Supplementary Material Available: Synthetic procedures and data for **20**, **22**, and **23** and ^{1}H NMR spectra for **22** and **23** (4 pages). Ordering information is given on any current masthead page.

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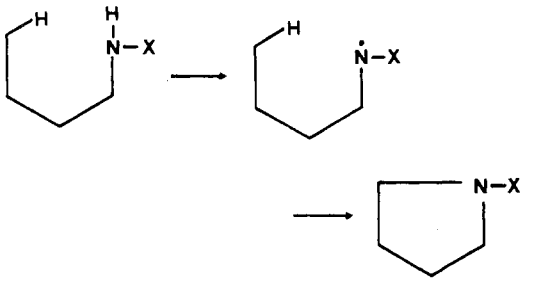
Intramolecular Functionalization of Phosphoramidate Radicals. Synthesis of 1,4-Epimine Compounds

Summary: Photolysis of the diethyl, diphenyl, and dibenzyl phosphoramidates **1a-c**, **3**, and **5a** in the presence of lead tetraacetate and iodine results in the formation of the corresponding *N*-dioxyphosphinyl 1,4-epimine compounds **2a-c**, **4**, and **6**, respectively, in excellent yields, thus providing an effective synthetic method for pyrrolidines.

Sir: Intramolecular hydrogen abstraction from hetero radicals which leads to the remote functionalization of nonactivated carbon centers is an important target for organic chemists.[1-3] Although the reactions initiated by oxy radicals have been the subject of numerous studies,[2] those associated with nitrogen radicals have received comparatively little attention.[3] The sole reaction[4] of this type which has proved of significant value for the preparation of cyclic amines is the thermal or photochemical fragmentation of *N*-halo amines (Hofmann-Löffler-Freytag reaction). In spite of the fact that this reaction represents the earliest example of intramolecular functionalization of a nonactivated carbon, only limited use has been made of it in complex or sensitive molecules owing to the highly acidic conditions required.[8] Furthermore, secondary cyclic amines are only obtained in poor yields when the Hofmann-Löffler-Freytag reaction was applied to primary amines.

Recently we reported[9] the intramolecular functionalization of the C-18 and C-19 steroidal methyl groups by neutral aminyl radicals of the R-N̈-NO_2 (R = steroidal nucleous) type, generated in situ by photolysis of *N*-iodo nitroamines. This procedure provides a convenient synthesis of *N*-nitro 1,4-epimine compounds under mild conditions, and it is an advantageous alternative method to the Hofmann-Löffler-Freytag reaction which overcomes the problem associated with the strong acidic media required in the latter.

Continuing our investigations in this field, we now report the synthesis of epimine compounds by remote functionalization initiated by phosphoramidate radicals which were generated by photolysis of the corresponding *N*-iodo derivatives (eq 1). In all the reported cases, the epimine



(1)

X = $P(O)(OEt)_2$, $P(O)(OPh)_2$, $P(O)(OCH_2Ph)_2$

compounds were obtained with excellent yields. When the free secondary cyclic amines are desired, the dioxyphosphinyl moiety could be easily removed, especially when compared with the nitro group, initially used as the nitrogen radical stabilizing group.

Diethyl *N*-(3β-acetoxy-5α-cholestan-6β-yl)phosphoramidate (**1a**) was prepared by reaction of 6β-amino-5α-cholestan-3β-ol[10] (1 mmol) with diethyl phosphorochloridate (1.1 mmol) in dry chloroform (1 mL) in the presence of triethylamine (2 mmol) and subsequent acetylation. Intramolecular cyclization of the diethyl phosphoramidate **1a** (1 mmol) was accomplished by reaction with lead tetraacetate (10 mmol) and iodine[11] (5 mmol) in cyclohexane (75 mL) under reflux and irradiation with two 100-W tungsten-filament lamps for 2 h, yielding quantitatively diethyl *N*-(3β-acetoxy-5α-cholestan-6β,19-epimino)phosphonate (**2a**). All spectroscopic data[12] (IR, ^{1}H NMR, and MS) are consistent with the structure proposed for the product; thus, high-resolution mass spectroscopy indicates a molecular formula of $C_{33}H_{58}NO_5P$, and in its ^{1}H NMR spectrum the two protons at C-19 appear as a broad singlet at δ 3.08.

