reagents for organic synthesis

Reagents for Organic Synthesis

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Reagents for Organic Synthesis

PREFACE

A precursor of this book which appeared as a 49-page section in *Experiments in Organic Chemistry*, 3rd edition, 1955 was received with sufficient enthusiasm to encourage us to undertake this more extensive book describing 1,120 reagents of use to organic chemists.

The reagents are listed alphabetically, and for each we give the structural formula, molecular weight, physical constants, preferred methods of preparation or purification, suppliers, and examples of significant uses, each documented with references and with flow sheets showing at a glance the molar ratio of the reactants, the reaction conditions, and the yield. Where a choice exists, we have given preference to examples that compare the reagent in question with alternative reagents, that explain details of the experimental procedure, or that seem otherwise particularly informative. Where the reaction cited is part of a significant synthetic sequence, the formulation often includes enough preceding or succeeding steps to bring out points of interest. In deciding whether to regard a given compound as a reagent or merely a starting material, we probably have been swayed somewhat by the consideration of interest.

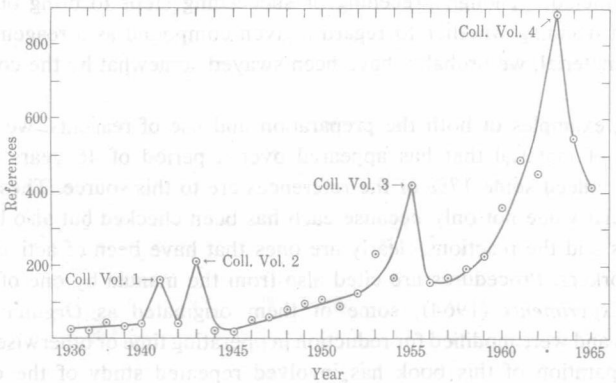
In citing examples of both the preparation and use of reagents, we have made liberal use of material that has appeared over a period of 46 years in *Organic Syntheses*; indeed some 17% of the references are to this source. These examples are of special value not only because each has been checked but also because the compounds and the reactions clearly are ones that have been of active interest to modern workers. Procedures are cited also from the manual by one of us entitled *Organic Experiments* (1964); some of them originated as *Organic Syntheses* procedures and were modified for reduction in operating time or otherwise simplified.

The preparation of this book has involved repeated study of the question of excess reagent. Is it a good plan to routinely employ a reagent in 1.2 times the theoretical amount? In our opinion the answer is in the affirmative in only two situations. In a study of a particular Diels-Alder reaction presented in this book it is shown that with 1.5 equivalents of the dienophile the reaction in tetrachloroethylene at 78.8° was complete in 8.0 hrs., but that the time can be reduced to 2.4 hrs. by use of 3.0 equivalents of the dienophile. In determining the time required for reaction in 50 other solvents, use of a threefold excess of the dienophile seemed indicated. In many permanganate oxidations, use of excess oxidant is justified because considerable permanganate decomposes in the process with liberation of oxygen. In all situations except those of the two types exemplified, we recommend use of a reagent in the exact theoretical amount. We regard as faulty a procedure that specifies use of excess reagent without presenting evidence that the excess is beneficial.

The precursor of this book included a section on the properties of solvents and methods for their purification. After some study of the problem, we decided against an extensive coverage of solvent purification. Abundant references are available to procedures for the purification and drying of solvents, but the papers present no evidence of the degree of purity achieved and hence provide little basis for their evaluation. We place more confidence in the 44 purified solvents now available

from five competing U.S. firms and have listed them in a section on **Solvents**. It stands to reason that a firm specializing in solvent purification is in a position to make a long-range study of each problem undertaken and to install efficient techniques of distillation and drying and effective measures for product control. At least some of the prominent industrial research groups find it expedient to purchase purified solvents rather than utilize their own manpower for the purpose. The relatively few detailed procedures for solvent purification included in this book are supplemented by descriptions of drying with lithium aluminum hydride, calcium hydride, and molecular sieves. Properties of the pure solvents available commercially are recorded in tables in which solvents are arranged in order of boiling point in each of five solubility types (aprotic and water-immiscible, etc.).

The impact of *Organic Syntheses* on the development and use of reagents is evident from the chart. Not shown at the left is an almost straight-line section extending back to 1900 and beginning to rise slowly from 5–10 references per year only in about 1925. Then come four collective-volume peaks, each surging higher than before.



