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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.

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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.

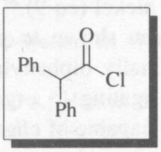
Volume 8 also contains a Formula Index, listing all reagents covered in the Encyclopedia.

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.

Dip

Diphenylacetyl Chloride

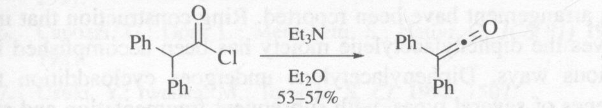


[1871-76-7] $C_{14}H_{11}ClO$ (MW 230.70)

(preparation of diphenylketene[1])

Physical Data: mp 49–53 °C; bp 175–176 °C/17 mmHg.
Form Supplied in: 90% technical grade.
Preparative Method: by the action of ***Thionyl Chloride*** on diphenylacetic acid.[2]
Handling, Storage, and Precautions: corrosive; a lachrymator. Use in a fume hood.

Diphenylacetyl chloride is used as the principal reagent in the preparation of diphenylketene.[1] Diphenylacetyl chloride reacts with ***Triethylamine*** in an inert solvent such as ether or benzene, at rt, to give 53–57% yield of diphenylketene (eq 1). The ketene may be isolated for subsequent use (eq 2).[2] More frequently, diphenylketene is generated in situ (eq 3).[3]



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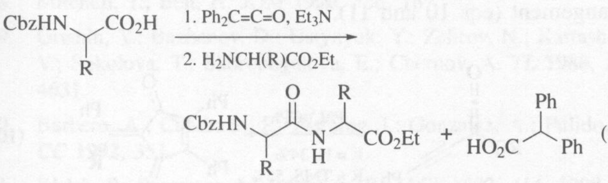

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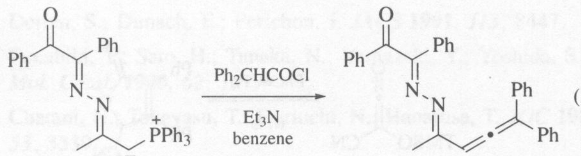
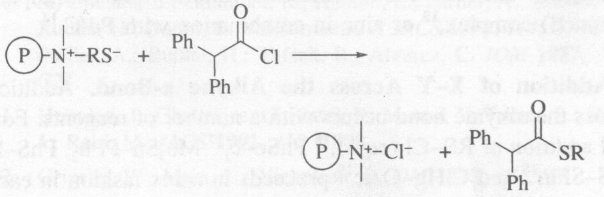


(3)

Diphenylacetyl chloride has been used in the synthesis of thiol esters via thiolate ions supported on the anion exchanger Amberlyst A-26. Many acid chlorides have been reacted in this manner (eq 4).[4]



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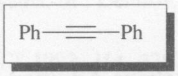
Regina Zibuck
Wayne State University, Detroit, MI, USA

Diphenylacetylene



[501-65-5] $C_{14}H_{10}$ (MW 178.24)

(precursor to substituted stilbenes[1,2] and benzil;[3] participant in cycloaddition chemistry;[4] symmetrical π-acidic ligand used widely in organometallic chemistry[5])

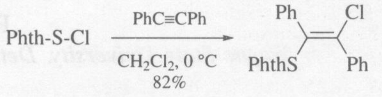
Physical Data: mp 62.5 °C; bp 90–97 °C/0.3 mmHg; *d* 0.990 g cm^{-3}.
Solubility: sol ether, hot alcohol.
Form Supplied in: colorless solid; widely available.
Handling, Storage, and Precautions: low oral toxicity; possible danger from absorption through skin.

Introduction. Due to the symmetry and high degree of planarity of diphenylacetylene, it has enjoyed enormous success as a highly Lewis acidic and sterically accessible alkyne for use in various areas of organic chemistry, as well as in organometallic chemistry where it serves as an excellent ligand of varying hapticity.

Oxidation and Reduction. The oxidation of diphenylacetylene is reported to proceed under a variety of conditions. Its cleavage to benzoic acid has been accomplished by molybdenum(VI) and tungsten(VI) polyoxometalates,[6] as well as by [bis(trifluoroacetoxy)iodo]pentafluorobenzene.[7] Chromium-based complexes,[3] zinc/chromium,[8] electrooxidation,[9] and ***Barium Manganate***,[10] among others,[11] have been successfully utilized in the oxidation of diphenylacetylene to benzil. However, methods for its oxidation to the monoketone are scarce.[12]

The reduced states of diphenylacetylene are attainable via several efficient methods. (*E*)-Stilbene is produced in 80% yield with the aid of $NiCl_2{\cdot}4PPh_3$.[1] Hydrogenation over a ruthenium catalyst[2] provides (*Z*)-stilbene, as does the use of $CoCl_2{\cdot}4PPh_3$/SmI_2/AcOH[13] or zinc in combination with Pd/C.[14] Reduction of the alkyne bond to the alkane level is achieved with the use of hydrogen and a montmorillonite–(diphenylphosphine)palladium(II) complex,[15] or zinc in combination with Pd/C.[14]

Addition of X–Y Across the Alkyne π-Bond. Addition across the alkynic bond occurs with a number of reagents. Formal addition of RS–Cl (eq 1),[16] PhSe–F,[17] Me_3Sn–PPh_2, PhS–F, PhS–SPh,[18] and ClHg–OAc[19] proceeds in *trans* fashion in each instance. However, similar addition of Bu_3Sn–H (eq 2),[20] RNH–H,[21] and HO_2C–H[22] leads to the formation of *cis*-stilbene derivatives. H–CN,[23] TMS–CN,[24] X_2 (X = halogen),[25] Et–$AlEt_2$,[26] and Al–H[27] additions to diphenylacetylene have also been reported.



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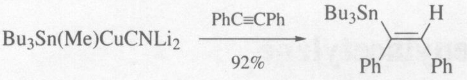
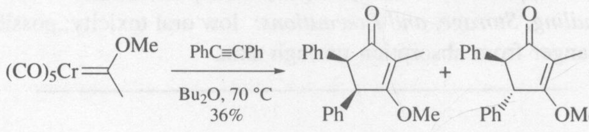


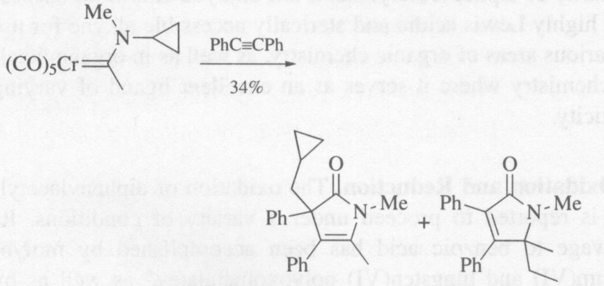
(2)