The triterpene 3β-phosphoramidate derivative **3**[13] also reacted smoothly, under similar conditions, to give the 3β,24-epimine compound **4** in 90% yield.[14]

We next turned our attention to the functionalization of the C-18 methyl group in the steroidal 20(*S*)-

(1) Heusler, K.; Kalvoda, J. In "Organic Reactions in Steroid Chemistry"; Fried, J., Edwards, J. A., Eds.; Van Nostrand-Reinhold: New York, 1971; Vol. 2, pp 237-287. Kirk, D. N.; Hartshorn, M. P. In "Steroid Reaction Mechanisms"; Elsevier: Amsterdam, 1968; pp 394-411.

(2) Kalvoda, J.; Heusler, K. *Synthesis* **1971**, 501. Heusler, K.; Kalvoda, J. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 525.

(3) Neale, R. S. *Synthesis* **1971**, 1. Schönberg, A. In "Preparative Organic Photochemistry"; Springer-Verlag: West Berlin, 1968; pp 242-247. Wolff, M. E. *Chem. Rev.* **1963**, *63*, 55.

(4) Hydrogen abstraction by nitrogen radicals has also been postulated by Barton et al[5] during the photolysis of *N*-iodo amides, although only lactones have been isolated from this reaction. The formation of epimine compounds by photolysis of steroidal azides has been the object of controversy,[6] but at least in one case[7] 6β,19-epimino-5α-pregnane has been obtained in low yield (6%) from 6β-azido-5α-pregnane.

(5) Barton, D. H. R.; Beckwith, A. L. J.; Goosen, A. *J. Chem. Soc.* **1965**, 181.

(6) Barton, D. H. R.; Morgan, L. R. *J. Chem. Soc.* **1962**, 624. Wasserman, E.; Smolinsky, G.; Yager, W. A. *J. Am. Chem. Soc.* **1964**, *86*, 3166. Saunders, W. H.; Caress, E. A. *Ibid.* **1964**, *86*, 861. Moriarty, R. M.; Rahman, M. *Tetrahedron* **1965**, *21*, 2877. Barton, D. H. R.; Starratt, A. N. *J. Chem. Soc.* **1965**, 2444.

(7) Pancrazi, A.; Khuong-Huu, Q.; Goutarel, R. *Tetrahedron Lett.* **1972**, 5015. Farid, A. M.; McKenna, J.; McKenna, J. M.; Wall, E. N. *J. Chem. Soc., Chem. Commun.* **1969**, 1222.

(8) Neale, R. S.; Walsh, M. R.; Marcus, N. L. *J. Org. Chem.* **1965**, *30*, 3683.

(9) Hernández, R.; Rivera, A.; Salazar, J. A.; Suárez, E. *J. Chem. Soc., Chem. Commun.* **1980**, 958.

(10) Shoppee, C. W.; Evans, D. E.; Summers, G. H. R. *J. Chem. Soc.* **1957**, 97.

(11) Lead tetraacetate and iodine were added in portions every 15 min along the reaction.

(12) Compound **2a**: amorphous; IR ($CHCl_3$) ν_{max} 1720, 1230 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.71 (3 H, s, C-18 H), 3.08 (2 H, br s, C-19 H), 3.57 (1 H, m, $W_{1/2}$ = 10 Hz, C-6α H); MS, *m/e* (assignment, relative intensity) 579.4016 (M^+, $C_{33}H_{58}NO_5P$, 10), 316.1309 ($C_{14}H_{23}NO_5P$, 100).

(13) Betancor, C.; Freire, R.; González, A. G.; Salazar, J. A.; Pascard, C.; Prange, C. *Phytochemistry* **1980**, *19*, 1989.

(14) Compound **4**: mp 154-156 °C (*n*-pentane); $[\alpha]_D$ +18° ($CHCl_3$); IR ($CHCl_3$) ν_{max} 1730, 1230 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.45 (1 H, m, $W_{1/2}$ = 11 Hz, C-3α H), 2.76, 3.56 (2 H, AB, *J* = 11 Hz, C-24 H); MS, *m/e* (relative intensity) 619 (M^+, 100).

