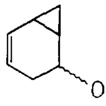
anol–benzene (90:10) at 40° define rather broadly at this time the limits of reactivity under relatively mild conditions. Putting this another way, in the reactions of ethers promoted by Ag^+, successful rearrangement due to methoxyl group ionization could conceivably occur if the resulting carbonium ion is at least 10^4 times more kinetically accessible than the cyclohexyl cation.[16] Since many molecular types do fall into this category, the implications are potentially far-reaching. These implications are currently under active study.[17] It should be emphasized, however, that our data now serve as a caveat regarding the validity of mechanistic interpretations based on the nature of ether products derived from silver ion promoted reaction of strained-ring hydrocarbons in the presence of alcohol trapping agents.[2b] The structure of such ether products need not reflect that of a true carbonium ion intermediate, if one exists, since they may result from secondary transition metal catalyzed reaction of ephemeral trapping product(s) *via* carbon–oxygen bond heterolysis.

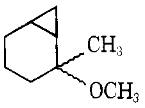
Acknowledgment. The financial support of the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the National Cancer Institute is gratefully acknowledged.

[16] S. Winstein, M. Shatavsky, C. Norton, and R. B. Woodward, *J. Amer. Chem. Soc.*, 77, 4183 (1955).

[17] As examples of the generality of such reactions we cite the Ag^+-catalyzed conversion of i to cycloheptatriene[6] and of ii to 2-methyl-2-norcarene (S. E. Wilson, unpublished).



i



ii

Leo A. Paquette,* Gerald Zon
Department of Chemistry, The Ohio State University
Columbus, Ohio 43210

Received March 13, 1972

N,N,N′,N′-Tetramethylphosphorodiamidate Group. A Useful Function for the Protection or Reductive Deoxygenation of Alcohols and Ketones[1]

Sir:

We recently reported[2] that the lithium–amine reduction of enol diethyl phosphates prepared by phosphorylation of enolate anions was an efficient method for the regiospecific formation of olefins. Further investigation of the scope of this reduction reveals that the diethyl phosphates (DEP) and *N,N,N′,N′*-tetramethylphosphorodiamidates (TMPDA) of alcohols, as well as ketone enolates, are also readily reduced in high yield by lithium–ethylamine solution. In addition to making possible the direct cleavage of the hydroxyl function the two-step process for the reductive removal of a ketone, *i.e.*, $RCOR' \rightarrow RCHOHR' \rightarrow RCH_2R'$, has certain advantages over the Wolff–Kishner reduction in some cases. Also, the TMPDA grouping appears to be a useful blocking group for the hydroxyl function, as it is stable to a variety of reaction conditions, and yet the original alcohol may be regenerated in near quantitative yield under relatively mild conditions.

The DEP and TMPDA derivatives are readily prepared by phosphorylation of the corresponding enolate or alcoholate anions. The former may be generated from α,β-unsaturated ketones by lithium–ammonia reduction[3] or conjugate organometallic addition or from saturated ketones by enolization with lithium–diisopropylamide. The latter are simply prepared from an alcohol by treatment with a slight molar excess of *n*-butyllithium. For the phosphorylation of these anions we have used 1 equiv of diethylphosphorochloridate or a fivefold excess of the less reactive *N,N,N′,N′*-tetramethyldiamidophosphorochloridate[4] and found that the best solvent system for the reaction is 4:1 dimethoxyethane–(or tetrahydrofuran–) *N,N,N′,N′*-tetramethylethylenediamine. In general, the reaction is complete after stirring for 1–2 hr at 25°, and chromatography and/or crystallization of the product after work-up afforded the desired ester. The yields of these phosphorylations are uniformly high, and the choice of which ester is formed depends on the proposed subsequent use.

While either derivative is satisfactory for the reductive formation of olefins from the enol system, the TMPDA grouping is more necessary for the deoxygenation of primary and secondary alcohols. More by virtue of its greater ease of formation than a significant difference in the reduction stage, the DEP grouping appears better for the reductive removal of tertiary alcohols.

