Encyclopedia of Reagents for Organic Synthesis

Editor-in-Chief
Leo A. Paquette

Volume 3
Dib - Dio

TQ421-61
W123

ENCYCLOPEDIA

of

Reagents

for

Organic Synthesis

Editor-in-Chief

Leo A. Paquette
The Ohio State University, Columbus, OH, USA

江苏工业学院图书馆
藏书章

Volume 3

Dib – Dio

JOHN WILEY & SONS
Chichester · New York · Brisbane · Toronto · Singapore

Copyright © 1995 by John Wiley & Sons Ltd
Baffins Lane, Chichester
West Sussex PO19 1UD, England

Telephone National (01243) 779777
International (+44) 1243 779777

All rights reserved.

No part of this book may be reproduced by any means,
or transmitted, or translated into a machine language
without the written permission of the publisher.

Other Wiley Editorial Offices

John Wiley & Sons, Inc., 605 Third Avenue,
New York, NY 10158-0012, USA

Jacaranda Wiley Ltd, 33 Park Road, Milton,
Queensland 4064, Australia

John Wiley & Sons (Canada) Ltd, 22 Worcester Road,
Rexdale, Ontario M9W 1L1, Canada

John Wiley & Sons (SEA) Pte Ltd, 37 Jalan Pemimpin #05-04,
Block B, Union Industrial Building, Singapore 2057

British Library Cataloguing in Publication Data

A catalogue record for this book is available from the British Library

ISBN 0 471 93623 5

Chemical structures produced in ChemDraw by Synopsys, Leeds
Data Management and Typesetting by Reed Technology and Information Services, London
Printed and bound in Great Britain by BPC Wheatons, Exeter

This book is printed on acid-free paper responsibly manufactured from sustainable forestation,
for which at least two trees are planted for each one used for paper production.

Editorial Board

Editor-in-Chief

Leo A. Paquette
The Ohio State University, Columbus, OH, USA

Editors

Steven D. Burke
University of Wisconsin at Madison, WI, USA

Robert M. Coates
University of Illinois at Urbana-Champaign, IL, USA

Rick L. Danheiser
Massachusetts Institute of Technology, Cambridge, MA, USA

Scott E. Denmark
University of Illinois at Urbana-Champaign, IL, USA

David J. Hart
The Ohio State University Columbus, OH, USA

Lanny S. Liebeskind
Emory University Atlanta, GA, USA

Dennis C. Liotta
Emory University Atlanta, GA, USA

Anthony J. Pearson
Case Western Reserve University, Cleveland, OH, USA

Hans J. Reich
University of Wisconsin at Madison, WI, USA

James H. Rigby
Wayne State University Detroit, MI, USA

William R. Roush
Indiana University Bloomington, IN, USA

Assistant Editors

James P. Edwards
Ligand Pharmaceuticals San Diego, CA, USA

Mark Volmer
Emory University Atlanta, GA, USA

International Advisory Board

Leon A. Ghosez
Université Catholique de Louvain, Belgium

Jean-Marie Lehn
Université Louis Pasteur Strasbourg, France

Steven V. Ley
University of Cambridge UK

Chun-Chen Liao
National Tsing Hua University, Hsinchu, Taiwan

Lewis N. Mander
Australian National University, Canberra Australia

Giorgio Modena
Università di Padua Italy

Ryoji Noyori
Nagoya University, Japan

Gerald Pattenden
University of Nottingham UK

Edward Piers
University of British Columbia, Vancouver Canada

Pierre Potier
CNRS, Gif-sur-Yvette France

W. Nico Speckamp
Universiteit van Amsterdam The Netherlands

Hishashi Yamomoto
Nagoya University, Japan

Ekkehard Winterfeldt
Universität Hannover Germany

Managing Editor

Colin J. Drayton
Woking, Surrey, UK

Preface

The extent to which organic synthetic methodology has developed and flourished during the past several decades has placed unusually heavy demands on the broad range of scientists who utilize chemical reagents. There exists the vital need to know which reagent will perform a specific transformation. Since a number of reagents are often amenable to similar objectives, a researcher's ability to access readily a comparative summary of those features that distinguish one reagent from another can result in a considerable economy of time. The purpose of the *Encyclopedia of Reagents for Organic Synthesis* is to incorporate into a single work a genuinely authoritative and systematic description of the utility of all reagents used in organic chemistry. Its comprehensiveness is further served by an unrivaled ease to locate any specific entry or topic.

These objectives have been met by inviting practicing chemists from throughout the world to provide specific contributions in their area of expertise. Furthermore, the masthead for each of the 3000 reagents provides valuable information concerning physical data, solubility, form supplied in, purification, and, where relevant, preparative methods. The CAS registry number, handling/storing information, and precautions will further serve potential users. The first literature reference in each entry provides reviews, if available, dealing with the subject reagent. The critical coverage of all relevant literature is extensive.

The goal of the *Encyclopedia of Reagents for Organic Synthesis* is to serve as a reference work where the retrievability of useful information concerning any specific reagent is made facile. For this reason there is a detailed subject index and, in addition, a formula index of all the reagents, and also two further indexes that list the reagents by structural class and by function.

In any undertaking of this type, it is important that the term 'reagent' be clearly defined. The guideline that has dominated the thinking of the members of the Editorial Board is that a reagent be an agent or a combination of agents which with some generality effects the transformation of a substrate into a product. In addition, many useful building blocks have been included. As a consequence, we anticipate that a work has been produced that will serve biochemists, material scientists, pharmacologists, and chemical engineers, in addition to chemists from all disciplines, in that manner most conducive to accelerating progress in their respective fields of research.

The entries highlight the various uses characteristic of each reagent, with specific examples illustrative of these chemical reactions. The contributions are organized alphabetically and the cross-referencing to other reagents is liberal. Thus, a concerted effort has been made to bring together in one place a detailed compilation of the uses of those reagents that will serve both the beginning and experienced investigator. The wealth of facts contained within the *Encyclopedia of Reagents for Organic Synthesis* has been assimilated in a manner which will cause all scientists to want this source of information kept in close proximity to their laboratory.

A work of this magnitude could not have been brought to realization without the input of a great deal of time, effort, and dedication on the part of a large number of highly responsible individuals. I am especially indebted to the editors – Steven Burke, Robert Coates, Rick Danheiser, Scott Denmark, David Hart, Lanny Liebeskind, Dennis Liotta, Anthony Pearson, Hans Reich, James Rigby, and William Roush – for their tremendously valuable enthusiasm, intensive work, and unstinting persistence. A most critical role has been played by Colin Drayton, not only in conceiving the project but also as a consequence of his range of knowledge of the publishing business in steering us continually in the proper direction and in overseeing the massive editing operation. James Edwards and Mark Volmer are also to be thanked for their central role as assistant section editors. The body of this encyclopedia was composed by over 1000 authors from 40 countries around the world. The knowledge and expertise contributed by these experienced investigators in the form of authoritative treatises dealing with reagents with which they are thoroughly familiar constitutes the scientific underpinning of the entire undertaking. The enlightening end product of their contributions will have a major impact on the conduct of research in organic chemistry and I thank each of these individuals for their insightful entries.

The large contingent of organic chemists alluded to above, directly and indirectly, expects the *Encyclopedia of Reagents for Organic Synthesis* to play a vital role in stimulating creative research in organic chemistry in the years immediately ahead. All of us hope that you will share in this excitement by perusing its many pages and creatively adapting the valuable information contained therein.

Leo A. Paquette
The Ohio State University
Columbus, OH, USA

此为试读,需要完整PDF请访问: www.ertongbook.com

Foreword

This Encyclopedia covers comprehensively over 3000 reagents, alphabetically arranged using IUPAC nomenclature. The articles are self-contained but ***Bold Italics*** are used within each article to indicate other reagents that have their own entries in the Encyclopedia. A list of related reagents is given at the end of articles.

Although most articles are devoted to a single reagent, in some cases closely related reagents are covered under one heading, e.g. Methyl Trimethylsilylacetate is discussed in the article on Ethyl Trimethylsilylacetate, and Lithium Trimethoxyaluminum Hydride in the article on Lithium Tri-*t*-butoxyaluminum Hydride.

A particular reagent can be found either directly, by going to the appropriate place in the Encyclopedia, or from the Subject Index in Volume 8. Numerous other topics, such as types of reaction, named reactions, named reagents, general substrates or products, and specific substrates or products, are included in this index.

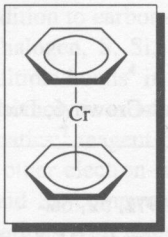
Volume 8 also contains a Formula Index, listing all reagents covered in the Encyclopedia.

In addition, there are two further compilations of all the reagents in Volume 8, a Reagent Structural Class Index and a Reagent Function Index. The former groups the reagents under headings such as Dienes, Hydrides, and Titanium Reagents, while the latter has headings such as Alkylating Agents, Desilylation Reagents, and Ring Expansion Agents.

The abbreviations used for journals in the references are on the front endpapers of all volumes, while the back endpapers list other abbreviations used throughout the Encyclopedia.

Dib

Dibenzenechromium



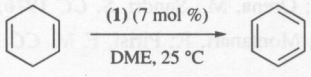
[1271-54-1] $C_{12}H_{12}Cr$ (MW 208.22)

(dehydrogenation catalyst[1])

Alternate Name: bis(η^6-benzene)chromium.
Physical Data: mp 284–285 °C.
Solubility: sol benzene; slightly sol ether.
Form Supplied in: brown-black crystals.
Purification: sublimed at 160 °C in vacuo.
Handling, Storage, and Precautions: air sensitive.