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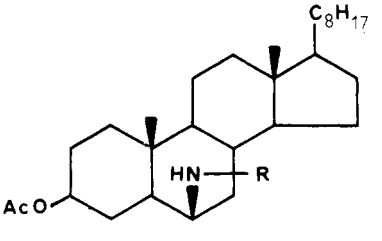
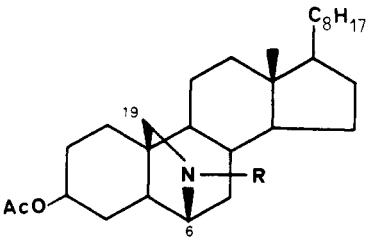
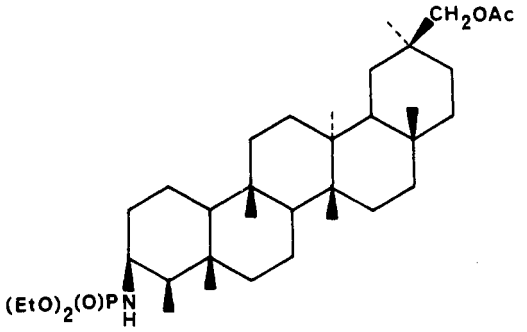
Chart I



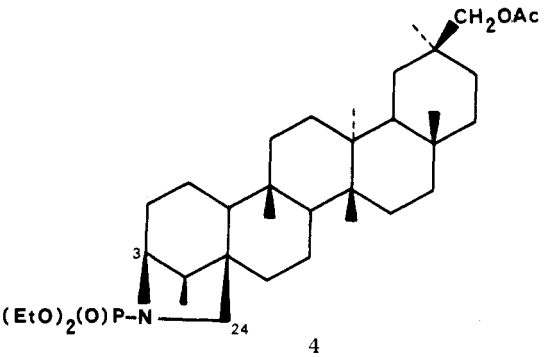
1a, R = $P(O)(OEt)_2$
b, R = $P(O)(OPh)_2$
c, R = $P(O)(OCH_2Ph)_2$



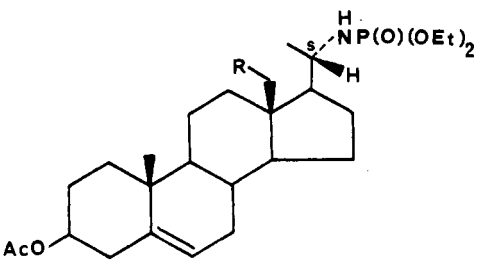
2a, R = $P(O)(OEt)_2$
b, R = $P(O)(OPh)_2$
c, R = $P(O)(OCH_2Ph)_2$
d, R = H



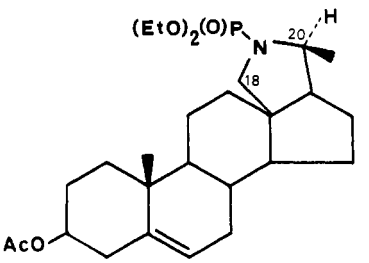
3



4



5a, R = H
b, R = I



6

phosphoramidate **5a**.[15] The photolysis of **5a** in the presence of $I_2/Pb(OAc)_4$ (0.5 mmol/3 mmol per mmol of **5a**) was faster than those already described (50 °C, 1 h), giving the C-18 iodine **5b** (60%)[17] and the 18,20(*S*)-epimine derivative **6** (10%).[18] Attempts to improve the yield of **6**, by increasing the reaction time as well as raising the temperature, led to evidently inferior results. The transformation of **5b** into **6** was accomplished in 90% yield with an excess of silver acetate in acetone at room temperature for 18 h.

After the success in the synthesis of epimine compounds by photolysis of diethyl phosphoramidates we tried to extend this reaction by introducing radical-stabilizing phosphonic groups that eventually could be removed more easily than the diethoxyphosphinyl moiety after the cyclization step. Hence, irradiation of the diphenyl and dibenzyl phosphoramidates **1b** and **1c**[19,20] under the conditions specified for the obtention of **2a** gave in 100% yield the 6β,19-epimine compounds **2b** and **2c**, respectively.[21]

(15) Compound **5a** has been prepared from 3β-hydroxy-20(*S*)-aminopregn-5-ene[16] and diethyl phosphorochloridate as described for **1a**.

(16) Janot, M. M.; Devissaguet, P.; Pais, M.; Khuong-Huu, Q.; Jarreau, F. X.; Goutarel, R. *Bull. Soc. Chim. Fr.* **1967**, 4567.