Susceptibility to Carbene Addition. Diphenylacetylene undergoes addition with chromium, tungsten, and cobalt[28] carbenes. Chromium Fischer-type carbenes react with diphenylacetylene to form cyclopentenones (eq 3).[29] Pyrrolinones are accessed when nitrogen is present in the chromium carbene reagent (eqs 4 and 5).[30] Tungsten carbenes of the Fischer class respond differently in that they form seven-membered rings (eq 6).[31] Diphenylacetylene has also demonstrated an ability to undergo facile cycloaddition with *ortho*-manganated aryl ketones to afford inden-1-ols (eq 7).[32]



(3)

cis:*trans* = 43:21



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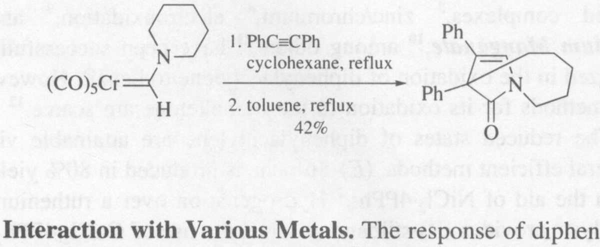

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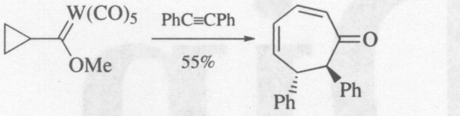

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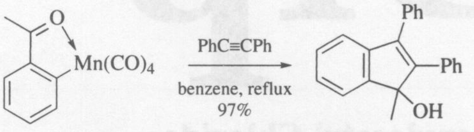
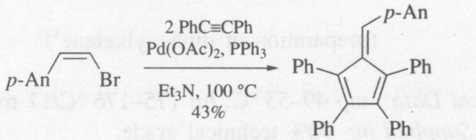


(7)

Interaction with Various Metals. The response of diphenylacetylene to palladium in coupling[33] and annulation (eq 8)[34] transformations is well documented. Spiroannulation has been effected with the aid of nickel (eq 9),[35] and insertion into zirconium complexes has been shown to provide a variety of unsaturated molecules.[36] Finally, diphenylacetylene has exhibited a general propensity for ligating to organometallic complexes[37] and clusters,[38] and to be capable of engaging in metathesis reactions.[39]



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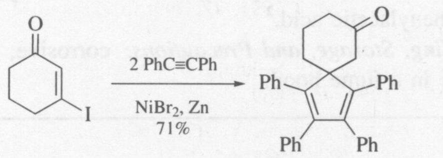
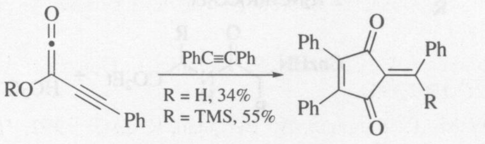


(9)

Ring Formation and Cycloaddition. Incorporation of a vicinal diphenyl group into rings of various types has been demonstrated repeatedly. Oxazoles,[40] benzothiophenes,[41] indoles,[42] pyrroles,[43] and furan-2(5*H*)-ones[44] among others[45] containing this arrangement have been reported. Ring construction that involves the diphenylacetylene moiety has been accomplished in various ways. Diphenylacetylene undergoes cycloaddition to ketenes of several types, with subsequent fragmentation and rearrangement (eqs 10 and 11).[46]



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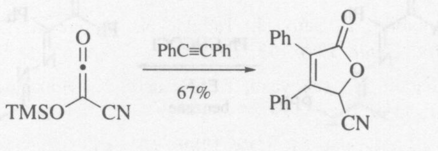
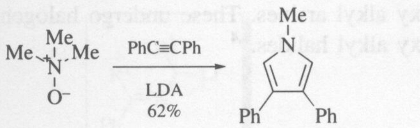


(11)

Diphenylacetylene participates satisfactorily in Pauson–Khand reactions.[47] Furthermore, [3 + 3] cycloaddition with azomethine ylides provides the respective pyrrole in good yield (eq 12).[48] Examples of [4 + 2],[49] [2 + 2],[50] 1,3-dipolar,[51] and other cycloadditions[52] have been widely reported.

Related Reagents. Dimethyl Acetylenedicarboxylate.



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(Diphenylarsinyl)methyllithium[1]

$\boxed{Ph_2As(O)CH_2Li}$

[61024-99-5] $C_{13}H_{12}AsLiO$ (MW 266.11)

(indirect nucleophilic halomethylation[2] and haloalkylation[3] of aldehydes, ketones, alkyl halides, and epoxides; synthesis of 2-hydroxy-1,2λ^5-oxarsolanes,[1,4] 1,2-bis(diphenylarsinyl)ethane, 1,2-bis(diphenylarsino)ethane ('diars'), and 1-diphenylarsino-2-(diphenylarsinyl)ethane[5])

Solubility: sol THF.

Preparative Method: quantitatively formed as a yellow solution in THF by treating the easily accessible (diphenylarsinyl)-methane[6] with LDA at −40 °C (eq 1).

$$\mathrm{As_2O_3} \xrightarrow[\text{2. SO}_2\ 74\%]{\text{1. MeI, NaI}} \mathrm{I_2AsMe} \xrightarrow[\text{2. H}_2\text{O}_2\ 70\%]{\text{1. 2 equiv PhMgBr}} \mathrm{Ph_2As(O)Me} \xrightarrow[\text{quant.}]{\text{LDA}} \mathrm{Ph_2As(O)CH_2Li} \quad (1)$$

Handling, Storage, and Precautions: handle and store the THF solution of $Ph_2As(O)CH_2Li$ under N_2 or Ar; $Ph_2As(O)Me$ (mp 153–154 °C) is stable in air but toxic. Use in a fume hood.

Indirect Nucleophilic Halomethylation and α-Haloalkylation. $HalCH_2Li$ and HalCH(Alk)Li would be interesting reagents for nucleophilic halomethylation and α-haloalkylation, but they are quite unstable due to carbene formation. Ph_2AsCH_2Li[7] is an attractive synthetic equivalent for $HalCH_2Li$, but $Ph_2As(O)CH_2Li$ is more accessible and more reactive. Treatment of this reagent with electrophiles (aldehydes, ketones, alkyl halides) followed by ***Lithium Aluminum Hydride*** and then with halogen (Br_2, I_2) or ***Thionyl Chloride*** affords halogen compounds (e.g. β-hydroxy alkyl halides) in preparatively useful yields (eq 2; R = H).[2] The yield determining step is the reaction with the electrophile, according to eqs 3 and 4.