Dehydrogenation Catalyst. Treatment of dibenzenechromium with potassium produces the corresponding radical anion (eq 1), which is an effective catalyst for the conversion of 1,4-cyclohexadiene to benzene (eq 2).[1] The scope and limitations of the process have not been tested.

$$(C_6H_6)_2Cr \xrightarrow{K} \underset{\textbf{(1)}}{[(C_6H_6)_2Cr]^{-\bullet}} \quad (1)$$

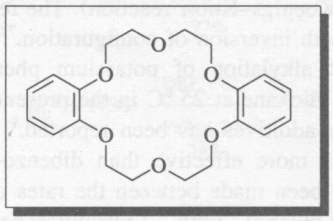


(2)

1. Fochi, G. *OM* **1988**, *7*, 2255.

James W. Herndon
University of Maryland, College Park, MD, USA

Dibenzo-18-crown-6



[14187-32-7] $C_{20}H_{24}O_6$ (MW 360.41)

(solubilization and activation of a variety of potassium salts)

Physical Data: mp 162.5–163.5 °C. UV maxima: (MeOH solution) 223 nm (ε 17 500) and 275 nm (ε 5500). ^{1}H NMR: ($CDCl_3$) 6.8–7.0 ppm (8H multiplet) and 3.8–4.3 ppm (16H multiplet).
Form Supplied in: white fibrous needles.
Preparative Methods: dibenzo-18-crown-6 was first prepared in 39–48% yield from the reaction of catechol and bis(2-chloroethyl) ether using sodium hydroxide as the base and *n*-butanol as the solvent.[1] The ditosylate of diethylene glycol has been substituted for the dichloride with accompanying yields of 32–35%.[2]
Handling, Storage, and Precautions: toxic; use in a well-ventilated fume hood.

Complexation With Metal Salts. The cavity diameter of dibenzo-18-crown-6 is estimated to be 2.6–3.2 Å, which is ideal for complexing with a potassium cation (ionic diameter 2.66 Å).[3] While the selectivity of dibenzo-18-crown-6 for potassium salts is well documented, this macrocyclic multidentate ligand will also effectively complex with other alkali metal cations.[3] The solubility of potassium acetate in ***Acetonitrile*** is greater in the presence of dibenzo-18-crown-6 compared to ***18-Crown-6***.[4] The solubility of potassium acetate in the presence of a variety of other ligands was also reported. Arguments related to cavity diameter, lipophilicity, and rigidity were advanced to explain, at least partially, the observed structure–solubilization order.

Reactions.

Halides. The catalytic activity of a number of macrocyclic polydentate ligands in the reaction of 1-octyl bromide with ***Potassium Iodide*** to produce the 1-octyl iodide has been reported.[5] Dibenzo-18-crown-6 appears to be less effective than ***Dicyclohexano-18-crown-6***.[5]

Oxygen Anions. The reaction of potassium acetate activated by a wide variety of macrocyclic polydentate ligands with benzyl chloride in acetonitrile indicates that dibenzo-18-crown-6 is somewhat less effective than 18-crown-6 or dicyclohexano-18-crown-6.[4] At –45 °C in dry THF, sodium 3-(fluoren-9-ylidene)-2-phenylacrylate decarboxylated very slowly. In the presence of dibenzo-18-crown-6 the reaction proceeded at a rapid rate, indicating that the nature of the ion pair was critical in influencing the reaction rate profile.[6]

Dibenzo-18-crown-6 has been used in the reaction of an acetylated halo sugar with a series of alcohols catalyzed by ***Silver(I) Nitrate*** (Koenigs–Knorr reaction). The reaction proceeds in good yield with inversion of configuration.[7,8]

The rates of alkylation of potassium phenoxide with 1-bromobutane in dioxane at 25 °C in the presence of linear and cyclic polyether additives has been reported.[9] Dicyclohexano-18-crown-6 was more effective than dibenzo-18-crown-6. A comparison has been made between the rates of reaction of *t*-butoxide in *t*-butanol with 2-nitrofluorobenzene and 4-nitrofluorobenzene where the counter cation was potassium and potassium/dibenzo-18-crown-6 and the corresponding reaction of potassium methoxide in methanol.[10] Potassium methoxide was 30 times more reactive than ***Potassium t-Butoxide*** but in the presence of dibenzo-18-crown-6 the reverse was true.

Dibenzo-18-crown-6 is an effective phase-transfer catalyst in the reactions of 4-chloromethyl-1,3-dioxolane with mono- and dihydric phenols in the presence of metal hydroxides.[11]

The effect of dibenzo-18-crown-6 on the reaction of sodium 9-fluorenone oximate with ***Iodomethane*** in 33.5% acetonitrile and 66.5% *t*-butyl alcohol has been studied. The crown ether increased the fractional *O*-alkylation.[12,13]

Carbon Anions. The effects of dibenzo-18-crown-6 on (a) the simultaneous base-catalyzed racemization, isotopic exchange, and isomerization of optically pure (–)-3-*t*-butyl-1-methylindene-1-*h* and its deuterated counterpart in the 1-position to 1-*t*-butyl-3-methylindene under a variety of conditions,[14] (b) the isotopic exchange and racemization of (–)-4-biphenylylphenylmethoxydeuteromethane with potassium *t*-butoxide,[15] (c) the stereochemistry accompanying the cleavage of (+)-4-phenyl-3,4-dimethyl-3-hexanol with potassium *t*-butoxide,[12] and (d) the rates of isotopic exchange and racemization of (+)-2-methyl-2,3-dihydro-2-deuterobenzo[*b*]thiophene 1,1-dioxide with potassium methoxide[12] have been reported.

The lithium, sodium, and potassium salts of 4*H*-cyclopenta[*def*]phenanthrene radical anion are considerably more stable in the presence of dibenzo-18-crown-6, especially when sodium or potassium is the counter cation.[16] The presence of crown also affected the rate of decay of the radical anion.

The use of dibenzo-18-crown-6 as a liquid–liquid phase–transfer catalyst in the generation and reaction of carbanions and halocarbenes has been studied.[17] Among the reactions studied were the alkylation of carbon acids, reactions involving trichloromethyl anions and dichloromethylene, reactions of carbanions with nitro compounds, and Darzens condensations.

Sulfur Anions. The solid–liquid phase-transfer catalytic reaction between ***Benzyl Chloride*** and ***Potassium Thiocyanate*** produces a ratio of benzyl thiocyanate to benzyl isothiocyanate of 71:29 in the presence of dibenzo-18-crown-6.[18]

Reductions. Studies related to the use of ***Sodium Borohydride*** in toluene in the reduction of a variety of ketones (acetophenone, cyclohexanone, methyl *n*-pentyl ketone, methyl isopropyl ketone) in the presence of equivalent amounts of dibenzo-18-crown-6, diglyme, or dimethoxyethane have been reported.[19] In general, the crown was the most effective ligand. Potassium borohydride required longer reactions times.

Oxidations. The preparation of *N*-(arylsulfonyl)sulfoximines by oxidation of the sulfilimines with ***Sodium Hypochlorite*** in an aqueous methylene chloride–ethyl acetate two-phase system has been reported.[20]

The reaction of ***Potassium Chromate*** with primary alkyl halides in HMPA containing dibenzo-18-crown-6 at 100 °C produces aldehydes in good yields.[21] The chromate ion behaves as both a nucleophile and an oxidant.

The oxidation of 1-octene to *n*-heptanoic acid with a saturated aqueous ***Potassium Permanganate***–benzene two-phase system proceeds in 80% yield at rt in the presence of dibenzo-18-crown-6.[22]

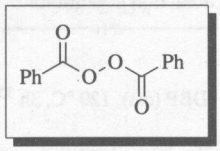
Related Reagents. 18-Crown-6; Dicyclohexano-18-crown-6.

1. Pedersen, C. J. *OS* **1972**, *52*, 66.
2. Ashby, J.; Hull, R.; Cooper, M. J.; Ramage, E. E. *SC* **1974**, *4*, 113.
3. Liotta, C. L. In *Synthetic Multidentate Macrocyclic Compounds*; Izatt, R. M.; Christensen, J. J., Eds.; Academic: New York, pp 111–205.
4. Knochel, A.; Oehler, J.; Rudolph, G. *TL* **1975**, 3167.
5. Cinquini, M.; Montanari, F.; Rundo, P. *CC* **1975**, 393.
6. Hunter, D. H.; Lee, W.; Sins, S. K. *CC* **1974**, 1018.
7. Knochel, A.; Rudolph, G. *TL* **1974**, 3739.
8. Knochel, A.; Rudolph, G.; Thiem, J. *TL* **1974**, 551.
9. Thomassen, L. M.; Ellingsen, T.; Ugelstad, J. *ACS* **1971**, *25*, 3024.
10. Cima, F.; Biggi, G.; Pietra, F. *JCS(P2)* **1973**, *2*, 55.
11. Ufa Petroleum Institute. Translated from *Zh. Prikl. Khim.* **1990**, *63*, 1383.
12. Smith, S. G.; Milligan, D. V. *JACS* **1968**, *90*, 2393.
13. Smith, S. G.; Hanson, M. P. *JOC* **1971**, *36*, 1931.
14. Almy, J.; Garwood, D. C.; Cram, D. J. *JACS*, **1970**, *92*, 4321.
15. Roitman, J. N.; Cram, D. J. *JACS* **1971**, *93*, 2231.
16. Tabner, B. J.; Walker, T. *JCS(P2)* **1973**, 1201.
17. Makosza, M.; Ludwikow, M. *AG(E)* **1974**, *13*, 665.
18. Dehmlow, E. V.; Torossian, G. O. *ZN(B)* **1990**, *45b*, 1091.
19. Matsuda, T.; Koida, K. *BCJ* **1973**, *46*, 2259.
20. Akutagawa, K.; Furukawa, N. *JOC* **1984**, *49*, 2282.
21. Cardillo, G.; Orena, M.; Sandri, S. *CC* **1976**, 190.
22. Landini, D.; Montanari, F.; Pirisi, F. M. *CC* **1974**, 879.