The reductive cleavage of either the DEP or TMPDA groups may be accomplished by the addition of a solution of the derivative and 2–4 equiv of *tert*-butyl alcohol in tetrahydrofuran to an ice-cooled, argon-protected solution of 10 equiv of lithium in dry ethylamine. After stirring for 20–30 min, the reaction mixture is quenched with water, and the product isolated by ether extraction. Chromatography and/or crystallization of the crude product affords the reduced material in high yield. The reduction is very fast and in the absence of a proton source the TMPDA group is reduced without concomitant reduction of an anisole ring. When the immediate objective is the removal of an oxygen function, this reduction procedure may be performed on unpurified phosphorus ester without any adverse effect on the yield.

The following examples[5] (Chart I) serve to document these generalizations and provide a basis for evaluation of the scope of the process.

The utility of this sequence for the reductive removal of a ketone function is illustrated by the cases in Chart II. In neither case was it necessary (or advantageous) to purify material at the intermediate stages, although in each instance this was done initially. In both instances the indicated transformations were not as satisfactorily accomplished by other means due to the acid–base

---

[1] The support of this research by the National Science Foundation is gratefully acknowledged.

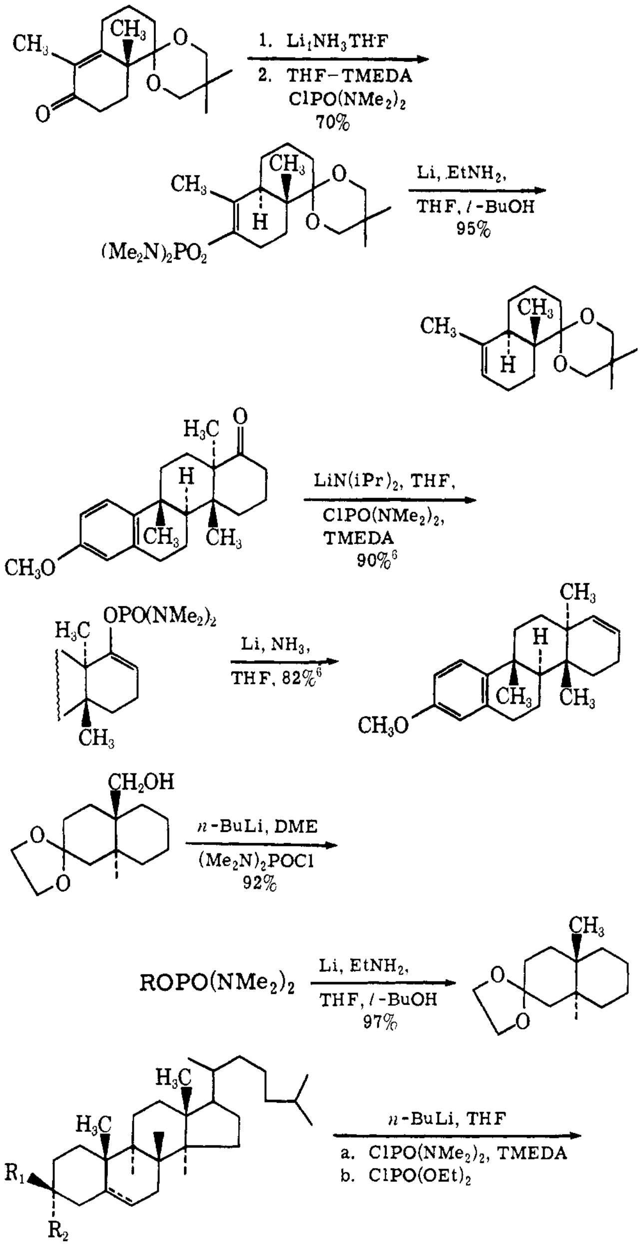
[2] R. E. Ireland and G. Pfister, *Tetrahedron Lett.*, 2145 (1969); see also, M. Fetizon, M. Jurion, and N. T. Anh, *Chem. Commun.*, 112 (1969).