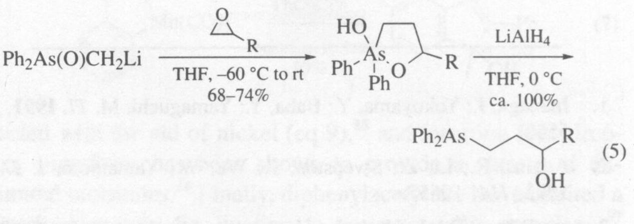
$$\mathrm{Ph_2As(O)CH(R)Li} \xrightarrow[\text{2. LiAlH}_4]{\text{1. electrophile}} \mathrm{PhAsCH(R)E} \xrightarrow[\text{2. heat}]{\text{1. Hal}_2\text{ or SOCl}_2} \mathrm{HalCH(R)E} \quad (2)$$

$$\mathrm{Ph_2As(O)CH_2Li} \xrightarrow[\text{THF, }-40\ ^\circ\text{C to rt}\ 56\text{–}72\%]{\text{HalAlk}} \mathrm{Ph_2As(O)CH_2Alk} \quad (3)$$

$$\mathrm{Ph_2As(O)CH_2Li} \xrightarrow[\text{THF, }-40\ ^\circ\text{C to rt; 2. H}_2\text{O}\ 53\text{–}82\%]{\text{1. RCOR}^1} \mathrm{Ph_2AsCH_2C(OH)RR^1} \quad (4)$$

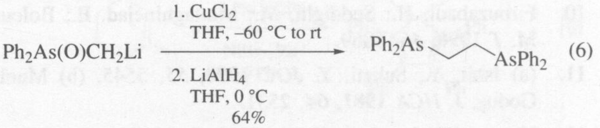
Like $Ph_2As(O)Me$, the higher homologs (prepared as in eq 3) can be lithiated at the methylene group α to the As atom by ***Lithium Diisopropylamide***. The resulting compounds provide entry to functionalized hydrocarbons according to eq 2 (R = Alkyl).[3] ***Sulfuryl Chloride*** is particularly useful as a reagent for replacing the diphenylarsino group by chlorine. Also the methine group of *s*-butyldiphenylarsine oxide is lithiated by LDA (80%). α-Lithiated alkyldiphenylarsine oxides react extremely diastereoselectively with benzaldehyde or acetophenone.[3b]

Synthesis of 2,2-Diphenyl-2-hydroxy-1,2λ^5-oxarsolanes. The treatment of terminal epoxides with $Ph_2As(O)CH_2Li$ and subsequently with H_2O leads to 2,2-diphenyl-2-hydroxy-1,2λ^5-oxarsolanes (eq 5), which are smoothly reduced by $LiAlH_4$ to γ-hydroxy alkyl arsines. These undergo halogenolysis to give γ-hydroxy alkyl halides.[1,4]



(5)

Coupling. $Ph_2As(O)CH_2Li$ reacts with ***Copper(II) Chloride*** to give 1,2-bis(diphenylarsinyl)ethane (64%), which is quantitatively reduced by $LiAlH_4$ to 1,2-bis(diphenylarsino)ethane, the important ligand 'diars' for transition metals (eq 6). ***Sodium Borohydride*** can be used to obtain the corresponding monooxide (88%).[5]



(6)

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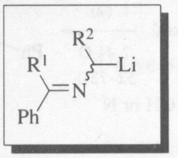
1,1-Diphenyl-2-azaallyllithium[1]



(1; R^1 = Ph, R^2 = H)
[64042-43-9] $C_{14}H_{12}LiN$ (MW 201.21)
(2; R^1 = H, R^2 = Ph)
[37019-83-3]

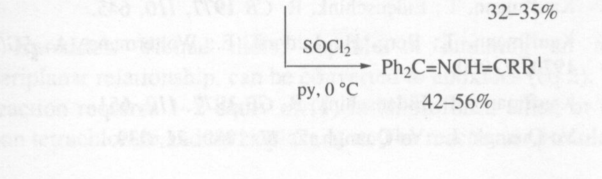
(agents for the nucleophilic aminomethylation of ketones and alkyl halides;[2] react with C=C, C=N, C=S, and N=N double bonds as well as with C≡C and C≡N triple bonds by [3 + 2] cycloaddition with high regioselectivity and stereospecificity;[3] corresponding cycloadditions with *N*-benzylidenebenzylamine[1])

Solubility: sol THF; slightly sol Et_2O.

Preparative Methods: 1,1-diphenyl- (**1**) and 1,3-diphenyl-2-azaallyllithium (**2**)[4] are prepared by deprotonation of *N*-(diphenylmethylene)methylamine or *N*-benzylidenebenzylamine, respectively, with ***Lithium Diisopropylamide*** in THF or Et_2O/THF at ca. –60 °C. Solutions thus prepared contain diisopropylamine. Amine-free solutions of *cis,trans*-(**2**) are obtained by thermal conrotatory ring opening of *N*-lithio-*cis*-2,3-diphenylaziridine in THF.[4] *cis,trans*-(**2**) is labile[4] and isomerizes readily at 20 °C[1] to give *trans,trans*-(**2**); 1-phenyl-2-azaallyllithium is prepared similarly.[1] Aliphatic substituted 2-azaallyllithium reagents are prepared by stannyl–lithium exchange.[5]

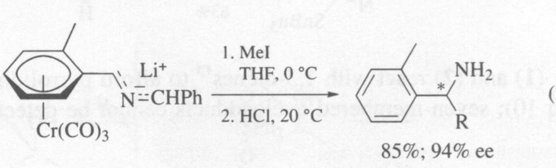
Handling, Storage, and Precautions: solutions of (**1**) and *trans,trans*-(**2**) in THF are stable at –30 °C under N_2 or Ar for days. No special precautions are necessary.

Indirect Nucleophilic Aminomethylation and Synthesis of 2-Azabutadienes. Reaction of (**1**) with ketones yields hydroxy azomethines which are of preparative interest since they provide β-amino alcohols on hydrolytic cleavage with acids (eq 1).[2] Dehydration of the hydroxy azomethines with ***Thionyl Chloride/Pyridine*** provides an entry to 2-azabutadienes.[2c] Nucleophilic aminomethylation of alkyl bromides is also possible (eq 2).[2a,c] With a chiral, optically active derivative of (**2**), a highly enantioselective amine synthesis has been developed (eq 3).[6] In addition, from the 3-cyano analog a synthesis of α-amino acids (eq 4) has been developed,[7] and the 3-vinyl analog is known.[8]



(1)

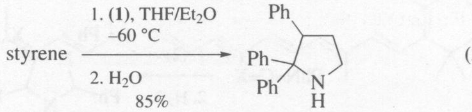
$$RBr \xrightarrow[-60\ ^\circ C\text{ to rt}\ \ 22\text{–}64\%]{(1),\ THF} Ph_2C{=}NCH_2R \xrightarrow{HCl} H_2NCH_2R \qquad (2)$$