Charles L. Liotta

Georgia Institute of Technology, Atlanta, GA, USA

Dibenzoyl Peroxide[1–4]



[94-36-0] $C_{14}H_{10}O_4$ (MW 242.23)

(initiator for radical reactions such as allylic and benzylic halogenation,[5] radical addition to carbon–carbon multiple bonds to form C–heteroatom (halogen, S, Si, Ge, P, and N) bonds,[2] C–H additions across multiple bonds[4] in an intermolecular[1] and intramolecular[6] fashion, homolytic aromatic substitution in electron-deficient heteroaromatics;[7] reagent for benzoyloxylation of enolates, enamines, and other electron-rich systems;[8] oxidizing agent for N, P, Si, S, and Se compounds; oxidizing agent in redox chain reactions with transition metals[9])

Alternate Name: DBP.

Physical Data: mp 103–106 °C (dec).

Solubility: sparingly sol water or alcohol; sol benzene, chloroform, and ethers.

Form Supplied in: white crystalline powder.

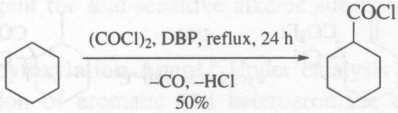
Analysis of Reagent Purity: the peroxide content can be established by iodometric titration.[10]

Handling, Storage, and Precautions: explosive; harmful if exposed by ingestion or skin contact; strong oxidizer; susceptible to explosion by shock, friction or heat; autoignition temperature 79 °C. *Caution*: all experiments involving peroxy compounds should be carried out behind a safety shield. Excess peroxide should be destroyed before working up the reaction.[11]

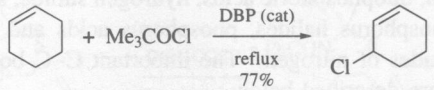
Introduction. Dibenzoyl peroxide is a widely used initiator for radical reactions. It undergoes thermal homolytic cleavage of the O–O bond with a half-life of about 1 h at 95 °C (eq 1).[12] This homolysis may also be effected by light as well as transition metal catalysts.[9]

$$(PhCO_2)_2 \longrightarrow 2\ PhCO_2\bullet \longrightarrow Ph\bullet + CO_2 \qquad (1)$$

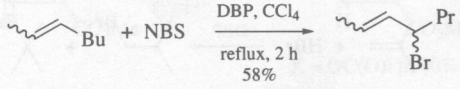
Initiator for Halogenation Reactions. Even though DBP has been used as an initiator for functionalization of unactivated hydrocarbons (eq 2), more common are the applications for halogenations of allylic (eqs 3 and 4)[5,13] and benzylic (eq 5)[14] positions. DBP also serves as an initiator for halogenation of silanes by replacement of a Si–H bond.[15]



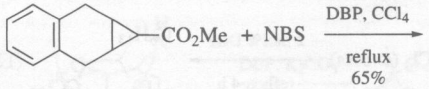
(2)

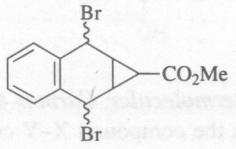


(3)



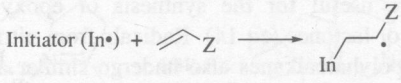
(4)



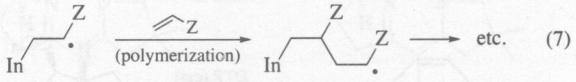


(5)

Initiator for Radical Additions to Unsaturated Compounds. The primary steps in the radical addition of X–Y to unsaturated compounds are shown in eqs 6–10. By far the largest application of this reagent[16] is in radical chain polymerization of vinyl compounds such as vinyl chloride, vinyl acetate, butadiene derivatives, styrene, and various acrylic monomers. The topic of polymerization is beyond the scope of this article. Excellent monographs and reviews dealing with this subject are available.[17]

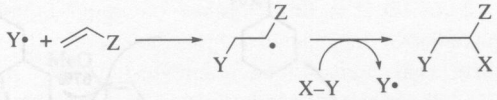


(6)



(7)

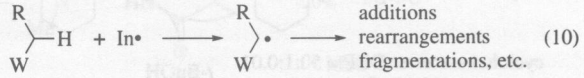
(8)



(9)

repeat ⟶ 1:1 adduct of the alkene and X–Y

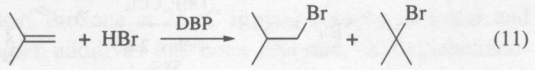
when X–Y contains an activated C–H:



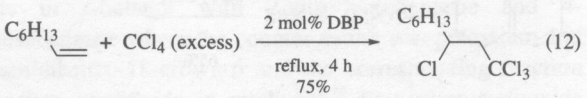
(10)

Formation of a 1:1 adduct (eq 9) will be favored when X–Y is an efficient chain transfer agent. For reactions of short chain lengths, an excess of X–Y and a steady concentration of the initiator should be present in the reaction medium.[2] Since the original discoveries of the anti-Markovnikov addition of HBr (eq 11),[18] and of carbon tetrachloride to alkenes (eq 12),[1] a large number of related reactions have been reported. DBP catalyzes the addition of a wide variety of X–Y type compounds to carbon–carbon multiple bonds. These include H–Br, thiols, mer-

capto acids, thiophosphoric acids, hydrogen sulfide, silanes, germanes, phosphorus halides, phosphorus acids and esters, and various oxides of nitrogen.[2] The important C–C bond-forming reactions are described below.



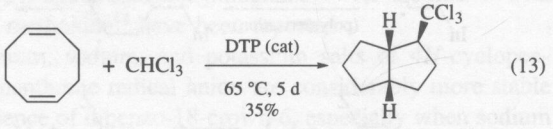
(11)



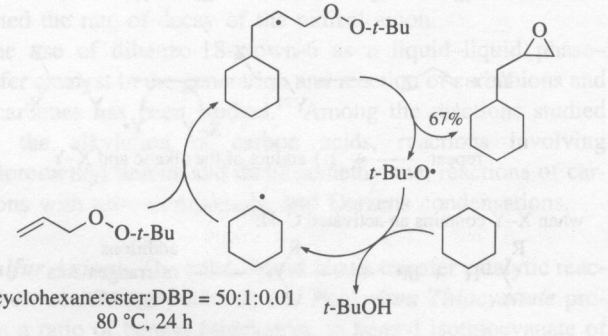
(12)

Intermolecular Carbon–Carbon Bond Forming Reactions. When the compound X–Y contains an activated C–H bond, initiators such as DBP and di-*t*-butyl peroxide initiate the radical reactions by abstraction of this hydrogen (eq 10) from the substrate, and the resultant radical enters the radical chain cycle. Substrates of this kind are poor chain transfer agents and typically a higher concentration of the substrate and a steady supply of the initiator are needed for a viable reaction. Representative examples of carbon–carbon bond forming reactions initiated by DBP are listed in Table 1[11,41–45] (see also ***1,1-Di-t-butyl Peroxide***). A more complete list is available in two excellent reviews.[1,4]

The intermolecular additions may be coupled to an intramolecular cyclization (eq 13)[19] or an S_H2 reaction.[20] The S_H2 reactions are useful for the synthesis of epoxy compounds (Scheme 1) or lactones (eq 14). Radicals from nitriles, ketones, ethers, and polyhaloalkanes also undergo similar addition–substitution reactions.