(17) Compound **5b**: decomposes over 200 °C; IR ($CHCl_3$) ν_{max} 3400, 1720, 1230 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.01 (3 H, s, C-19 H), 3.22 (2 H, br s, C-18 H), 3.6 (1 H, m, $W_{1/2}$ = 22 Hz, C-20 H); MS, *m/e* (assignment, relative intensity) 478.2715 ($C_{26}H_{41}NO_5P$, 55), 418.2468 ($C_{24}H_{37}NO_3P$, 100).

(18) Compound **6**: mp 116–118 °C (*n*-pentane); $[\alpha]_D$ −9° ($CHCl_3$); IR ($CHCl_3$) ν_{max} 1720, 1230 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95 (3 H, s, C-19 H), 3.06 (2 H, m, $W_{1/2}$ = 7 Hz, C-18 H), 3.7 (1 H, m, $W_{1/2}$ = 22 Hz, C-20 H); MS, *m/e* (assignment, relative intensity) 493.2927 (M^+, $C_{27}H_{44}NO_5P$, 2), 418.2484 ($C_{24}H_{37}NO_3P$, 100).

(19) The diphenyl phosphoramidate **1b** was prepared by reaction of 6β-amino-5α-cholestan-3β-ol[10] with diphenyl phosphorochloridate in the presence of 2 molar equiv of triethylamine and subsequent acetylation. The dibenzyl phosphoramidate **1c** was prepared according to: Kenner, G. W.; Told, A. R.; Weymouth, F. J. *J. Chem. Soc.* **1952**, 3675.

(20) Wolfrom, M. L.; Conigliaro, P. J.; Soltes, E. J. *J. Org. Chem.* **1967**, *32*, 653. Wolman, Y. In "The Chemistry of the Amino Group"; Patai, S., Ed.; Interscience: London, 1968; p 678. Ballou, C. E.; MacDonald, D. L. In "Methods in Carbohydrate Chemistry"; Whistler, R. L.; Wolfrom, M. L., Ed.; Academic Press: New York, 1963; Vol. 2, pp 270–297.

We believe that these reactions ilustrate the synthetic potential of the stabilized phosphoramidate radicals in pyrrolidine synthesis. At present, we are thoroughly studying these and related reactions, and further applications of these results to the synthesis of heterocyclic natural products are under investigation and will be reported in due course.

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Registry No. **1a**, 87509-76-0; **1b**, 87509-77-1; **1c**, 87509-78-2; **2a**, 87509-79-3; **2b**, 87509-80-6; **2c**, 87509-81-7; **2d**, 87509-82-8; **3**, 87509-83-9; **4**, 87509-84-0; **5a**, 87509-85-1; **5b**, 87509-86-2; **6**, 87509-87-3; 6β-amino-5α-cholestan-3β-ol, 87509-88-4; diethyl phosphorochloridate, 814-49-3; 3β-hydroxy-20(*S*)-aminopregn-5-ene, 5035-10-9; diphenyl phosphorochloridate, 2524-64-3.

Supplementary Material Available: IR, ^{1}H NMR, and mass spectral data for **1a–c**, **2a–c**, **3**, **4**, **5a,b**, and **6**. (5 pages). Ordering information is given on any current masthead page.

(21) Compound **2b**: mp 123–126 °C (*n*-pentane); $[\alpha]_D$ −24° ($CHCl_3$); IR ($CHCl_3$) ν_{max} 1725, 1590, 1490, 1230 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.27, 3.11 (2 H, AB, J = 11 Hz, C-19 H), 3.78 (1 H, m, $W_{1/2}$ = 10 Hz, C-6α H); MS, m/e (assignment, relative intensity) 675.4086 (M^+, $C_{41}H_{58}NO_5P$, 10), 352.1129 ($C_{20}H_{19}NO_3P$, 100). Compound **2c**: mp 137–141 °C (MeOH); $[\alpha]_D$ −13° ($CHCl_3$); IR ($CHCl_3$) ν_{max} 1720, 1230 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.06 (2 H, br s, C-19 H), 3.61 (1 H, m, $W_{1/2}$ = 10 Hz, C-6α H); MS, m/e (assignment, relative intensity) 703 (M^+, 2), 440.1675 ($C_{24}H_{27}NO_5P$, 100). Catalytic hydrogenation[20] over PtO_2 of **2c** followed by acid treatment [HCl(dil), pH 4, 25°C, 0.5 h] and subsequent neutralization (NaOH aqueous) afforded **2d**: 70% yield; IR ($CHCl_3$) ν_{max} 3400, 1720 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.70 (3 H, s, C-18 H), 3.00 (2 H, br s, C-19 H), 3.45 (1 H, m, $W_{1/2}$ = 10 Hz, C-6α H); MS, m/e 443.3755 (M^+, $C_{29}H_{49}NO_2$).