[3] G. Stork, P. Rosen, N. Goldman, R. V. Coombs, and J. Tsuji, *J. Amer. Chem. Soc.*, 87, 275 (1965).

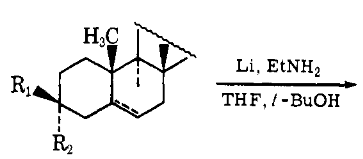
[4] E. Crunden and F. Hudson, *J. Chem. Soc.*, 3591 (1962); H. G. Cook, J. D. Ilett, B. C. Saunders, G. J. Stacey, H. G. Watson, I. G. Wilding, and S. J. Woodcock, *ibid.*, 2921 (1949).

[5] All new compounds were characterized by ir and nmr spectroscopy and behavior on glpc and tlc, and had satisfactory (±0.2%) combustion analyses.

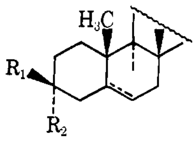
Chart I



R_1 = OH; R_2 = H; 5αH
R_1 = OH; R_2 = H; Δ^5
R_1 = CH_3; R_2 = OH; 5αH



R_1 = $OPO(NMe_2)_2$; R_2 = H; 5αH (91%)
R_1 = $OPO(NMe_2)_2$; R_2 = H; Δ^5 (not purif)
R_1 = CH_3; R_2 = $OPO(OEt)_2$; 5αH (82%)



R_1 = R_2 = H; 5αH (99%)
R_1 = R_2 = H; Δ^5 (96%)
R_1 = CH_3; R_2 = H; 5αH (91%)

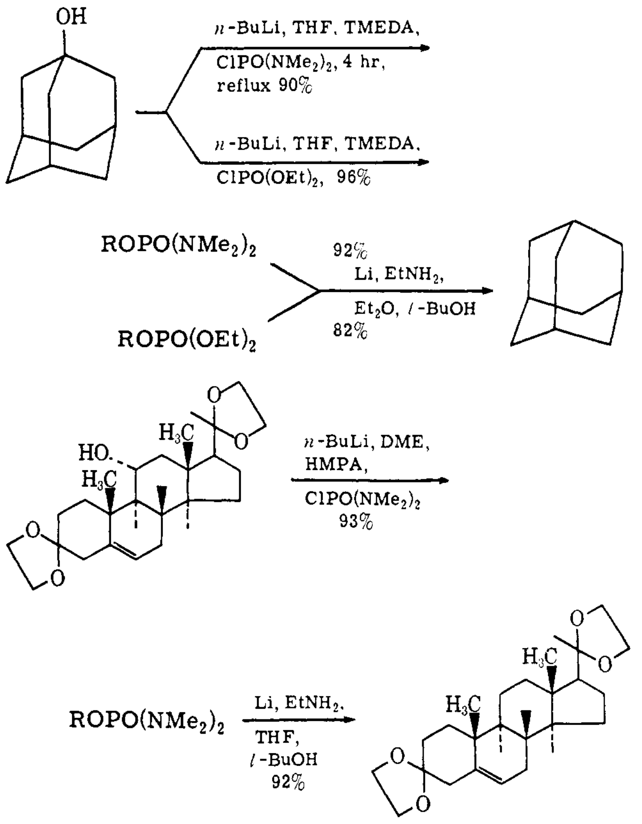
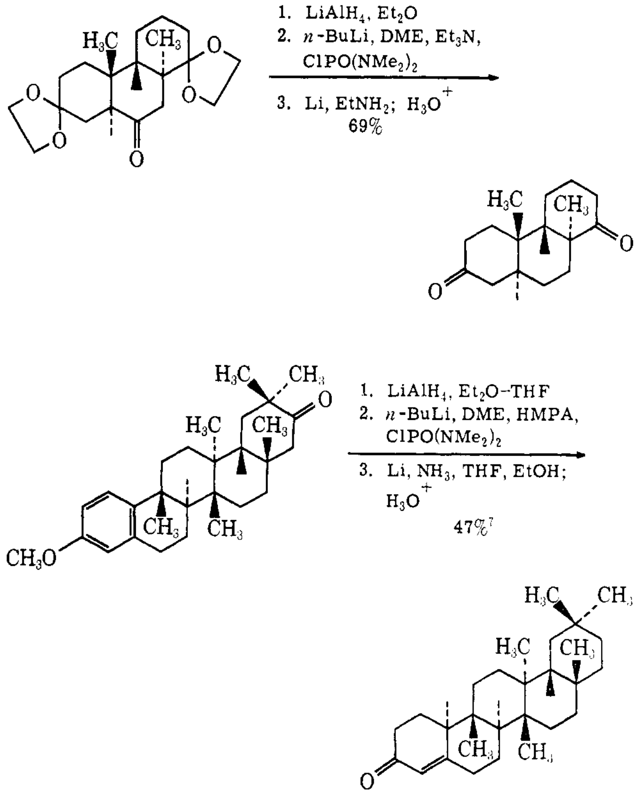