(13)

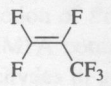
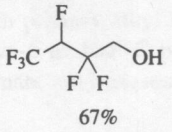
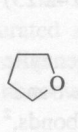
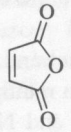
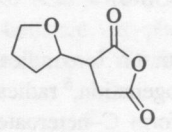
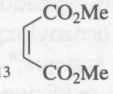
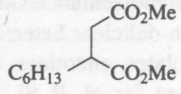
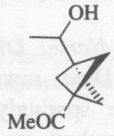
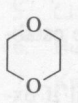
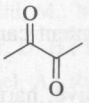
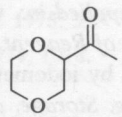
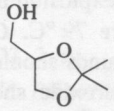


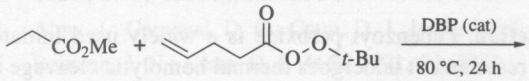
Scheme 1 Intermolecular addition–S_H2 reaction of peresters

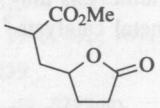
Addition of various α-carboxyl radicals to alkenes is best carried out with a high temperature initiator such as di-*t*-butyl peroxide, although reports of using DBP are known. This subject has been extensively reviewed.[21]

Intramolecular Additions. The intramolecular versions of the C–H additions mentioned above have been extensively studied

Table 1 Intermolecular C–C Forming Reactions via Radicals

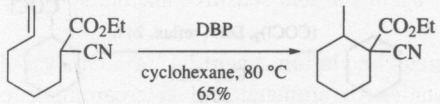
Precursor	Alkene	Reaction conditions	Product
MeOH		DBP (cat), 120 °C, 3h [11]	 67%
		DBP (cat), 65 °C [41]	 70%
		DBP (cat), 87 °C, 24 h [42]	 71%
		DBP [43]	
		DBP, 80 °C, 2 h [44]	 48%
	CH_2O	DBP, *hv* [45]	 86%



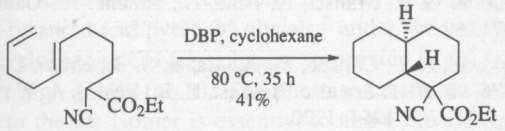


(14)

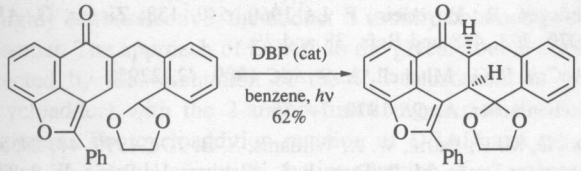
by Julia and co-workers (eqs 15 and 16).[6] These reactions, while not very practical from a synthetic standpoint, nonetheless have played a key role in the development of radical synthetic methodology.[22,23] A related cyclization (eq 17) was used by Barton and co-workers for the synthesis of a tetracycline intermediate.[24] An interesting variant of this reaction is the cyclization of geranyl acetate to a benzoyloxyfarnesyl acetate (eq 18).[25] The radical reaction is initiated by DBP and the Cu salt serves as an oxidant for the final cyclized radical.



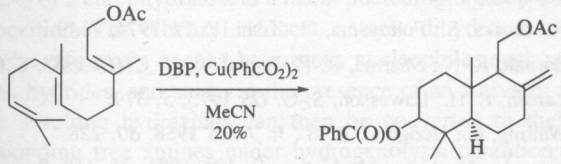
(15)



(16)

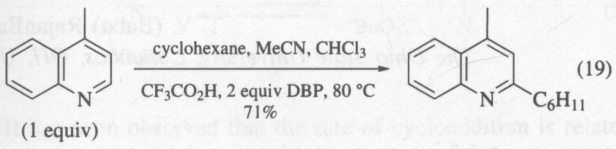


(17)



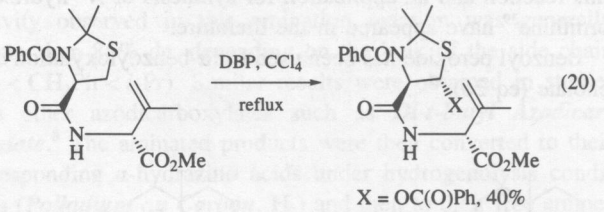
(18)

Initiator for Radical Additions to Electron-Deficient Heteroaromatic Compounds. Minisci and co-workers have developed radical-mediated homolytic substitution reactions for various electron-deficient aromatic nuclei.[7] Radicals derived from alkyl halides, dioxane,[26] dimethylformamide,[27] and even cyclohexane[26] can be added to protonated heteroaromatic compounds. The addition of a cyclohexyl radical (eq 19) proceeds in good yields even when the reaction medium contains a large excess of chloroform and acetonitrile. The highly electrophilic nature of the $\bullet CCl_3$ and $\bullet CH_2CN$ completely inhibits the reaction towards the protonated heterocycle. Under these conditions, ethyl acetate gives the electrophilic radical $\bullet CH_2CO_2Et$ and the nucleophilic radical $MeCO_2\dot{C}HMe$, but only the latter adds.

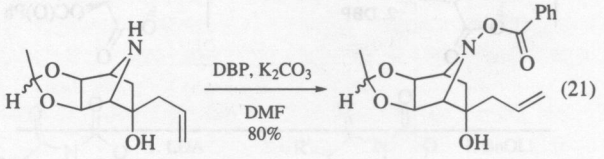


(19)

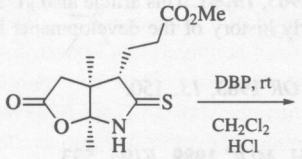
As an Oxidant. Benzoyl peroxide oxidizes ethers to α-benzoyloxy ethers, and alkyl sulfides to α-benzyloxy sulfides (eq 20).[28] Tertiary amines are oxidized to amine oxides, while secondary amines give *N*-benzoyloxy amines (eq 21).[29] In the presence of a mild base, DBP acts as a very selective oxidizing agent for hydroquinones.[30] Aldehydes and benzylic positions are not affected. Two key steps in the Eschenmoser synthesis of the corrin nucleus make use of DBP (eqs 22 and 23).[31] Secondary alcohols are oxidized to ketones with dibenzoyl peroxide and ***Nickel(II) Bromide*** (eq 24).[32] A benzoyl peroxide-mediated annulation used by Kishi in the synthesis of sporidesmin B (eq 25)[33] is likely to be an ionic (vis-á-vis radical) reaction. A 1:1 mixture of DBP and ***Hexamethyldisilazane*** has been used as an epoxidizing agent for acid-sensitive alkenic substrates.[34]

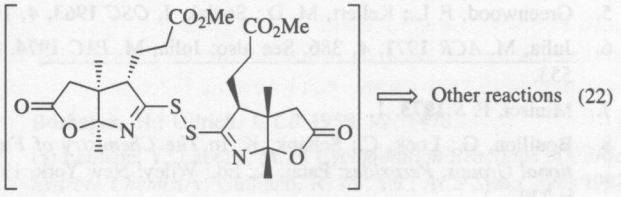


(20)

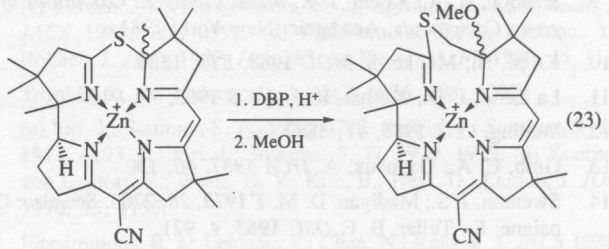


(21)

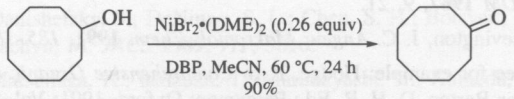




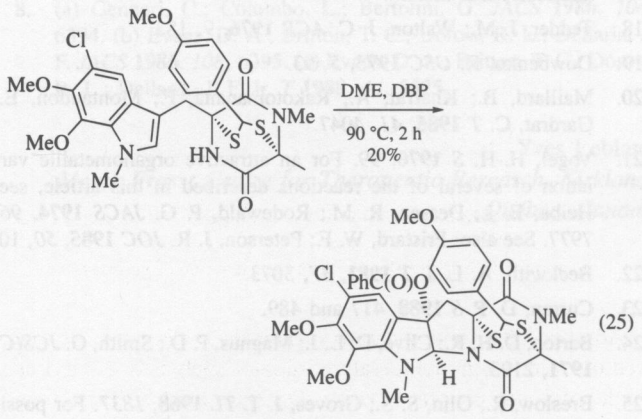
(22)



(23)



(24)



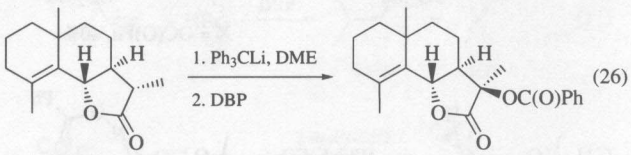
(25)

As a Benzoyloxylation Agent.[8] Under catalysis by ***Iodine***, benzoyloxylation of aromatic and heteroaromatic compounds takes place. Nucleophilic compounds such as malonates,[35] phenols,[36] enamines, and indoles[37] also react with DBP to give benzoyloxylation products. Secondary amines are converted into *N*-benzyloxy amines (eq 20).[29] An improved protocol[38] for

此为试读,需要完整PDF请访问: www.ertongbook.com

this reaction and an application for synthesis of N^5-hydroxy-L-ornithine[39] have appeared in the literature.