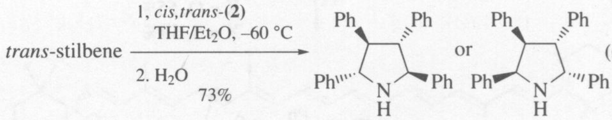
(3)

$$RX + Ph_2C{=}NCH_2CN \xrightarrow[\text{catalyst, phase transfer, } 75\text{–}95\%]{\text{aq NaOH, toluene}} Ph_2C{=}NCH(R)CN \xrightarrow{HCl} H_2NCH(R)CO_2H \qquad (4)$$

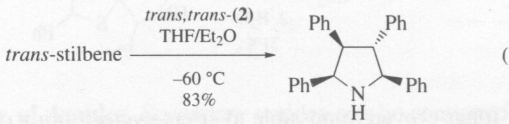
Stoichiometric 1,3-Anionic Cycloaddition. (**1**) and (**2**) react with C=C, C=N, N=N, and C=S double bonds as well as with C≡C and C≡N triple bonds by [3 + 2] cycloadditions. In contrast to unstrained isolated C=C double bonds, one of the strained isolated C=C double bonds of norbornadiene undergoes 1,3-anionic cycloaddition with (**1**) or (**2**) to give pyrrolidines.[1] Compounds with an alkenic double bond conjugated with an aromatic system[3,9] or an organoelement group[10] (PhS–, PhSe–, Ph_2P–, Ph_2As–, Ph_3Ge–, $Ph_2(O)P$–, $Ph_2(O)As$–; not PhTe–, Ph_2Sb–, Ph_3Sn–, Ph_3Pb–) are better 1,3-anionophiles. The cycloadditions with (**1**) can occur with high regioselectivity (e.g. eq 5) with aryl alkenes.[4] In addition, the cycloaddition of *cis,trans*-(**2**) with *trans*-stilbene (eq 6) or of *trans,trans*-(**2**) with *trans*-stilbene (eq 7) or with *cis*-stilbene occurs stereospecifically with respect to the alkene and the 2-azaallyl component (*cis* addition in each case).[4,11]



(5)



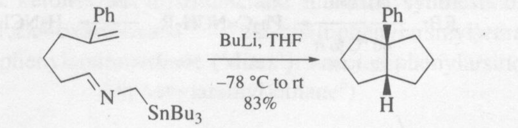
(6)



(7)

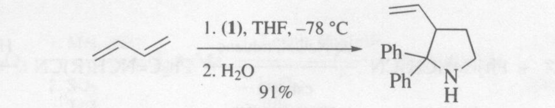
Cycloaddition of the 1,3-diphenyl-2-azaallyl anion (generated by a phase transfer technique) to cyclohex-2-enone derivatives yields bicyclic pyrrolidine derivatives (eq 8).[12] An intramolecular 2-azaallyl anion [3 + 2] cycloaddition has also been reported (eq 9).[5]

(8)



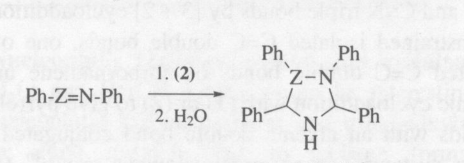
(9)

(1) and **(2)** react with 1,3-dienes[13] to afford pyrrolidines (e.g. eq 10); seven-membered cycloadducts cannot be detected.



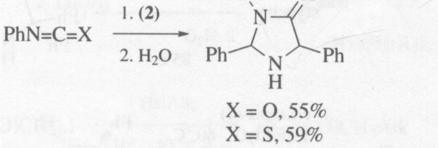
(10)

(2) undergoes cycloaddition to aromatic azomethines and azo compounds (e.g. eq 11).[14] In contrast, **(1)** (which is generally more prone to form open-chain adducts than **2**) gives the expected cycloadduct only with *p,p′*-azotoluene, but with azobenzene and azomethines open-chain adducts are formed.[1]

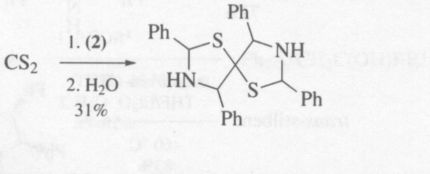


(11)

(2) reacts with ***Phenyl Isocyanate*** and ***Phenyl Isothiocyanate*** according to eq 12.[15] **(2)** also reacts with phenylallenes[16] to produce methylenepyrrolidines. The use of diphenylcarbodiimide and CS$_2$ as substrates generates cycloadducts to which a secondary reaction occurs (e.g. eq 13), whereas CO$_2$ gives an open-chain product.

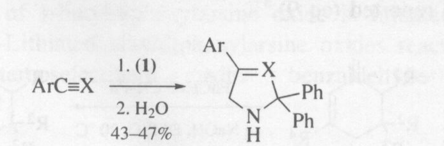


(12)

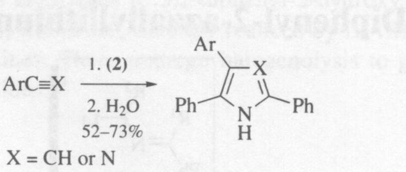


(13)

It has proved impossible to effect cycloaddition of **(1)** and **(2)** with terminal alkynes or with aliphatic nitriles having a hydrogen in the α-position to the cyano group. Internal alkynes and nitriles[1,17] normally react with **(1)** to give a cycloaddition product (e.g. eq 14). However, with **(2)**, the corresponding aromatic ring system is generated instead of the cycloadduct (e.g. eq 15).

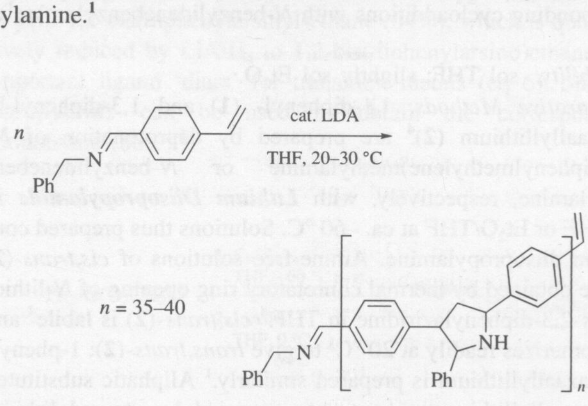


(14)



(15)

Catalytic 1,3-Anionic Cycloaddition with LDA as Catalyst. Whereas, for unknown reasons, the use of *N*-(diphenylmethylene)methylamine (educt of **1**) in such reactions has produced satisfactory results only in two cases, the yields of the cycloadducts obtained with benzylidenebenzylamine (educt of **2**) are generally good, and both *trans,trans*-**(2)** and *cis,trans*-**(2)** participate in cycloaddition.[1] Eq 16 shows the LDA-catalyzed polymerization of a vinyl derivative of *N*-benzylidenebenzylamine.[1]



(16)