The prognosis for the next few years is clear, and it is evident that if this book meets with favor it will need to be revised or supplemented in the near future. We expect to keep abreast of the new literature in preparation for a possible paperback supplement to be published whenever enough new and revised material accumulates. We cordially invite fellow chemists to submit corrections, comments, suggestions, and contributions. If you think of reagents or references we have missed, do send in either notes and references or else a finished contribution which we can use with minor editing and with acknowledgment of the source. Scattered throughout the present volume are contributions submitted originally for a book planned by Melvin S. Newman and Robert E. Ireland and kindly turned over to us when the project was abandoned.

It is a pleasure to acknowledge with sincere thanks the generous help of several people in the preparation of this book. Outside readers included Drs. Elmore L. Martin of du Pont, William P. Schneider of Upjohn, John J. Baldwin, John M. Chemerda, Stanton A. Harris, James H. Jones, Larry J. Loeffler, Arthur A. Patchett, Peter I. Pollak, David C. Remy, Walfred S. Saari, and David Taub of Merck Sharp and Dohme Research Laboratories. Co-workers who proofread manuscript and

checked references are Drs. Makhluf J. Haddadin, Musa Z. Nazer, E. Paul Papadopoulos, Joseph P. Schirmer, Jr., and Mr. Edwin Arima. We are indebted also to investigators who provided explanations or supplied additional information. Suppliers of chemicals and apparatus were also highly cooperative.

We alone are to blame for some duplication of references, discovered only in the course of preparing the indexes. A reaction involving A and B and cited as an attribute of A is easily forgotten and later cited as an attribute of B with repetition of the reference, rather than by cross reference. We apologize for such blemishes.

Our closing date was August 23, 1966; journals received after that date could not be reviewed. Even so, there are 182 references to papers of 1966.

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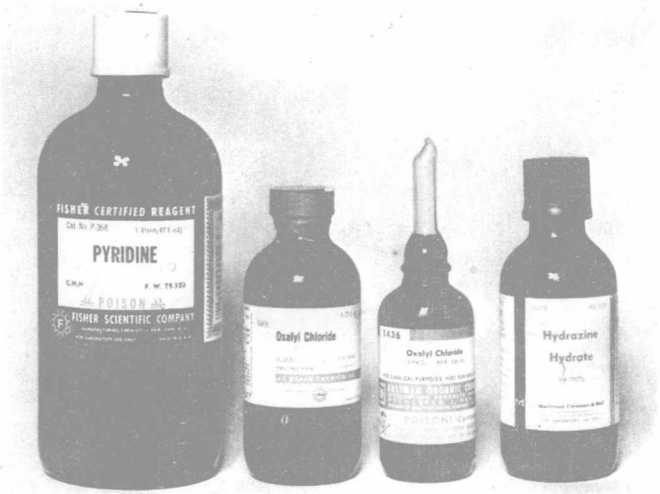


CONTENTS

Introduction

Arrangement. Suppliers mentioned in the text are listed in a section placed before the indexes and easily located by an indenture.

For enhanced usefulness the book is provided not only with a subject and an author index but also with an index of types, that is, types of reactions or types of compounds, for example: acetylation, bromination, characterization (of a, b, c, etc.), decarboxylation, or: π-acids, benzyne precursors, carbene precursors, diimide precursors. Listed alphabetically under each such entry are all the reagents which figure in the operation or group cited, whether as prime reactant, catalyst, solvent, scavenger, etc. A given reagent may fit appropriately in two or more categories. When a reagent does not fit easily into a reasonable category, we leave it unclassified rather than make a forced assignment. With no less than 92 reagents available as oxidants and 101 for use as reducing reagents, it seemed out of the question to attempt to indicate in the index of types further details about these general reactions. In a few instances a procedure cited for the preparation of one reagent provides a good example of the use of another one. For example, a preferred route to allene is by reaction of 2,3-dichloropropene with zinc dust and ethanol; in the index of types the entries under "Dechlorination" include "Zinc dust–ethanol, *see* Allene, preparation."

Names and spelling. One guideline we have followed is the rule recently adopted by *Organic Syntheses* that when an ester, ether, or peroxide contains two or more alkyl, aryl, or acyl groups the name must indicate the number of such groups:

Formula	*Correct*	*Incorrect*
$(CH_3)_2O$	Dimethyl ether	Methyl ether
$(C_2H_5O)_2SO_2$	Diethyl sulfate	Ethyl sulfate
$(C_6H_5)_2O$	Diphenyl ether	Phenyl ether
$(CO_2CH_3)_2$	Dimethyl oxalate	Methyl oxalate
$CH_2(CO_2C_2H_5)_2$	Diethyl malonate	Ethyl malonate
$(C_6H_5COO)_2$	Dibenzoyl peroxide	Benzoyl peroxide
$HC(OC_2H_5)_3$	Triethyl orthoformate	Ethyl orthoformate
$(C_2H_5O)_4C$	Tetraethyl orthocarbonate	Ethyl orthocarbonate