Benzoyl peroxide has been used for α-benzoyloxylation of an enolate (eq 26).[40]

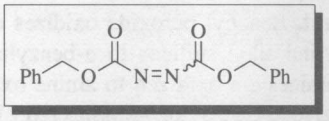


(26)

1. Walling, C.; Huyser, E. S. *OR* **1963**, *13*, 91. This article also gives an excellent account of the early history of the developments in radical chemistry.
2. Stacey, F. W.; Harris, J. F., Jr. *OR* **1963**, *13*, 150.
3. Kropf, H. *MOC* **1988**, *E13*.
4. Ghosez, A.; Giese, B.; Zipse, H. *MOC* **1989**, *E19a*, 533.
5. Greenwood, F. L.; Kellert, M. D.; Sedlak, J. *OSC* **1963**, *4*, 108.
6. Julia, M. *ACR* **1971**, *4*, 386. See also: Julia, M. *PAC* **1974**, *40*, 553.
7. Minisci, F. *S* **1973**, 1.
8. Bouillon, G.; Lock, C.; Schank, K. In *The Chemistry of Functional Groups, Peroxides*; Patai, S.; Ed.; Wiley: New York, 1983; p 279.
9. Sheldon, R. A.; Kochi, J. K. *Metal Catalyzed Oxidations of Organic Compounds*; Academic: New York, 1981.
10. Kropf, H.; Munke, S. *MOC* **1988**, *E13*, 1386.
11. La Zerte, J. D.; Koshar, R. J. *JACS* **1955**, *77*, 910.
12. Walling, C. *T* **1985**, *41*, 3887.
13. Grob, C. A.; Gagneux, A. *HCA* **1957**, *40*, 130.
14. Swenton, J. S.; Madigan, D. M. *T* **1972**, *28*, 2703. See also: Campaigne, E.; Tullar, B. F. *OSC* **1963**, *4*, 921.
15. Nagai, Y.; Yamazaki, K.; Shiojima, I.; Kobori, N.; Hayashi, M. *JOM* **1967**, *9*, 21.
16. Bevington, J. C. *Angew. Makromol. Chem.* **1991**, *185–186*, 1.
17. See for example: Hodge, P. In *Comprehensive Organic Chemistry*; Barton, D. H. R. Ed.; Pergamon: Oxford, 1991; Vol. 5, p 833 and references therein.
18. Tedder, J. M.; Walton, J. C. *ACR* **1976**, *9*, 183.
19. Dowbenko, R. *OSC* **1973**, *5*, 93.
20. Maillard, B.; Kharrat, A.; Rakotomanana, F.; Montaudon, E.; Gardrat, C. *T* **1985**, *41*, 4047.
21. Vogel, H.-H. *S* **1970**, 99. For an attractive organometallic variation of several of the reactions described in this article, see: Heiba, E. I.; Dessau, R. M.; Rodewald, P. G. *JACS* **1974**, *96*, 7977. See also: Fristard, W. F.; Peterson, J. R. *JOC* **1985**, *50*, 10.
22. Beckwith, A. L. J. *T* **1981**, *37*, 3073.
23. Curran, D. P. *S* **1988**, 417 and 489.
24. Barton, D. H. R.; Clive, D. L. J.; Magnus, P. D.; Smith, G. *JCS(C)* **1971**, 2193.
25. Breslow, R.; Olin, S. S.; Groves, J. T. *TL* **1968**, *1837*. For possible mechanisms, see: Kochi, J. K. *Science* **1967**, *155*, 415. See also: Lellemand, J. Y.; Julia, M.; Mansuy, D. *TL* **1973**, 4461.
26. Minisci, F.; Vismara, E.; Fontana, F.; Morini, G.; Serravalle, M.; Giordano, C. *JOC* **1986**, *51*, 4411.
27. Gardini, G. P.; Minisci, F.; Palla, G.; Arnone, A.; Galli, R. *TL* **1971**, 59.
28. Baldwin, J. E.; Christie, M. A.; Haber, S. B.; Kruse, L. I. *JACS* **1976**, *98*, 3045. See also: Henbest, H. B.; Reid, J. A. W.; Stirling, C. J. M. *JCS* **1964**, 1220.
29. Buchi, G.; Fliri, H.; Shapiro, R. *JOC* **1977**, *42*, 2192. See also: Huisgen, R.; Bayerlein, F. *LA* **1960**, *630*, 138; Zinner, G. *AP* **1970**, *303*, 488 and Refs. 38 and 39.
30. McCay, P. G.; Mitchell, A. S. *AJC* **1989**, *42*, 2295.
31. Eschenmoser, A. *QR* **1970**, *24*, 366.
32. Doyle, M. P.; Patrie, W. J.; Williams, S. B. *JOC* **1979**, *44*, 2955. See also: Doyle, M. P.; Dow, R. L.; Bagheri, V.; Patrie, W. J. *TL* **1980**, *21*, 2795.
33. Nakatsuka, S.; Fukuyama, T.; Kishi, Y. *TL* **1974**, 1549.
34. Baruah, R. N.; Sharma, R. P.; Baruah, J. N. *C1(L)* **1983**, 825.
35. Larsen, E. H.; Lawesson, S.-O. *OS* **1973**, *5*, 379.
36. Walling, C.; Hodgdon, R. B., Jr. *JACS* **1958**, *80*, 228.
37. Kanaoka, Y.; Aiura, M.; Hariya, S. *JOC* **1971**, *36*, 458. See also: Nishio, T.; Yuyama, M.; Omote, Y. *CL* **1975**, 480.
38. Biloski, A. J.; Ganem, B. *S* **1983**, 537. See also: White, E. H.; Ribi, M.; Cho, L. K.; Egget, N.; Dzadzic, P. M.; Todd, M. J. *JOC* **1984**, *49*, 4886.
39. Milewska, M. J.; Chimiak, A. *S* **1990**, 233. See also: Milewska, M. J.; Chimiak, A. *AJC* **1987**, *40*, 1919.
40. Greene, A. E.; Muller, J. C.; Ourisson, G. *TL* **1972**, 3375. See also: Huffman, J. W.; Desai, R. C.; Hillenbrand, G. F. *JOC* **1984**, *49*, 982.
41. Jacobs, R. L.; Ecke, G. G. *JOC* **1963**, *28*, 3036.
42. Patrick, T. M., Jr.; Erickson, F. B. *OSC* **1963**, *4*, 430.
43. Wiberg, K. B.; Waddell., S. T.; Laidig, K. *TL* **1986**, *27*, 1553.
44. Bentrude, W. G.; Darnall, K. R. *JACS* **1968**, *90*, 3588.
45. Sanderson, J. R.; Lin, J. J.; Duranleau, R. G.; Yeakey, E. L.; Marquis, E. T. *JOC* **1988**, *53*, 2859.

T. V. (Babu) RajanBabu
The Ohio State University, Columbus, OH, USA

Dibenzyl Azodicarboxylate[1]

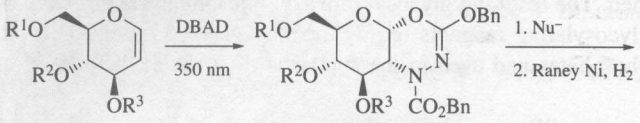


[2449-05-0] $C_{16}H_{14}N_2O_4$ (MW 298.30)

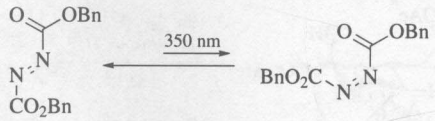
(efficient diene in the hetero Diels–Alder reaction with furanoid and pyranoid glycals;[2] source of positive nitrogen, used in the preparation of α-hydrazino and α-amino acids from chiral lithium enolates[3])

Alternate Name: DBAD.
Physical Data: mp 44–46 °C.
Solubility: sol CH_2Cl_2; insol cyclohexane.
Form Supplied in: orange solid.

Hetero Diels–Alder Reaction. Dibenzyl azodicarboxylate adds to furanoid and pyranoid glycals,[2] under irradiation at 350 nm in cyclohexane/CH_2Cl_2 solution, to provide [4 + 2] cycloadducts in high yields (eq 1). The photoisomerization[4] of *trans*-DBAD to the *cis* isomer is essential to allow the cycloaddition reaction to take place (eq 2). This cycloaddition reaction is highly stereoselective; the adduct is usually obtained as a single isomer. The approach of DBAD to the glycal double bond is directed by the orientation of the C-3 substituent to give the cycloadduct with the 2-amino function *trans* to the C-3 substituent. The cycloaddition reaction of DBAD and glycals allows, in a single operation, the introduction of an amino moiety at C-2 of a carbohydrate and a latent nucleofugal group at the C-1 position. The dibenzyl adducts, namely dihydrooxadiazines, can be efficiently opened by various nucleophiles such as alcohols, hydrides, and acids, in the presence of an activator (eq 1). The resulting hydrazides can then be converted to their corresponding free amines under hydrogenolysis conditions. This methodology has been applied to the synthesis of simple and complex 2-amino saccharides.[5] The cycloaddition reaction of DBAD with galactal and glucal was used for the synthesis of subunits of tunicamycin.[6]



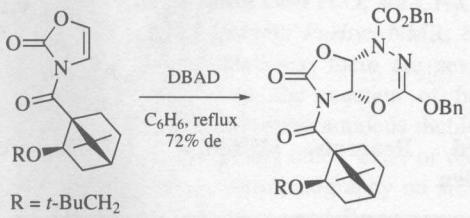
R^3 = TBDMS, Me (1)



(2)

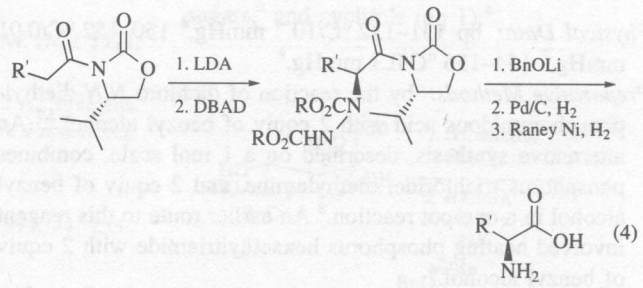
It has been observed that the rate of cycloaddition is related to the electronic nature of the C-3 substituent.[2a,b] The cycloaddition reaction does not take place with substrates having electron-withdrawing groups at the C-3 position.