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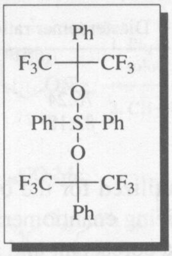
Diphenylbis(1,1,1,3,3,3-hexafluoro-2-phenyl-2-propoxy)sulfurane[1]

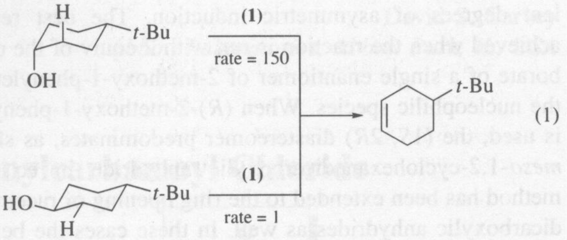


[32133-82-7] $C_{30}H_{20}F_{12}O_2S$ (MW 672.57)

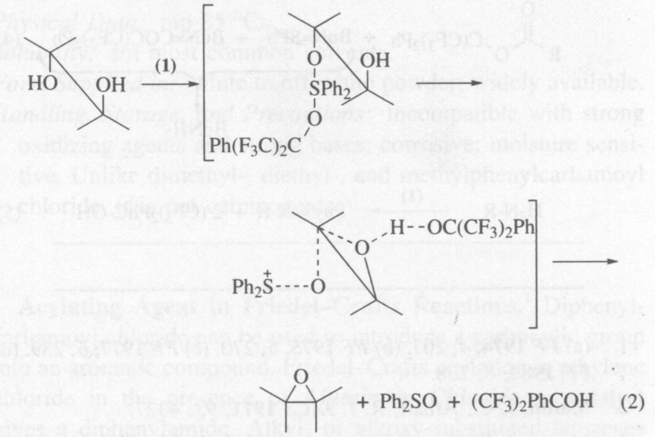
(dehydration of alcohols;[2] synthesis of epoxides and cyclic ethers;[3] cleavage of amides;[5] oxidation of amines[6])

Physical Data: mp 107–109 °C.
Solubility: sol ether, benzene, acetone, alcohols.
Form Supplied in: white crystals.
Analysis of Reagent Purity: NMR, IR.
Preparative Method: by the reaction of the potassium salt of 1,1,1,3,3,3-hexafluoro-2-phenylisopropanol with diphenyl sulfide in the presence of chlorine in ether at −78 °C.[1a]
Handling, Storage, and Precautions: avoid moisture; readily hydrolyzed; stable at rt; decomposes slowly at rt in solution.

Dehydration of Alcohols. The title reagent (**1**) is useful for the dehydration of alcohols. In general, tertiary alcohols are dehydrated instantaneously at rt. Some secondary alcohols are dehydrated. In cyclohexane rings, a *trans*-diaxial orientation of the leaving groups significantly increases the rate of elimination (eq 1). Primary alcohols do not yield products of dehydration unless the β-proton is sufficiently acidic. In most cases, the ether [$(CF_3)_2PhCOR$] is obtained.[2]

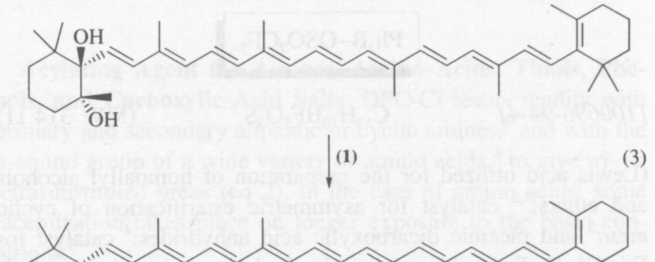


Epoxides. Vicinal diols, capable of attaining an antiperiplanar relationship, can be converted to epoxides (eq 2). The reaction requires 1–2 equiv of (**1**) in chloroform, ether, or carbon tetrachloride and takes place at rt. The reaction is postulated to take place via ligand exchange with the sulfone followed by decomposition to the epoxide, diphenyl sulfoxide, and 1,1,1,3,3,3-hexafluoro-2-phenylisopropanol.



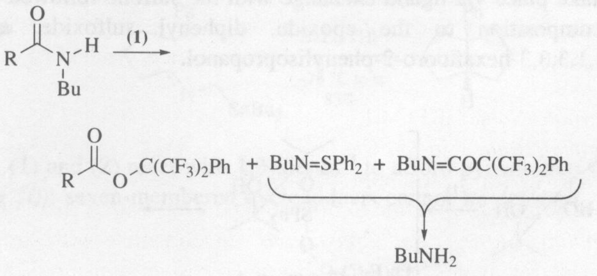
Other cyclic ethers have been prepared, but yields are highly dependent on product ring size. The following transformations are representative: 2,2-dimethyl-1,3-propanediol to 3,3-dimethyloxetane (86%), 1,4-butanediol to tetrahydrofuran (72%), 1,5-pentanediol to tetrahydropyran (39%), and diethylene glycol to dioxane (40%). Longer chain diols yield ethers [$(CF_3)_2PhCO(CH_2)_nOCPh(CF_3)_2$].[3]

Eschenmoser used this method to convert (5*R*,6*R*)-5,6-dihydro-β,β-carotene-5,6-diol to its epoxide (eq 3). This reagent is more effective than other reagents due to the unique solubility profile of the dihydrocarotenediol.[4]



Cleavage of Amides. Secondary amides can be converted to esters with (**1**). The rate is sensitive to steric constraints at the nitrogen and the acyl carbon. In most cases the amine portion is trapped as the sulfilimine and/or the imidate, which are easily converted back to the amine (eq 4). The dual nature of this reaction affords a mild conversion of amides to esters as well as a simple method for deprotection of *N*-acylated amines.[5]

Oxidation of Amines. In a related reaction, (**1**) reacts with primary amines (as well as amides and sulfonamides) to give sulfilimines (eq 5). Secondary amines are converted to imines on reaction with (**1**) whereas benzylamine is converted to benzonitrile (89%) with 2 equiv of (**1**).[6]



$$H_2N\text{-}R \xrightarrow{(1)} Ph_2S{=}N\text{-}R + 2\,(CF_3)_2PhC\text{-}OH \qquad (5)$$

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1. (a) *FF* **1974**, *4*, 205. (b) *FF* **1975**, *5*, 270. (c) *FF* **1977**, *6*, 239. (d) *FF* **1980**, *8*, 208.
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Diphenylboryl Trifluoromethanesulfonate

$Ph_2B\text{–}OSO_2CF_3$

[100696-94-4] $C_{13}H_{10}BF_3O_3S$ (MW 314.11)

(Lewis acid utilized for the preparation of homoallyl alcohols and ethers;[1,2] catalyst for asymmetric esterification of cyclic *meso*[3] and racemic dicarboxylic acid anhydrides;[4] catalyst for Friedel–Crafts acylation of acid anhydrides and acid chlorides[5])

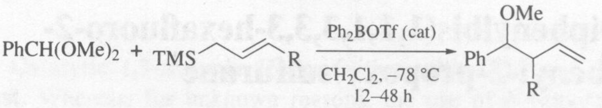
Alternate Name: diphenylboryl triflate.