That the situation previously was highly confused is evident from the following entries in the index of *Org. Syn., Coll. Vol.*, 4: "Diethyl oxalate" and "Diethyl malonate" (both correct), but "Ethyl orthoformate" and "Ethyl orthocarbonate" (both incorrect). The following entry is describable as a double error: "Triethyl orthoformate, *see* Ethyl orthoformate." To locate all references to a given ester, it is thus necessary to search under two names. We urge suppliers to revise their catalogs in accordance with the rule cited. In this book we do not even list, with cross references, names which we consider to be incorrect.

Similar reform in the nomenclature of polyhalogen compounds may come some day, but for the present we consider it imprudent to do more than make a start. Thus the correct names for BF_3 and for $ClCH_2CH_2Cl$ surely are boron trifluoride and ethylene dichloride, and we feel no restraint from using them. However, although the names methylene chloride for CH_2Cl_2 and aluminum chloride for $AlCl_3$ seem

incorrect, we cannot bring ourselves to break with tradition and employ other names.

As explained in our *Style Guide for Chemists* (p. 77), we disapprove of the weak-sounding dioxăn, furăn, tryptophăn, and urethăn and add the letter *e* to these words to produce the strong pronunciations dioxāne, furāne, tryptophāne, and urethāne. For the same reason we favor desoxo- and desoxy- over deoxo- and deoxy-.

Abbreviations. Short forms of abbreviations of journal titles are as follows:

Journal of the American Chemical Society
Angewandte Chemie
Annalen der Chemie
Annales de chimie (Paris)
Chemische Berichte (formerly Berichte der deutschen chemischen Gesellschaft)
Bulletin de la société chimique de France
Chemical Communications
Acta Chemica Scandinavica
Collection of Czechoslovak Chemical Communications
Comptes rendus hebdomadaires des séances de l'académie des sciences
Gazzetta chimica italiana
Helvetica Chimica Acta
Journal of the Chemical Society (London)
Journal of Organic Chemistry
Monatshefte für Chemie
Organic Syntheses
Organic Syntheses, Collective Volume
Recueil des travaux chimique des Pays-Bas (The Netherlands)

The book by one of us, *Organic Experiments*, D. C. Heath and Co., Boston (1964), is referred to as *Org. Expts.*

Abbreviations

Ac	Acetyl	MeOH	Methanol
AcOH	Acetic acid	Ms	Mesyl, CH_3SO_2
BuOH	Butanol	NBS	N-Bromosuccinimide
Bz	Benzoyl	Ph	Phenyl
Cathyl	Carboethoxy	Phth	Phthaloyl
Cb	Carbobenzoxy	PrOH	Propanol
Diglyme	Diethylene glycol dimethyl ether	Py	Pyridine
DMF	Dimethylformamide	THF	Tetrahydrofurane
DMSO	Dimethyl sulfoxide	Triglyme	Triethylene glycol dimethyl ether
DNF	2,4-Dinitrofluoro-benzene	Trityl	$(C_6H_5)_3C-$
DNP	2,4-Dinitrophenyl-hydrazone	Ts	Tosyl, p-$CH_3C_6H_4SO_2-$
EtOH	Ethanol	TsCl	Tosyl chloride
Glyme	1,2-Dimethoxyethane	TsOH	Tosic acid, p-$CH_3C_6H_4SO_3H$

A

Acetaldehyde, CH_3CHO. Mol. wt. 44.05, b.p. 20.8°, sp. gr. 0.78. Suppliers: B, E, F, MCB.

Preparation. (a) Measure 20 ml. (20 g.) of paraldehyde into a 50-ml. round-bottomed flask, add a cooled mixture of 0.5 ml. each of concd. sulfuric acid and water, attach a fractionating column, condenser, and ice-cooled receiver, and heat gently with a microburner at such a rate that acetaldehyde distils at a temperature not higher than 35°. To avoid charring of the mixture, continue only until about half of the material has been depolymerized.

(b) *p*-Toluenesulfonic acid has been recommended as catalyst for depolymerization of paraldehyde without specification of details.[1]

[1]N. L. Drake and G. B. Cooke, *Org. Syn., Coll. Vol.*, **2**, 407 (1943)

Acetaldoxime, $CH_3CH{=}NOH$. Mol. wt. 59.07, m. p. 47°. Suppliers: A, B, KK.