Under thermal conditions, DBAD undergoes a [4 + 2] cycloaddition reaction with derivatized 2-oxazolones. The reaction shows moderate diastereofacial selectivity (eq 3).[7]



R = *t*-$BuCH_2$ (3)

Synthesis of α-Hydrazino and α-Amino Acids. DBAD is an efficient source of electrophilic nitrogen and has been used in the preparation of α-hydrazino and α-amino acids.[3] Aminated carboximides were obtained from the condensation of (*Z*)-lithium enolates of chiral carboximides with DBAD (eq 4). The selectivity observed in this amination reaction was generally greater than 85% de, depending on the bulk of the side chain (Me < CH_2Ph < *i*-Pr). Similar results were obtained in studies with other azodicarboxylates such as ***Di-t-butyl Azodicarboxylate***.[8] The aminated products were then converted to their corresponding α-hydrazino acids under hydrogenolysis conditions (***Palladium on Carbon***, H_2) and then to their free amines with ***Raney Nickel***/H_2.

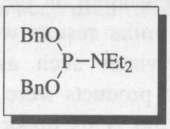


(4)

1. Böshagen, H.; Ullrich, J. *CB* **1959**, *92*, 1478.
2. (a) Leblanc, Y.; Labelle, M. In *Cycloaddition Reactions in Carbohydrate Chemistry*; Guiliano, R. M., Ed.; *ACS Symp. Ser.*, **1992**, *494*, 81. (b) Leblanc, Y.; Fitzsimmons, B. J. *TL* **1989**, *30*, 2889. (c) Leblanc, Y.; Fitzsimmons, B. J.; Springer, J. P.; Rokach, J. *JACS* **1989**, *111*, 2995. (d) Fitzsimmons, B. J.; Leblanc, Y.; Rokach, J. *JACS* **1987**, *109*, 285. (e) Fieser, M. *FF* **1990**, *15*, 111.
3. Trimble, L. A.; Vederas, J. C. *JACS* **1986**, *108*, 6397.
4. (a) Firl, J.; Sommer, S. *TL* **1972**, 4713. (b) Firl, J.; Sommer, S. *TL* **1971**, 4193. (c) Firl, J.; Sommer, S. *TL* **1970**, 1929. (d) Koerner von Gustorf, E.; White, D. V.; Kim, B.; Hess, D.; Leitich, J. *JOC* **1970**, *35*, 1155.
5. Fitzsimmons, B. J.; Leblanc, Y.; Chan, N.; Rokach, J. *JACS* **1988**, *110*, 5229.
6. Danishefsky, S.; DeNinno, S. L.; Chen, S. H.; Boisvert, L.; Barbachyn, M. *JACS* **1989**, *111*, 5810.
7. Matsunaga, H.; Ishizuka, T.; Marubayashi, N.; Kunieda, T. *CPB* **1992**, *40*, 1077.
8. (a) Gennari, C.; Columbo, L.; Bertolini, G. *JACS* **1986**, *108*, 6394. (b) Evans, D. A.; Britton, T. C.; Dorow, R. L.; Dellaria, J. F. *JACS* **1986**, *108*, 6395. (c) Evans, D. A.; Britton, T. C.; Dorow, R. L.; Dellaria, J. F. Jr. *T* **1988**, *44*, 5525.

Yves Leblanc
Merck Frosst Centre for Therapeutic Research, Kirkland, Québec, Canada

Dibenzyl *N,N*-Diethylphosphoramidite



[67746-43-4] $C_{18}H_{24}NO_2P$ (MW 317.40)

(phosphorylation of simple alcohols,[1] serine,[2] threonine,[3] and tyrosine;[4] synthesis of glycosyl phosphites and phosphates[5])

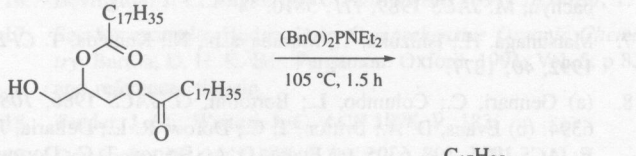
Physical Data: bp 131–132 °C/10^{-4} mmHg,[6] 150–152 °C/0.01 mmHg,[7] 154–156 °C/0.3 mmHg.[8]

Preparative Methods: by the reaction of dichloro *N,N*-diethylphosphoramidous acid with 2 equiv of benzyl alcohol.[3,7] An alternative synthesis, described on a 1 mol scale, combines phosphorus trichloride, diethylamine, and 2 equiv of benzyl alcohol in a one-pot reaction.[8] An earlier route to this reagent involved heating phosphorus hexaethyltriamide with 2 equiv of benzyl alcohol.[6]

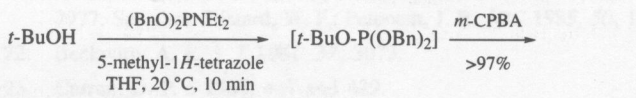
Purification: by distillation at reduced pressure.

Handling, Storage, and Precautions: reported to be stable at rt and has been kept for at least 6 months.[5]

Preparation of Organic Phosphite and Phosphate Esters. While dibenzyl *N,N*-diethylphosphoramidite will form phosphite triesters upon heating with 1,2-diacylglycerols in an uncatalyzed reaction (eq 1),[6] phosphitylation of alcohols has more recently been accomplished at ambient temperature in nearly quantitative yield in the presence of added 5-methyl-1*H*-tetrazole, 1*H*-tetrazole, or 1,2,4-triazole.[1,3,8] The phosphate triester has commonly been obtained by in situ oxidation of the phosphite ester intermediate using ***m*-Chloroperbenzoic Acid**,[1] ***t*-Butyl Hydroperoxide**,[3] or aqueous 30% ***Hydrogen Peroxide***.[8] *t*-Butyl dibenzyl phosphate has been obtained in excellent yield (eq 2).[1]

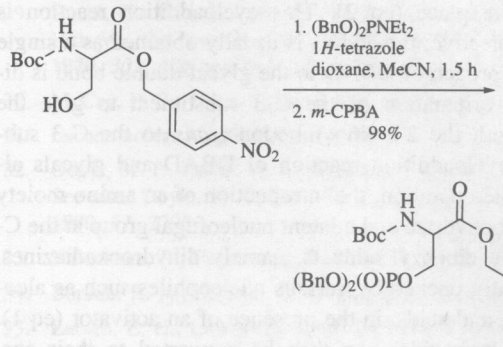


(1)



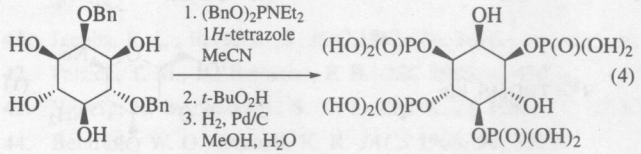
(2)

Protected serine and threonine derivatives have been phosphorylated for subsequent incorporation into peptides as the phosphate triesters (eq 3).[2,3,9,10] Similarly, dibenzyl *N,N*-diethylphosphoramidite has been used to prepare both Boc and Fmoc tyrosine derivatives for use in peptide synthesis.[4,11–14] Use of dibenzyl *N,N*-diethylphosphoramidite in phosphorylation of the side chain hydroxyls of serine- and threonine-containing peptides has been demonstrated.[2,7,15–18]

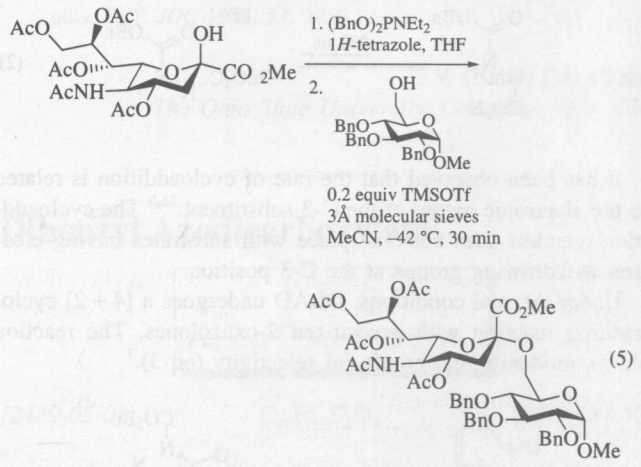


(3)

Dibenzyl *N,N*-diethylphosphoramidite has been used in phosphorylation sequences yielding dihydroxyacetone phosphate, D-*myo*-inositol 1,3,4,5-tetrakisphosphate (eq 4), and an inositol monophosphatase inhibitor.[8,19,20] Phosphitylation of the anomeric hydroxy groups of a series of sugars has been examined. The resulting glycosyl dibenzyl phosphites are effective as glycosylating reagents (eq 5), or they may be oxidized to the phosphates and used in the synthesis of sugar nucleotides.[5,21]



(4)



(5)

Related Reagents. Dibenzyl *N,N*-Diisopropylphosphoramidite.

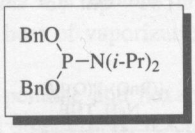
---

1. Perich, J. W.; Johns, R. B. *TL* **1987**, *28*, 101.
2. Perich, J. W.; Johns, R. B. *TL* **1988**, *29*, 2369.
3. De Bont, H. B. A.; Veeneman, G. H.; Van Boom, J. H.; Liskamp, R. M. J. *RTC* **1987**, *106*, 641.
4. Perich, J. W.; Reynolds, E. C. *SL* **1991**, 577.