Solubility: sol common inert organic solvents such as CH_2Cl_2 and toluene.

Preparative Method: generated in situ from equimolar amounts of ***Silver(I) Trifluoromethanesulfonate*** and diphenylchloroborane. The reactants are mixed in toluene at 0 °C and stirred for 1 h. The reagent is then used immediately.

Handling, Storage, and Precautions: solutions are moisture and air sensitive and therefore they should be used under a dry inert atmosphere.

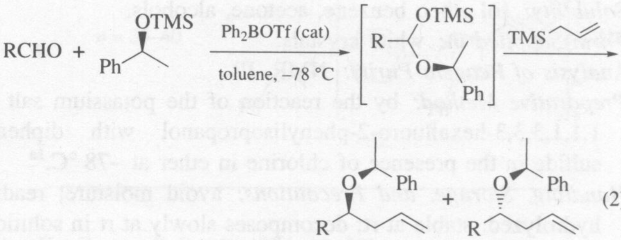
Allylation. Ph_2BOTf is a mild and effective catalyst for the addition of allylsilanes to acetals to afford the corresponding homoallyl ethers. These reactions proceed at –78 °C in good yield, and with modest diastereoselectivity when a substituted allylsilane is utilized (eq 1). The allylation reaction of acetals is not catalyzed by either Ph_2BCl or AgOTf, nor is it catalyzed by Bu_2BOTf. Thus it has been postulated that stabilization of the boryl triflate by the two phenyl groups yields a boron atom with significant cationic character and it is this property that allows Ph_2BOTf to serve as the activator of the reaction.[1]



(1)

R	Diastereomer ratio	Yield
H	–	71%
Me	76:24	69%
Ph	82:18	73%

Ph_2BOTf has been utilized for the one-pot asymmetric allylation of aldehydes utilizing enantiomerically pure 1-phenylethyl trimethylsilyl ether as a coreactant and source of asymmetric induction (eq 2). The highest diastereomeric product ratios are typically observed with reactions run at –78 °C in toluene. The protecting group on the resulting homoallylic ethers can be easily removed via catalytic hydrogenation or by treatment with ***Iodotrimethylsilane***.[2]

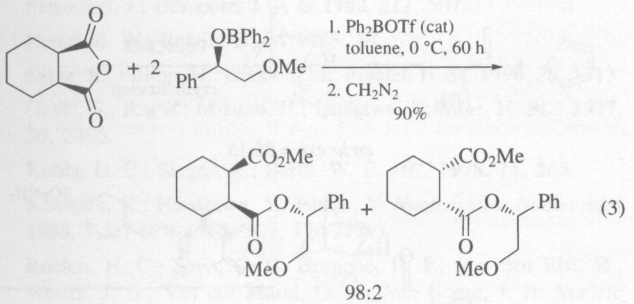


(2)

R		
Ph(CH2)2	96:4	71%
Cy	93:7	74%
Ph	74:26	77%

Asymmetric Esterification. Ph_2BOTf is a very efficient catalyst for the asymmetric esterification of cyclic *meso* and racemic dicarboxylic anhydrides. Various enantiomerically pure derivatives of mandelic acid have been utilized in reactions with anhydrides of cyclic *meso*-dicarboxylic acids with good to excellent degrees of asymmetric induction. The best results are achieved when the reaction is run with 2 equiv of the diphenylborate of a single enantiomer of 2-methoxy-1-phenylethanol as the nucleophilic species. When (*R*)-2-methoxy-1-phenylethanol is used, the (1*S*, 2*R*) diastereomer predominates, as shown for *meso*-1,2-cyclohexanedicarboxylic anhydride in eq 3.[3] This method has been extended to the ring opening of racemic cyclic dicarboxylic anhydrides as well. In these cases the best results are achieved when >2 equiv of the anhydride per equivalent of nucleophile are used. Yields for the reported examples average approximately 75%, a typical example being shown in eq 4.[4]

Friedel–Crafts Acylation. Ph_2BOTf has been reported to be an effective catalyst for the acylation of aromatic compounds



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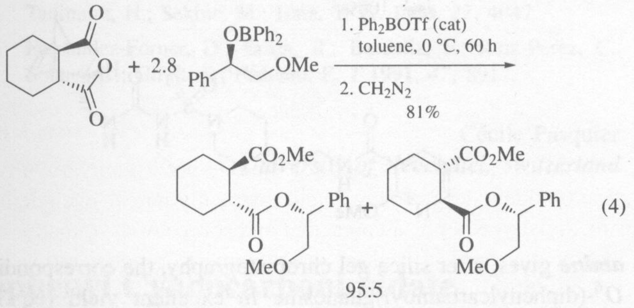
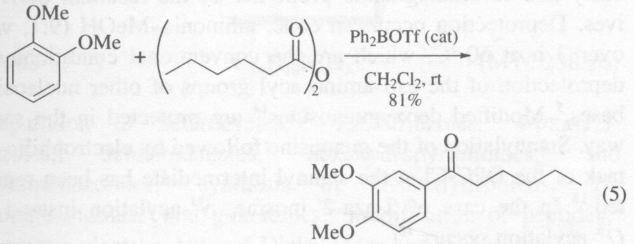


(4)

with acid chlorides or acid anhydrides under mild conditions (eq 5).[5]



(5)

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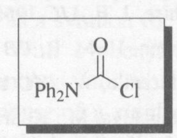
Diphenylcarbamoyl Chloride

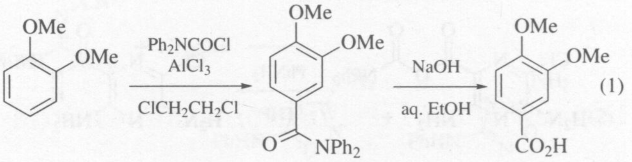


[83-01-2] $C_{13}H_{10}ClNO$ (MW 231.69)

(acylating agent in Friedel–Crafts reactions;[1] acylating agent for amines,[2] amino acids,[3] thiols,[2] phenols,[4] and carboxylic acid salts;[5] protecting group in oligonucleotide synthesis[6])

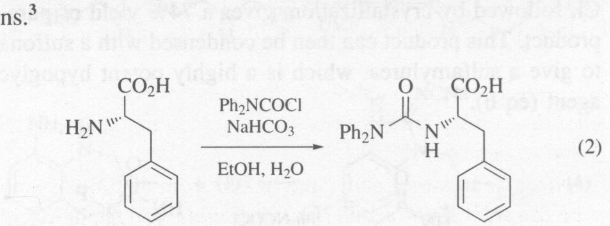
Alternate Name: DPC-Cl.
Physical Data: mp 85 °C.
Solubility: sol most common solvents.
Form Supplied in: white to off-white powder; widely available.
Handling, Storage, and Precautions: incompatible with strong oxidizing agents and strong bases; corrosive; moisture sensitive. Unlike dimethyl-, diethyl-, and methylphenylcarbamoyl chloride, it is not carcinogenic.