The reagent reacts with a diazonium salt to form an oxime which on acid hydrolysis affords an aryl methyl ketone.[1]

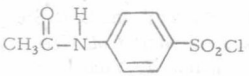
$$ArN_2Cl + CH_3CH{=}NOH \longrightarrow ArC(CH_3){=}NOH \xrightarrow{H^+} ArC(CH_3){=}O$$

[1]W. F. Beech, *J. Chem. Soc.*, 1297 (1954)

Acetamide, CH_3CONH_2. Mol. wt. 59.07, m.p. 82°. Suppliers: A, B, E, F, KK, MCB.

Acetamide is useful in the bromination of acid-sensitive compounds since it forms a stable complex with hydrogen bromide, $CH_3CONH_2 \cdot HBr$, which is insoluble in common bromination solvents.[1]

[1]K. Zeile and H. Meyer, *Ber.*, **82**, 275 (1949)

***p*-Acetamidobenzenesulfonyl chloride,** 

Mol. wt. 233.68, m.p. 149°. Suppliers: E, F, MCB.

Preparation from acetanilide and chlorosulfonic acid.[1] Use as catalyst for the Beckmann rearrangement of oximes in pyridine.[2]

[1]S. Smiles and J. Stewart, *Org. Syn., Coll. Vol.*, **1**, 8 (1941)
[2]St. Kaufmann, *Am. Soc.*, **73**, 1779 (1951); H. Heusser *et al.*, *Helv.*, **38**, 1399 (1955); G. Rosenkranz, O. Mancera, F. Sondheimer, and C. Djerassi, *J. Org.*, **21**, 520 (1956)

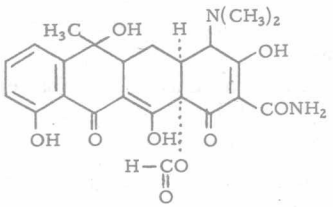
Acetic anhydride, $(CH_3CO)_2O$. Mol. wt. 102.09, b.p. 139.6°, sp. gr. 1.08.

Reagent that has stood for a time after a bottle has been opened should be tested either in a preliminary run or by shaking a sample with ice water and rapidly titrating the free acetic acid. Fractionation affords pure anhydride; material of practical grade should first be distilled from anhydrous sodium acetate to eliminate halogen compounds and metals.

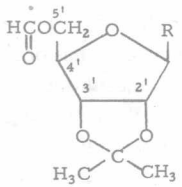
Procedures for acetylation described in *Organic Experiments*: DL-alanine (Chapt. 28); of amines in aqueous solution (Chapts. 34.3, 53.4); reductive acetylation (Chapt. 42.4); salicylic acid, order catalytic activity: $H_2SO_4 > BF_3 > Py > NaOAc$ (Chapt. 48).

Acetic–formic anhydride, $CH_3C(=O)-O-CH=O$. The reagent is prepared by cooling 2 volumes of acetic anhydride to 0°, slowly adding 1 volume of 100% formic acid, heating at 50° for 15 min., and cooling immediately to 0°.[1] It formylates alcohols, including tertiary alcohols that are dehydrated on attempted acetylation, and so is useful for the analysis of oils containing such alcohols.[1]

It has been used for the preparation in high yield of O[12a]-formyltetracycline (1)[2] and of 5′-O-formyl derivatives of nucleoside 2′,3′-acetonides (2),[3] in each case in piperidine at −20 to 0°. The O-formyl group is suggested for the protection of the



(1)



(2)

5′-hydroxyl group since it is cleaved more readily than an acetyl group; for example, it is removed by boiling methanol.

Japanese chemists[4] prepare the reagent either by the reaction of acetyl chloride with sodium formate or of formic acid with ketene. The reagent formylates amino acids in formic acid as solvent. The N-formyl group is useful as a blocking group in peptide synthesis. It is surprisingly resistant to basic hydrolysis but readily solvolyzed in dilute acid.[5]

[1]V. C. Mehlenbacher, *Org. Analysis*, **1**, 37 (1953); W. Stevens and A. Van Es, *Rec. trav.*, **83**, 1287, 1294 (1964)

[2]R. K. Blackwood, H. H. Rennhard, and C. R. Stephens, *Am. Soc.*, **82**, 5194 (1960)

[3]J. Žemlička, J. Beránek, and J. Smrt, *Coll. Czech.*, **27**, 2784 (1962)

[4]L. Muramatsu, M. Murakami, T. Yoneda, and A. Hagitani, *Bull. Chem. Soc. Japan*, **38**, 244 (1965)

[5]J. C. Sheehan and D.-D. H. Yang, *Am. Soc.*, **80**, 1154 (1958)

Acetoacetyl fluoride, CH_3COCH_2COF. Mol. wt. 104.08, b.p. 132–134°.