5. Sim, M. M.; Kondo, H.; Wong, C. H. *JACS* **1993**, *115*, 2260.
6. Smirnova, L. I.; Malenkovskaya, M. A.; Predvoditelev, D. A.; Nifantev, E. E. *ZOR* **1980**, *16*, 1170.
7. Perich, J. W.; Johns, R. B. *AJC* **1990**, *43*, 1623.
8. Pederson, R. L.; Esker, J.; Wong, C. H. *T* **1991**, *47*, 2643.
9. Perich, J. W.; Alewood, P. F.; Johns, R. B. *AJC* **1991**, *44*, 253.
10. Perich, J. W.; Alewood, P. F.; Johns, R. B. *AJC* **1991**, *44*, 377.
11. Perich, J. W.; Johns, R. B. *S* **1989**, 701.
12. Perich, J. W.; Johns, R. B. *JOC* **1989**, *54*, 1750.
13. Kitas, E. A.; Wade, J. D.; Johns, R. B.; Perich, J. W.; Tregear, G. W. *CC* **1991**, 338.
14. Kitas, E. A.; Knorr, R.; Trzeciak, A.; Bannwarth, W. *HCA* **1991**, *74*, 1314.
15. De Bont, H. B. A.; Liskamp, R. M. J.; O'Brian, C. A.; Erkelens, C.; Veeneman, G. H.; Van Boom, J. H. *Int. J. Pept. Protein Res.* **1989**, *33*, 115.
16. Perich, J. W.; Johns, R. B. *AJC* **1990**, *43*, 1633.
17. Perich, J. W.; Alewood, P. F.; Johns, R. B. *AJC* **1991**, *44*, 233.
18. Perich, J. W.; Johns, R. B. *AJC* **1991**, *44*, 503.
19. Dreef, C. E.; Tuinman, R. J.; Elie, C. J. J.; Van der Marel, G. A.; Van Boom, J. H. *RTC* **1988**, *107*, 395.
20. Baker, R.; Carrick, C.; Leeson, P. D.; Lennon, I.; Liverton, N. J. *CC* **1991**, 298.
21. Ichikawa, Y.; Sim, M. M.; Wong, C. H. *JOC* **1992**, *57*, 2943.

Charles G. Caldwell
Merck Research Laboratories, Rahway, NJ, USA

Dibenzyl *N,N*-Diisopropylphosphoramidite[1]



[108549-23-1] $C_{20}H_{28}NO_2P$ (MW 345.42)

(phosphitylating reagent for alcohols; the resulting alkyl dibenzyl phosphite is transformed to the phosphoric monoesters by oxidation and subsequent debenzylation)[2]

Solubility: insol cold H_2O; sol CH_2Cl_2, THF, acetonitrile.

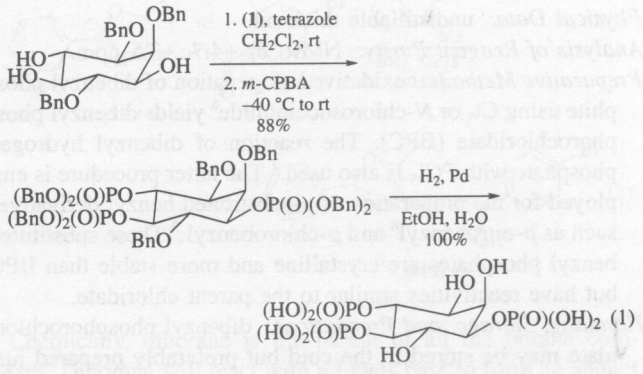
Analysis of Reagent Purity: NMR: δ_P ($CDCl_3$) +148.2.

Preparative Methods: there are several synthetic methods,[2-4] among which the reaction of benzyl alcohol with *N,N*-diisopropylphosphoramidous dichloride in the presence of *t*-amine in diethyl ether, THF, or dioxane is convenient.[5]

Purification: chromatography on silica gel.

Handling, Storage, and Precautions: can be stored in the absence of moisture and air for more than several months. A stock solution can be also prepared.

Phosphoric Monoester Synthesis. Dibenzyl phosphoramidites such as dibenzyl *N,N*-diisopropylphosphoramidite (**1**) (see also ***Dibenzyl N,N-Diethylphosphoramidite***) react quickly with various alcohols in the presence of 1*H*-tetrazole at room temperature to afford the phosphorus triesters which are oxidized in situ with an oxidant such as ***m-Chloroperbenzoic Acid***, ***t-Butyl Hydroperoxide***, or 30% ***Hydrogen Peroxide*** to give the corresponding alkyl dibenzyl phosphoric triesters in excellent yields. The triesters are deprotected by simple and clean catalytic hydrogenolysis on a Pd catalyst such as ***Palladium on Carbon*** or ***Palladium(II) Hydroxide***. The usefulness of the sequence has been demonstrated by many examples which involve synthesis of phosphate derivatives of amino acids,[2,6] peptides,[7] sugars,[8] and cyclitols (eq 1).[4]



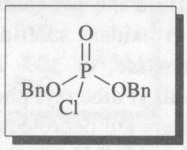
Dibenzyl phosphoric triesters are prepared alternatively by using ***Dibenzyl Phosphorochloridate***, tetrabenzyl pyrophosphate, or dibenzyl phosphorofluoridate. See also cyclic homologue of (**1**), ***o-Xylylene N,N-Diethylphosphoramidite***. These amidite reagents are more effective than P^V reagents, especially for phosphorylation of sterically hindered or base-sensitive alcohols, due to their high reactivity under milder conditions.

---

1. For a related review, see Beaucage, S. L.; Iyer, R. P. *T* **1992**, *48*, 2223.
2. Bannwarth, W.; Trzeciak, A. *HCA* **1987**, *70*, 175.
3. Smirnova, L. I.; Malenkovskaya, M. A.; Predvoditelev, D. A.; Nifant'ev, É. E. *ZOR* **1980**, *16*, 1011.
4. Yu, K.-L.; Fraser-Reid, B. *TL* **1988**, *29*, 979.
5. Fukase, K.; Kamikawa, T.; Iwai, Y.; Shiba, T.; Rietschel, E. T.; Kusumoto, S. *BCJ* **1991**, *64*, 3267.
6. de Bont, H. B. A.; Veeneman, G. H.; van Boom, J. H.; Liskamp, R. M. J. *RTC* **1987**, *106*, 641.
7. Perich, J. W.; Johns, R. B. *TL* **1988**, *29*, 2369.
8. Ichikawa, Y.; Sim, M. M.; Wong, C.-H. *JOC* **1992**, *57*, 2943.

Shoichiro Ozaki & Yutaka Watanabe
Ehime University, Matsuyama, Japan

Dibenzyl Phosphorochloridate[1]



[538-37-4] $C_{14}H_{14}ClO_3P$ (MW 296.69)

(phosphorylating reagent for alcohols,[2] phenols,[3] amines,[4] and amides;[5] removal of benzyl groups from the products affords phosphoric monoesters and monoamides respectively)

Alternate Name: BPC.

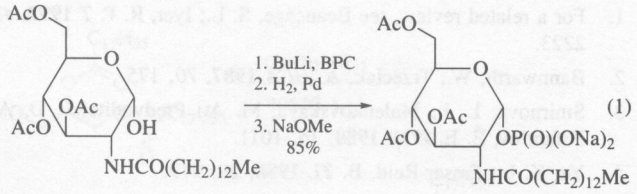
Physical Data: undistillable thick oil.

Analysis of Reagent Purity: NMR: δ_P +4.7, +3.5 ppm.

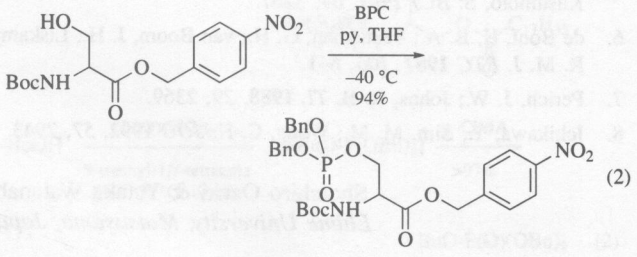
Preparative Methods: oxidative halogenation of dibenzyl phosphite using Cl_2 or *N*-chlorosuccinimide[6] yields dibenzyl phosphorochloridate (BPC). The reaction of dibenzyl hydrogen phosphate with PCl_5 is also used.[7] The latter procedure is employed for the preparation of *p*-substituted benzyl derivatives such as *p*-nitrobenzyl[8] and *p*-chlorobenzyl.[9] These substituted benzyl phosphates are crystalline and more stable than BPC but have reactivities similar to the parent chloridate.

Handling, Storage, and Precautions: dibenzyl phosphorochloridate may be stored in the cold but preferably prepared just prior to use. Distillation of the chloridate may cause violent decomposition.

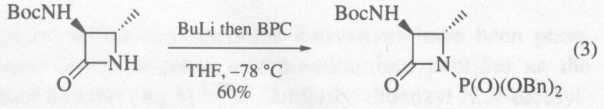
Phosphorylation. A variety of hydroxy compounds including nucleosides,[10] 1-hydroxy sugars (eq 1),[2] cyclitols,[11] and amino acids (eq 2),[12] as well as amines[4] and amides (eq 3),[5] have been phosphorylated with dibenzyl phosphorochloridate in the presence of a base, or after deprotonation, to afford the corresponding triesters and phosphoramidates, respectively.