Acylating Agent in Friedel–Crafts Reactions.[1] Diphenylcarbamoyl chloride can be used to introduce a carboxylic group into an aromatic compound. Friedel–Crafts acylation in ethylene chloride in the presence of ***Aluminum Chloride*** as catalyst gives a diphenylamide. Alkyl- or alkoxy-substituted benzenes are readily acylated, whereas fluoro or chloro derivatives are unreactive. With the exception of the sterically hindered amides obtained from mesitylene, durene, and pentamethylbenzene, the resultant diphenylamides are readily hydrolyzed by alkali (NaOH in 85% aq. EtOH or DMSO) to the parent carboxylic acids (eq 1).[7]



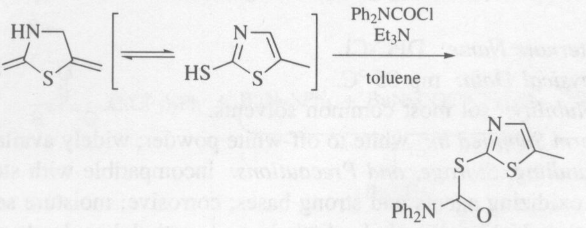
(1)

Acylating Agent for Amines, Amino Acids, Thiols, Phenols, and Carboxylic Acid Salts. DPC-Cl reacts readily with primary and secondary aliphatic or cyclic amines,[2] and with the α-amino group of a wide variety of amino acids,[3] to give tri- or tetrasubstituted ureas (eq 2). In the case of amino acids, some racemization takes place on longer exposure to the basic conditions.[3]



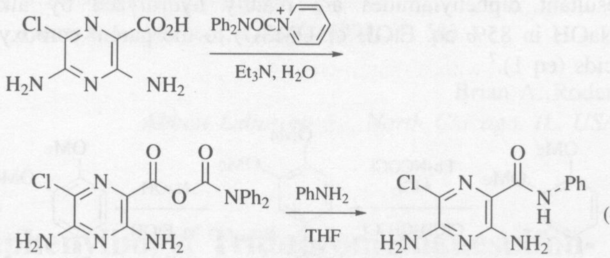
(2)

Reactions with thiols[2] can be carried out in aq. EtOH under basic conditions ($NaHCO_3$), to give good yields of *N,N*-diphenylthiocarbamates. Other carbamoyl derivatives such as dimethyl- and dibutylcarbamoyl chloride are not as useful because they are too unstable to basic conditions in water.[2] Imidazole in acetone or EtOH can be converted into its DPC derivative using an excess of imidazole as the base.[2] O-Methylhydroxylamine reacts readily with DPC-Cl in THF to give *N′*-methoxy-*N,N*-diphenylurea in 62% yield.[8] The reaction of 5-methylene-1,3-thiazolidine-2-thione with DPC-Cl traps only the aromatic thiazole tautomer, giving the *S*-substitution product (eq 3).[9]



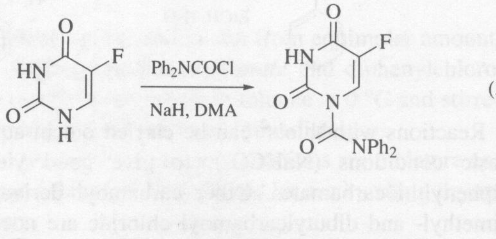
(3)

Phenols can be acylated by DPC-Cl in acetone[4] in the presence of ***Potassium Carbonate*** or in pyridine to give *N,N*-diphenylcarbamates.[10] Carboxylic *N,N*-diphenylcarbamic anhydrides have been isolated from the reaction of carboxylate salts with 1-(*N,N*-diphenylcarbamoyl)pyridinium chloride, prepared from DPC-Cl and pyridine, in aqueous or ethanolic solutions. In the presence of amino groups the reaction under these conditions is chemoselective and no carbamate is formed. These mixed anhydrides are stable, crystalline derivatives and are very reactive in acylation reactions (eq 4).[5]



(4)

The DPC group has been introduced in many pharmaceutical products. Hence the toxicity and tumor affinity of 5-fluorouracil have been modified by reacting it with DPC-Cl in DMA in the presence of ***Sodium Hydride*** to give the 1-DPC derivative (eq 5).[11] When excess DPC-Cl is employed in the presence of K_2CO_3, the 1,3-disubstituted derivative is also produced. Treatment of an 85/15 *endo*/*exo* mixture of bicyclo[2.2.1]hept-5-en-2-ylmethylamine obtained by Diels–Alder reaction with DPC-Cl, followed by crystallization, gives a 74% yield of pure *endo* product. This product can then be condensed with a sulfonamide to give a sulfamylurea, which is a highly potent hypoglycemic agent (eq 6).[12]



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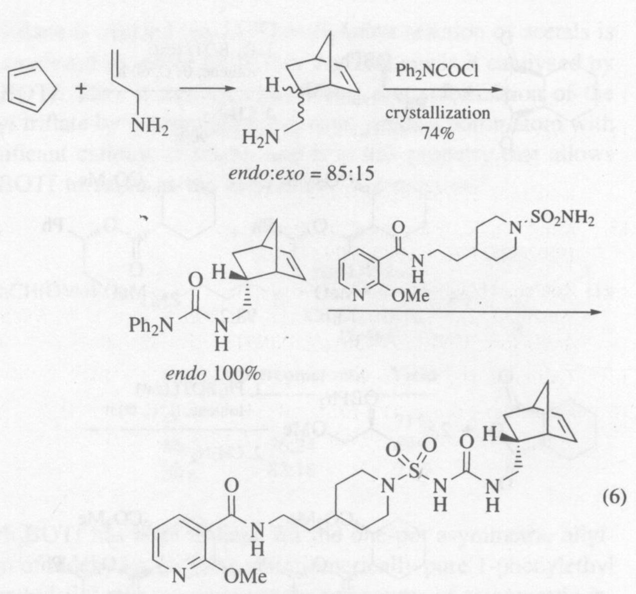
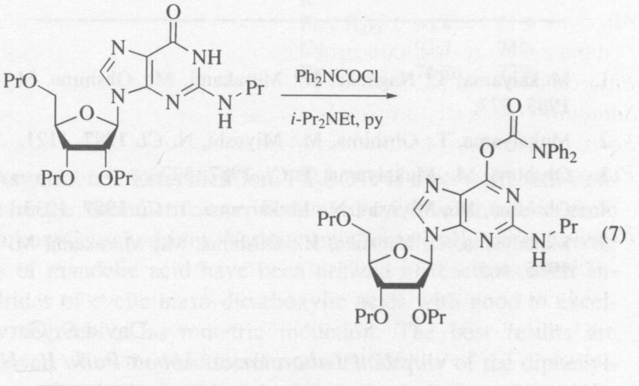