Prepared[1] by reaction of diketene with anhydrous hydrogen fluoride, the reagent can be stored for weeks at 0°, but at room temperature it slowly decomposes to form

$$CH_2{=}C(-O-C{=}O)-CH_2 \xrightarrow[60\%]{HF} CH_3COCH_2COF$$

dehydroacetic acid. It is unsatisfactory for Friedel-Crafts acylation, but serves as an acetoacetylating agent for alcohols and amines:

$$CH_3COCH_2COF \xrightarrow[68\text{-}86\%]{ROH} CH_3CCH_2COR + HF$$

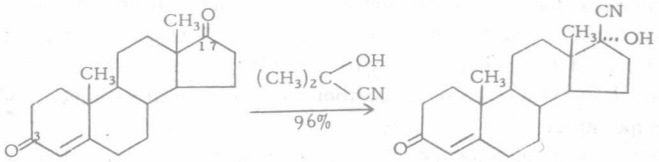
$$CH_3COCH_2COF \xrightarrow[56\text{-}87\%]{2\ RNH_2} CH_3CCH_2C(=O)NR + RNH_3F$$

[1]G. A. Olah and S. J. Kuhn, *J. Org.*, **26**, 225 (1961)

Acetone cyanohydrin, $(CH_3)_2C(OH)CN$. Mol. wt. 85.10, b.p. 80°/15 mm. Suppliers: Rohm and Haas, Union Carbide, A, B, MCB.

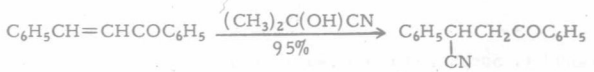
Preparation. (a) By addition of 40% sulfuric acid to an aqueous solution of acetone and sodium cyanide at 10–20°.[1] (b) Reaction of potassium cyanide with the sodium bisulfite addition compound of acetone gives material which is less pure but satisfactory for immediate use.[2]

Use for ***transcyanohydrination***: preparation in high yield of the 17-monocyanohydrin of a 3,17-diketo-Δ^4-steroid by hydrogen cyanide exchange with the reagent.[3]

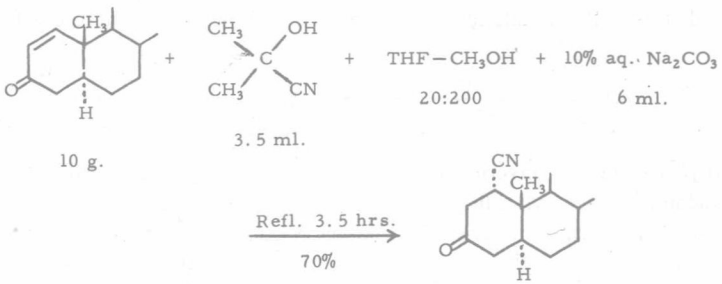


Δ^4-Androstene-3,17-dione

Use for the ***addition of hydrogen cyanide*** to benzalacetophenone and other α,β-unsaturated ketones; 5–10% aqueous sodium carbonate is the most satisfactory



catalyst.[4] The addition of hydrogen cyanide to conjugated steroid ketones usually gives mixtures and poor yields, but Julia *et al.*[5] achieved smooth addition to Δ^1-5α-cholestene-3-one as follows. A solution of the ketone and acetone cyanohydrin in tetrahydrofurane–methanol was treated with a little aqueous sodium carbonate



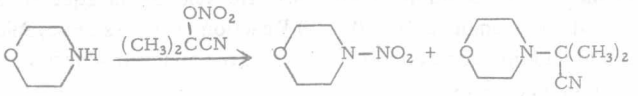
and refluxed for 3.5 hrs. After evaporation in vacuum, chromatography separated 1.2 g. of starting material and afforded 1α-cyano-5α-cholestane-3-one in good yield.

[1]R. F. B. Cox and R. T. Stormont, *Org. Syn., Coll. Vol.*, **2**, 7 (1943)
[2]E. C. Wagner and M. Baizer, *ibid.*, **3**, 324 (1955)
[3]A. Ercoli and P. de Ruggieri, *Am. Soc.*, **75**, 650 (1953)
[4]B. E. Betts and W. Davey, *J. Chem. Soc.*, 4193 (1958)
[5]S. Julia, H. Linarès, and P. Simon, *Bull. soc.*, 2471 (1963)

$$\begin{matrix} & ONO_2 & \\ & | & \\ (CH_3)_2CCN & & \end{matrix}$$

Acetone cyanohydrin nitrate, $(CH_3)_2CCN$. Mol. wt. 130.11, b.p. 65–66°/10 mm. Supplier: Aldrich. Preparation by nitration of acetone cyanohydrin with fuming nitric acid and acetic anhydride.[1] *Caution*: moderately explosive.