Chart II



lability of the first substrate[8] and the steric congestion[8,9] about the carbonyls in both molecules.

---

[6] Experiment performed by J. W. Tilley, Ph.D. Thesis, California Institute of Technology, 1972.

[7] Experiment performed by A. Hagenbach, unpublished results in these laboratories.

Our stability studies were conducted on 3β-cholestanyl TMPDA, and less than 5% reaction was observed when this material was treated with CH_3Li–Et_2O (2.5 hr at 25°), $LiAlH_4$–Et_2O (2.5 hr at 25°), 1 *N* KOH–EtOH (15 hr at reflux), and 0.2 *N* aqueous HCl–acetone (2 hr at 25°). Prolonged treatment (12 hr at 25°) with 0.2 *N* aqueous HCl–acetone resulted in recovery of only 59% of the original TMPDA, but *no* 3β-cholestanol was found. Regeneration of progesteron-11α-yl TMPDA from the corresponding diketal was accomplished in 91% yield by treatment of the diketal TMPDA with 0.2 *N* aqueous HCl–acetone for 2 hr at 25°. The regeneration of 3β-cholestanol from its TMPDA was accomplished in *quantitative yield* after treatment with 5 equiv of *n*-butyllithium in TMEDA for 30 min at 25°.

The mechanism and stereochemical outcome of the reduction of saturated DEP and TMPDA derivatives are presently under investigation.

---

[8] R. E. Ireland and U. Hengartner, *J. Amer. Chem. Soc.*, **94**, 3652 (1972).

[9] R. E. Ireland and S. C. Welch, *ibid.*, **92**, 7232 (1970).

[10] National Defense Education Act Trainee, 1967–1971.

[11] Fellow of Stiftung für Stipendien auf dem Gebiete der Chemie, Switzerland.

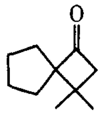
Robert E. Ireland,* David C. Muchmore,[10] Urs Hengartner[11]
Contribution No. 4462, Gates and Crellin Laboratories of Chemistry
California Institute of Technology, Pasadena, California 91109

Received May 18, 1972

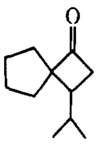
Two Novel Routes to Spiro[3.4]octan-1-ones

Sir:

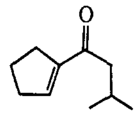
In this communication we outline briefly two independent syntheses of spiro[3.4]octan-1-ones **1** and **2**, representatives of a class of compounds with few previously known members.