(6)

Protecting Group in Oligonucleotide Synthesis. The lactam function of the guanine residue is subject to side-reaction during oligonucleotide synthesis. It can be protected according to widely used procedure originally devised by Kamimura et al.[5,13] Treatment of the amino-protected oligonucleotide with DPC-Cl in dry pyridine containing ***Triethylamine*** or ***Diisopropylethylamine*** gives, after silica gel chromatography, the corresponding O^6-(diphenylcarbamoyl)guanosine in excellent yield (eq 7).[5] DPC-Cl is superior to dimethyl- and dimethylthiocarbamoyl chloride for this purpose. In addition to the successful protection of the guanine residue, introduction of DPC improves the solubility and chromatographic properties of the resultant derivatives. Deprotection occurs in conc. ammonia–MeOH (9:1, v/v) over 3 h at 60 °C, which are the conventional conditions for deprotection of the *exo*-amino acyl groups of other nucleoside bases.[5] Modified deoxyguanosines[14] are protected in the same way. Stannylation of the guanosine followed by electrophilic attack of the DPC-Cl at the stannyl intermediate has been reported.[15] In the case of 2-aza-2′-inosine, N^1-acylation instead of O^6-acylation occurs.[16]



(7)

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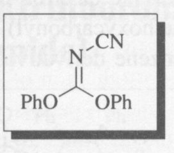
Diphenyl Cyanocarbonimidate

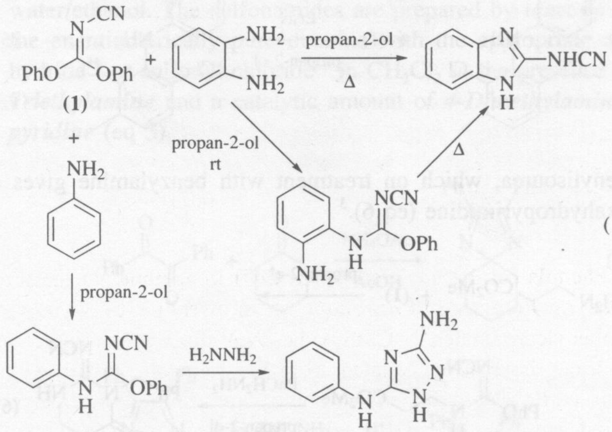


[79463-77-7] $C_{14}H_{10}N_2O_2$ (MW 238.26)

(preparation of heterocycles,[1,2] 1,2,4-triazoles,[1] 4-oxa-1,3-diazoles,[2] benzimidazoles,[1] hexahydropyrimidines,[3] and hydroquinazolines;[3] synthesis of *O*-phenylisoureas,[1] *N*-cyanoguanidines,[2] and guanidines;[4] modification of peptides;[5] reverse electron demand Diels–Alder heterodienophile[6])

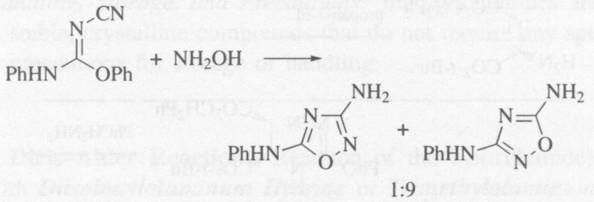
Alternate Names: DPCC; diphenoxymethylenecyanamide; diphenyl *N*-cyanoimidocarbonate.
Physical Data: mp 156–158 °C,[1] 161–163 °C (Aldrich).
Solubility: sol THF, propan-2-ol.
Form Supplied in: commercially available in ca. 97% purity.
Preparative Method: from diphenyl carbonate by treatment with PCl_5 followed by cyanamide.[1]
Handling, Storage, and Precautions: harmful if swallowed and irritating to the eyes and respiratory system. Care should be taken not to inhale the powder nor to allow it to come in contact with the skin. It is sensitive to moisture. It should be disposed of by dissolving in a solvent and burning the solution in an approved incinerator. Use in a fume hood.

Synthesis of Heterocycles. Diphenyl cyanocarbonimidate was originally described as a synthon for heterocyclic synthesis by Webb and Labaw.[1] With *o*-phenylenediamine in boiling propan-2-ol, 2-cyanoaminobenzimidazole is formed. At rt the *O*-phenylisourea, the product of a single displacement, can be isolated and converted to the benzimidazole on warming (eq 1). The sequential displacement of the two phenoxide ions illustrates a major advantage of DPCC as a reagent. Sequential reaction of aniline followed by ***Hydrazine*** gives 5-phenylamino-3-amino-1,2,4-triazole (eq 1). A variety of 1,2,4-triazoles have been prepared by this method.[7]



(1)

Treatment of the *O*-phenylisourea with ***Hydroxylamine*** gives two isomeric oxadiazoles, the predominant isomer arising from initial nucleophilic attack by the hydroxylamine nitrogen (eq 2).[2] Cyclization to give six-membered rings also occurs, forming substituted hydropyrimidines (eq 3).[8] Imidazole ring formation to give a tricyclic structure has been accomplished by reaction of DPCC with a diamine (eq 4).[9]



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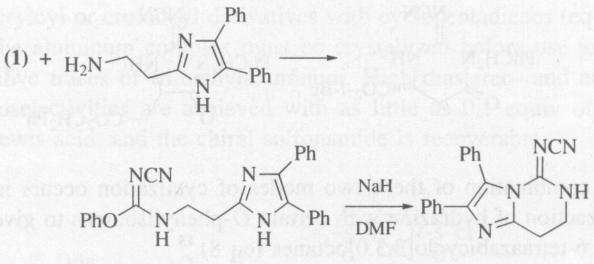

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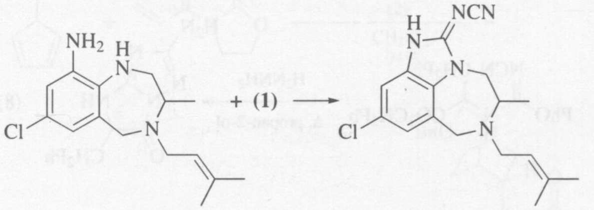

(4)

Oxadiazole ring formation occurs with a hydrazide in the presence of ***Triethylamine***, presumably involving the enol in the second nucleophilic displacement (eq 5).[10] Reaction of DPCC with 2-aminobenzyl alcohol gives a six-membered benzoazine.[11]

An alternative mode of ring formation involves sequential substitution with two different nitrogen nucleophiles, followed by ring closure between one nitrogen and a reactive center on the other nucleophile. Thus β-alanine methyl ester gives an *O*-