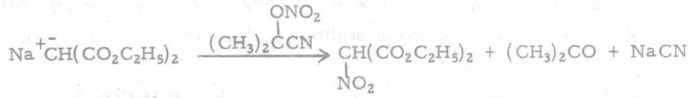
Acetone cyanohydrin nitrate is useful for conversion of primary and secondary amines into nitramines.[2] The reaction is unique in that nitration is carried out under



(1) (2)

neutral or alkaline conditions. Thus N-nitromorpholine (1, m.p. 54°) is obtained in 57–64% yield by reaction of morpholine with 2 equivalents of the reagent;[1] hydrochloric acid is added to the reaction mixture to dissolve excess morpholine and the by-product (2), and (1) is extracted with methylene chloride. In nitrating other amines, particularly on a large scale, acetonitrile can be used as solvent for better control of temperature.

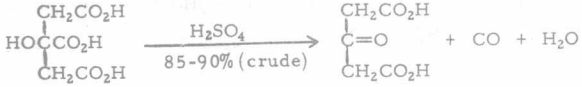
The reagent is useful also for the nitration of active-methylene compounds in the form of the sodio derivatives; this is the basis for a general synthesis of α-nitro esters.[3]



[1]J. P. Freeman and I. G. Shepard, *Org. Syn.*, **43**, 83 (1963)
[2]W. D. Emmons and J. P. Freeman, *Am. Soc.*, 77, 4387 (1955)
[3]*Idem, ibid.*, **77**, 4391 (1955)

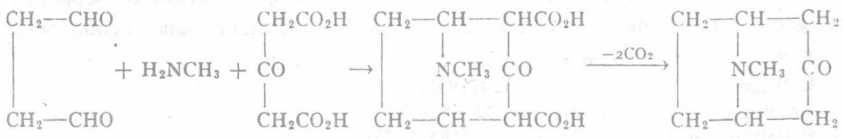
Acetonedicarboxylic acid, $HO_2CCH_2COCH_2CO_2H$. Mol. wt. 146.10, m.p. 138° dec. Suppliers: Baker, Eastern, Pfizer.

The diacid can be obtained in high yield by the action of fuming sulfuric acid on citric acid at 0–30°,[1] but material so prepared is not stable and should be crystallized



from ethyl acetate or converted into the diethyl ester by Fischer esterification.[2] Diethyl acetonedicarboxylate (b.p. 145–148°/17 mm.) is supplied by Aldrich.

Robinson's classical synthesis of tropinone was achieved by condensation of succindialdehyde and methylamine with acetonedicarboxylic acid.[3] Schöpf[4] later carried out the reaction in a solution buffered to pH 5 and at room temperature and



Tropinone

under these simulated physiological conditions the intermediate diacid loses carbon dioxide spontaneously and tropinone was obtained in yield as high as 90%. *See also* Glutaraldehyde.

[1]R. Adams, H. M. Chiles, and C. F. Rassweiler, *Org. Syn.*; *Coll. Vol.*, **1**, 10 (1941)
[2]R. Adams and H. M. Chiles, *ibid.*, **1**, 237 (1941)

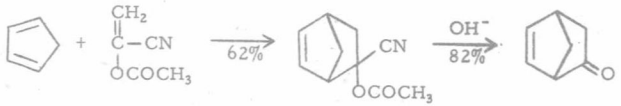
[3]R. Robinson, *J. Chem. Soc.*, **111**, 762 (1917)
[4]C. Schöpf and G. Lehmann, *Ann.*, **518**, 1 (1935)

Acetone dimethyl ketal, *see* 2,2-Dimethoxypropane.

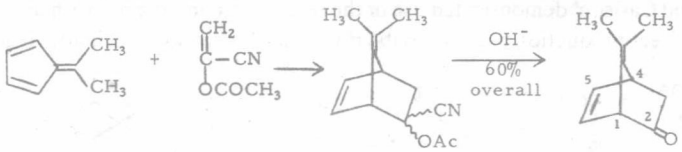
α-Acetoxyacrylonitrile, $CH_2{=}C(OCOCH_3){-}CN$. Mol. wt. 111.10., b.p. 173°/772 mm. Preparation by addition of hydrogen cyanide to ketene; best yields are obtained with a mildly basic catalyst such as potassium acetate.[1]

$$CH_2{=}C{=}O \xrightarrow{HCN} CH_2{=}C(OH){-}CN \xrightarrow{CH_2{=}C{=}O} CH_2{=}C(OCOCH_3){-}CN$$