(1)



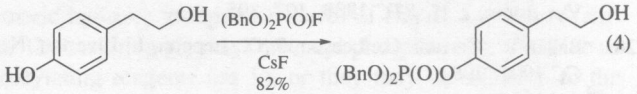
(2)



(3)

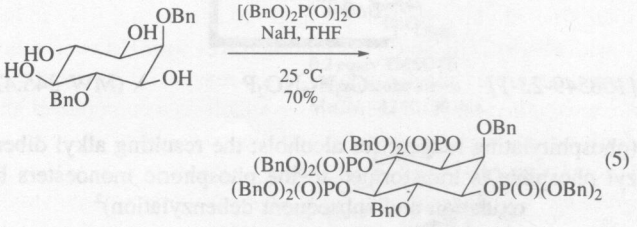
Deprotection of the dibenzyl phosphate derivatives is readily achieved by hydrogenolysis on a palladium catalyst such as ***Palladium on Carbon*** or Pd black, resulting in the formation of phosphoric monoesters and monoamides. Removal of the benzyl groups can be also carried out by ***Sodium–Ammonia***,[13] and ***Bromotrimethylsilane***[14] is useful when hydrogenation should be avoided. When removal of one of two benzyl groups is desired, various halides such as ***Sodium Iodide***[7] and other nucleophiles[15] are applied.

Synthetically Analogous Reagents. Dibenzyl phosphorofluoridate (colorless oil), a fluoro analog of BPC, is prepared by the action of 2-fluoro-1-methylpyridinium *p*-toluenesulfonate on dibenzyl hydrogen phosphate or by the reaction of tetrabenzyl pyrophosphate with CsF.[16] Unlike BPC, and dibenzyl phosphorobromidate and -iodidate, the fluoridate can be purified by distillation under reduced pressure (bp ca. 150 °C/0.2 mmHg) or chromatography on SiO_2. It reacts with alcohols and preferably with phenols in the presence of ***Cesium Fluoride*** (eq 4)[16] to give alkyl or aryl dibenzyl phosphates.



(4)

Tetrabenzyl pyrophosphate (needles, mp 60–61 °C), which is derived from dibenzyl hydrogen phosphate in the presence of ***1,3-Dicyclohexylcarbodiimide***,[17] can be used also for the phosphorylation of alcohols involving polyols (eq 5)[18] and amines. In the case of alcohols, generation of alkoxide by the action of strong bases such as ***n-Butyllithium***, ***Lithium Diisopropylamide***, ***Sodium Hydride***, or ***Potassium Hydride*** is necessary due to decreased reactivity relative to BPC. The pyrophosphate is crystalline solid and easy to handle, and can be stored in a desiccator.



(5)

Related Reagents. Dibenzyl *N,N*-Diethylphosphoramidite; *o*-Xylylene *N,N*-Diethylphosphoramidite.

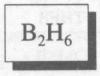
---

1. Slotin, L. A. *S* **1977**, 737. Brown, D. M. In *Advances in Organic Chemistry: Methods and Results*; Raphael, R. A.; Taylor, E. C.; Wynberg, H., Eds.; Interscience: New York, 1963; Vol. 3, p 75.
2. Inage, M.; Chaki, H.; Kusumoto, S.; Shiba, T. *CL* **1982**, 1281.
3. Valerio, R. M.; Alewood, P. F.; Johns, R. B.; Kemp, B. E. *TL* **1984**, *25*, 2609.
4. Khatri, H. N.; Stammer, C. H.; Bradford, M. M.; McRorie, R. A. *Biochem. Biophys. Res. Commun.* **1980**, *96*, 163.
5. Just, G.; Dugat, D.; Liu, W.-Y. *CJC* **1983**, *61*, 1730.

6. Atherton, F. R. *Biochem. Prep.* **1957**, *5*, 1.
7. Zervas, L. *N* **1939**, *27*, 317.
8. Zervas, L.; Dilaris, I. *JACS* **1955**, *77*, 5354.
9. Cosmatos, A.; Photaki, I.; Zervas, L. *CB* **1961**, *94*, 2644.
10. Baddiley, J.; Todd, A. R. *JCS* **1947**, 648. Michelson, A. M.; Todd, A. R. *JCS* **1949**, 2476.
11. Pietrusiewicz, K. M.; Salamończyk, G. M.; Bruzik, K. S.; Wieczorek, W. *T* **1992**, *48*, 5523.
12. Alewood, P. F.; Perich, J. W.; Johns, R. B. *AJC* **1984**, *37*, 429.
13. Baddiley, J.; Thain, E. M. *JCS* **1953**, 1610.
14. Chouinard, P. M.; Bartlett, P. A. *JOC* **1986**, *51*, 75.
15. Baddiley, J.; Clark, V. M.; Michalski, J. J.; Todd, A. R. *JCS* **1949**, 815.
16. Watanabe, Y.; Hyodo, N.; Ozaki, S. *TL* **1988**, *29*, 5763.
17. Khorana, H. G.; Todd, A. R. *JCS* **1953**, 2257.
18. Billington, D. *CSR* **1989**, *18*, 83. Potter, B. V. L. *Natur. Prod. Rep.* **1990**, *7*, 1.

Shoichiro Ozaki & Yutaka Watanabe
Ehime University, Matsuyama, Japan

Diborane



[19287-45-7] B_2H_6 (MW 27.67)

(strong reducing agent for many functional groups; extremely efficient hydroborating reagent)

Physical Data: bp –92.5 °C; mp –165.5 °C; *d* 0.437 g cm^{-3} (liquid at –92.5 °C); heat of vaporization 3.41 kcal mol^{-1} (at –92.5 °C).

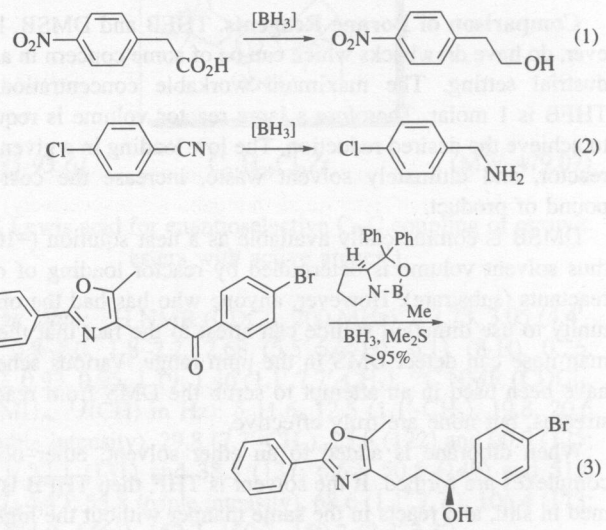
Solubility: slightly sol pentane and hexane; forms BH_3 adduct with DMS, THF, and other ethers; reacts with H_2O and protic solvents, releasing flammable hydrogen gas.

Form Supplied in: commercially available as a compressed gas.

Analysis of Reagent Purity: supplied as either 99.99% or >99.0% B_2H_6.

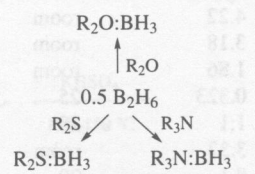
Handling, Storage, and Precautions: diborane is a toxic, pyrophoric gas and must be stored and handled accordingly. Feed lines and reactors should be flushed with N_2 and kept free of moisture. Cylinders should be hard-piped directly to reactor. When not in use, cylinder valve should be securely closed and capped. Cold (–20 to 0 °C) storage is recommended to ensure product purity. Decomposition products include higher boron hydrides and hydrogen gas.

Diborane and Borane Reagents. Borane complexes have been used in industrial-scale applications for years. In addition to their unique ability to add across carbon–carbon multiple bonds, boron hydrides reduce ketones, carboxylic acids, amides, and nitriles (eqs 1–3).[1] By the appropriate choice of borane reagent and reaction conditions, a significant degree of chemical selectivity can be achieved. This high level of selectivity and reactivity has found utility not only in classical organic synthesis,[2,3] but also in the area of asymmetric synthesis with the Corey–Itsuno catalyst serving as a prime example of a highly reactive and enantioselective reagent.[4]



Chemically, diborane is the parent of all the borane complexes. Diborane will react with a Lewis base to form an adduct in which the electron pair from the Lewis base is donated to the borane. This complexation alters the reactivity of the borane, subsequently changing its physical form. Diborane is a gas with a boiling point of –92.5 °C, whereas the borane complexes are either liquids or solids. As illustrated in the molecular model (**1**), diborane has some unusual bonding characteristics. The boron is so electron deficient that it resorts to sharing the electrons in the B–H bond, giving rise to bridging hydrogens. This electron deficiency allows formation of borane complexes with Lewis bases such as tetrahydrofuran (THF), dimethyl sulfide (DMS), and amines (Scheme 1).

(**1**)



Scheme 1

In the search for better borane reagents, a variety of complexes have been synthesized; almost all fit under one of the three following classifications: ether–borane complexes, sulfide–borane complexes, or amine–borane complexes.

A general trend of borane complexes is that the stronger the Lewis base, the weaker the reducing power of the resulting borane.[5] ***Borane–Tetrahydrofuran*** (THFB) is more reactive

此为试读,需要完整PDF请访问: www.ertongbook.com