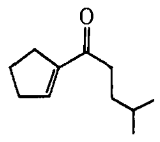
1



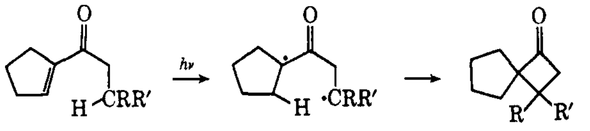
2



3



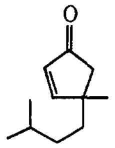
4



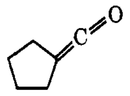
(1)

5

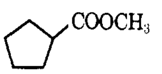
The first approach to these spiro ketones is a photochemical one and consists simply in photolysis of the related 1-acylcyclopentenes. The resulting reaction is quite clean, and although yields are modest, the only significant volatile products are those noted below. Starting materials are readily prepared through Friedel–Crafts reaction of cyclopentene with the appropriate acyl chloride.[1] Thus, irradiation[2] of 1-cyclopentenyl isobutyl ketone (**3**)[3] for 125 min caused complete destruction of starting material and formation of **1** in 35%[5] yield. Similarly, **4**[3] gave 36%[5] of **2**.[3] This photoisomerization is most easily explained as involving abstraction of a hydrogen atom by the β carbon atom of the enone system from the β′ carbon atom through a six-membered intermediate. As shown in eq 1, this process leads to a 1,4 biradical **5**, which may then collapse to the observed spiro ketone. A related intramolecular hydrogen abstraction by the β carbon atom of an α,β unsaturated ketone is responsible for the photochemical rearrangements of 4-isopentyl-4-methylcyclopentenone (**6**).[4] The suggestion that biradical **5** is an intermediate in the formation of **1** and **2** is supported by detection of ketene **7** as a concomitant product in photolysis of **3**. Infrared monitoring during this reaction revealed development of a sharp band at 2100 cm^{-1}; addition of methanol to the benzene solution after irradiation resulted in replacement of this band by new absorption at 1735 cm^{-1}, and subsequent isolation gave methyl cyclopentanecarboxylate (**8**, 25%[5]), which was identical with an authentic sample.[6,7] Formation of **7**, and presumably isobutylene, could occur most readily through simple fragmentation of biradical **5**. In connection with the mechanism (eq 1) it is noteworthy that the change of the β′ carbon atom from tertiary to secondary in passing from **3** to **4** does not reduce the yield of spiro ketone but does suppress formation of ketene **7**.[8]



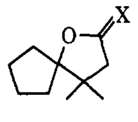
6



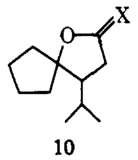
7



8



9



10

a, X = O
b, X = $(OC_2H_5)_2$
c, X = NNHTs
d, X = :

---

[1] N. Jones and H. T. Taylor, *J. Chem. Soc.*, 4017 (1959), and references cited therein.

[2] Irradiations were carried out at concentrations of about 1 mg/ml in benzene solution using a Hanovia Model L mercury lamp (No. 679A-36) in a quartz immersion well and a Corning No. 3320 uranium glass filter.

[3] This new compound gave satisfactory elemental analysis for carbon and hydrogen after purification by preparative vapor phase chromatography (vpc) over Carbowax under conditions similar to those described in ref 4.

[4] W. L. Schreiber and W. C. Agosta, *J. Amer. Chem. Soc.*, **93**, 3814 (1971); S. Wolff, W. L. Schreiber, A. B. Smith, III, and W. C. Agosta, *ibid.*, in press.

[5] Yields were obtained by calibrated vpc measurements.

[6] D. W. Goheen and W. R. Vaughan, "Organic Syntheses," Collect. Vol. IV, Wiley, New York, N. Y., 1963, p 594.

[7] For preparative purposes ketene **7** can be removed by washing the benzene solution with aqueous sodium bicarbonate after irradiation, leaving **1** as the only volatile product.

[8] Apparently even abstraction of methyl hydrogen is feasible in this series, since photolysis of 1-cyclopentenyl ethyl ketone gives a low but useful yield (8%) of the parent spiro[3.4]octan-1-one as the sole volatile product. This compound was identified by comparison of its ir and nmr spectra with those of authentic material [H. H. Wasserman and D. C. Clagett, *J. Amer. Chem. Soc.*, **88**, 5368 (1966)]. We are grateful to Professor Harry H. Wasserman for supplying these data.