The reagent is useful as a dienophile because the product on hydrolysis affords a ketone, as in the synthesis of dehydronorcamphor:[2]



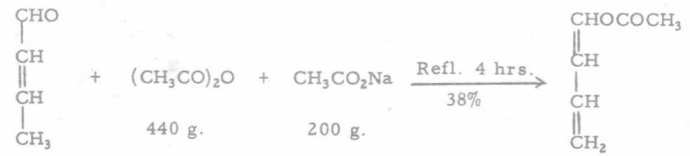
A further example is in the synthesis of 7-isopropylidenebicyclo[2.2.1]-5-heptene-2-one:[3]



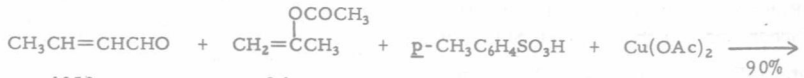
[1]S. Deakin and N. T. M. Wilsmore, *J. Chem. Soc.*, **97**, 1971 (1910); F. Johnston and L. W. Newton, U. S. patent 2,395,930 (1946) [*C.A.*, **40**, 4078 (1946)]; H. J. Hagemeyer, Jr., *Ind. Eng. Chem.*, **41**, 765 (1949)
[2]P. D. Bartlett and B. E. Tate, *Am. Soc.*, **78**, 2473 (1956)
[3]C. H. De Puy and P. R. Story, *Am. Soc.*, **82**, 627 (1960)

1-Acetoxybutadiene, Mol. wt. 112.16, b.p. 42–43°/16 mm., 51–52°/30 mm.

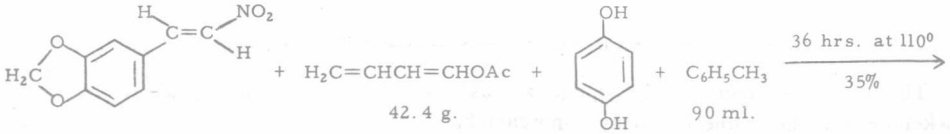
Preparation. This diene, the enol acetate of crotonaldehyde, can be prepared

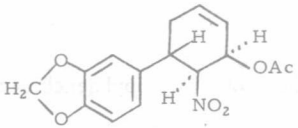


by refluxing the aldehyde with acetic anhydride and sodium acetate.[1] Workup includes removal of considerable crotonaldehyde (powerful lachrymator) with bisulfite; this fact together with the low yield[2] suggests that the reaction reaches equilibrium. A much better method described by Hagemeyer and Hull[3] consists in reaction of crotonaldehyde with isopropenyl acetate, a catalytic amount of *p*-toluenesulfonic acid, and a little copper acetate (function not stated). The aldehyde is added to the other components in 2–3 hrs. with provision for continuous removal of acetone to displace the equilibrium. The yield of twice-distilled 1-acetoxybutadiene is 90%.

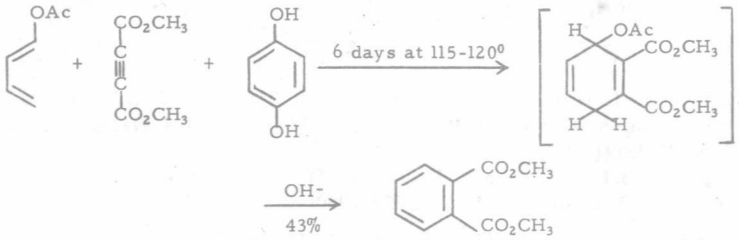


Diels-Alder reactions. Hill *et al.*[4] used the reagent in one step of a synthesis of the parent structure of lycorine.

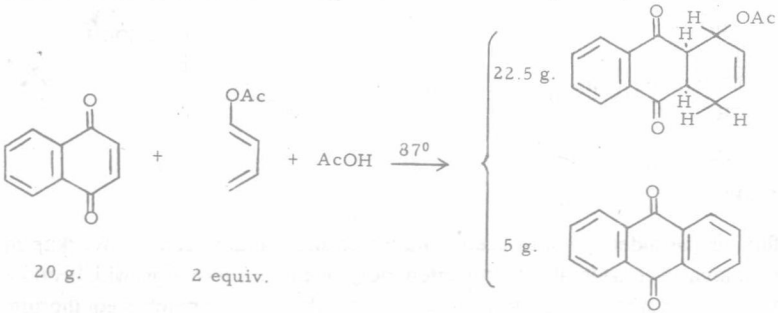




Hill and Carlson[5] demonstrated use of the reagent in combination with an acetylene for the direct production of an aromatic ring. The reagent adds normally to quinones,

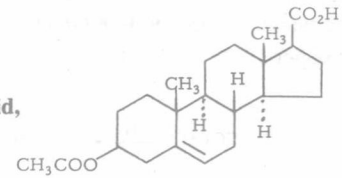


but in acetic acid at steam bath temperature the adduct is partially aromatized.[6]



[1]O. Wichterle and M. Hudlicky, *Coll. Czech.*, **12**, 564 (1947)
[2]P. Y. Blanc, *Helv.*, **44**, 1 (1961), used essentially the same procedure and reports a yield of 35%.
[3]H. J. Hagemeyer, Jr., and D. C. Hull, *Ind. Eng. Chem.*, **41**, 2920 (1949)
[4]R. K. Hill, J. A. Joule, and L. J. Loeffler, *Am. Soc.*, **84**, 4951 (1962)
[5]R. K. Hill and R. M. Carlson, *J. Org.*, **30**, 2414 (1965)
[6]W. Flaig, *Ann.*, **568**, 1 (1950)

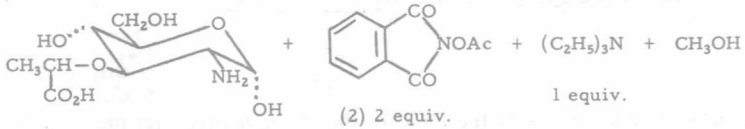
3β-Acetoxy-Δ⁵-etienic acid,



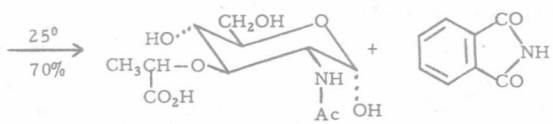
Mol. wt. 360.48, m.p. 238°. Preparation by hypobromite oxidation of pregnenolone acetate (available from Syntex S. A.).[1] The corresponding acid chloride has been used for the resolution of 1α-hydroxydicyclopentadiene,[2] of *cis,cis*-l-decalol,[3] and of *trans*-3-*t*-butylcyclohexanol[4] (in this case conventional resolution of acid phthalate salts with alkaloids failed).

[1]J. Staunton and E. J. Eisenbraun, *Org. Syn.*, **42**, 4 (1962)
[2]R. B. Woodward and T. J. Katz, *Tetrahedron*, **5**, 70 (1959)
[3]C. Djerassi and J. Staunton, *Am. Soc.*, **83**, 736 (1961)
[4]C. Djerassi, E. J. Warawa, R. E. Wolff, and E. J. Eisenbraun, *J. Org.*, **25**, 917 (1960)

N-Acetoxyphthalimide (2). The reagent is prepared by reaction of sodium N-hydroxyphthalimide (*which see*) with acetyl chloride.[1] It is recommended specifically[1,2] for N-acetylation of muramic acid (1), since acetylation with acetic anhydride and pyridine gives products of intramolecular cyclization (lactams). Osawa and Jeanloz[2] treated a solution of (1) in methanol at 0° with 2 equivalents of the reagent and 1 equivalent of triethylamine and let the mixture stand at room temperature for 20 hrs.



(1) 358 mg. (1 equiv.) (2) 2 equiv. 1 equiv.



(3)

After evaporation, the residue was extracted with water and the filtered solution adjusted to pH 3.5 with Amberlite IR 120 and extracted with ethyl acetate. The residual sirup crystallized spontaneously, and recrystallization from ethyl acetate–methanol afforded pure (3) in 70% yield. When the reaction was carried out with only 1 equivalent of N-acetoxyphthalimide,[1] the product was a mixture of (1) and (3).

[1]P. M. Carroll, *Nature*, **197**, 694 (1963)
[2]T. Osawa and R. W. Jeanloz, *J. Org.*, **30**, 448 (1965)

2- and 3-Acetoxypyridine, $C_5H_4NOCOCH_3$.[1] Mol. wt. 137.14.

Preparation. The 2-isomer (b.p. 110–112°/10 mm.) by the action of acetyl chloride on the sodium salt of 2-hydroxypyridine; the 3-isomer (b.p. 92°/9 mm.) from 3-hydroxypyridine and acetic anhydride.

Acetylation. The reagents can be used for the acetylation of alcohols, phenols, and amines and for Friedel-Crafts acetylation of reactive aromatics. In general 2-acetoxypyridine is more reactive than the 3-isomer.

[1]Y. Ueno, T. Takaya, and E. Imoto, *Bull. Chem. Soc. Japan*, **37**, 864 (1964)