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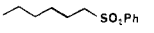
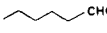
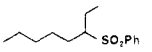
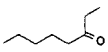
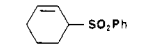
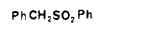
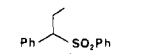
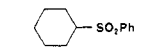
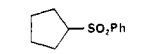
A Novel Oxidative Desulfonylation. Facile Conversion of Sulfones to Aldehydes or Ketones

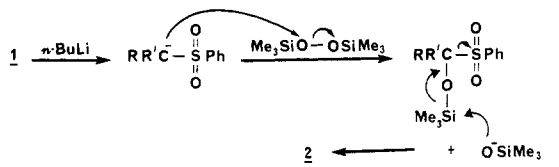
Summary: Alkyl, allylic, benzylic, and cycloalkyl sulfones can be converted to aldehydes or ketones in good-to-excellent yields by treatment with *n*-BuLi followed by $Me_3SiOOSiMe_3$. Preparation of ^{18}O-labeled carbonyl compounds with $Me_3Si^{18}O^{18}OSiMe_3$ was also successful.

Sir: The sulfone group is widely employed in organic synthesis.[1] However, this functional group must usually be removed after transformations have been completed. It has been proven that desulfonylation of sulfones to give carbonyl compounds can occur under basic conditions if an oxygen atom is located at the α position.[2] Recently, Little reported an elegant oxidative desulfonylation method to convert sulfones directly to ketones.[3] However, a 3-fold excess of the comparatively expensive oxidant, molybdenum peroxide (MoO_5·Py·HMPA)), is required. We report herein a general method for the conversion of sulfones to aldehydes or ketones using the readily available reagent bis(trimethylsilyl)perioxide[4] (BTSP). This method is also useful for the direct preparation of ^{18}O-labeled carbonyl compounds.

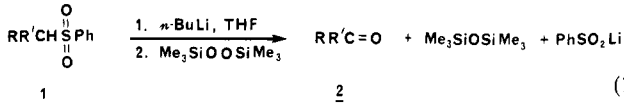
Table I. Conversion of Sulfones to Aldehydes or Ketones with BTSP

entry	sulfone	aldehyde or ketone[12]	yield, %
1			81
2			76
3			66
4			91
5			80
6			90
7			83

Scheme I



Removal of an α proton of phenylsulfone **1** with *n*-BuLi in tetrahydrofuran (THF) at −78 °C provides a bright yellow solution of the corresponding phenylsulfonyl carbanion. After 15 min, a slight excess of BTSP is injected to produce a reddish brown solution, which is then stirred overnight. A white precipitate appears, indicating the formation of the lithium salt of benzenesulfinic acid. After workup, aldehydes or ketones are obtained in good-to-excellent yields (see eq 1 and Table I.) This method has



(1)

been successful with some alkyl, allylic, benzylic, and cycloalkyl sulfones. For more hindered systems, such as cyclohexyl phenyl sulfone, refluxing is required to complete the reaction.

The mechanism of this two-step, one-pot reaction is illustrated in Scheme I. Owing to the low energy of O–O bonds and the high energy of O–Si bonds,[5] the trimethylsiloxyl anion (Me_3SiO^-) can behave as both an efficient leaving group and a back-attacking moiety.

In addition to requiring only simple manipulations and giving respectable yields, the method allows easy removal of byproducts.[6] It is therefore an attractive procedure for use in organic synthesis.

(1) (a) Vogtle, F.; Rossa, L. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 515. (b) Field, L. *Synthesis* **1978**, 713.
(2) (a) Magnus, P. D. *Tetrahedron* **1977**, *33*, 2019. (b) Tanaka, K.; Matsui, S.; Kagi, A. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 3619 and references therein.
(3) Little, R. D.; Myong, S. O. *Tetrahedron Lett.* **1980**, *21*, 3339.
(4) Cookson, P. G.; Davies, A. G.; Frazel, N. *J. Organomet. Chem.* **1975**, *99*, C31.
(5) The average bond energies for O–O and O–Si are 47 and 108 kcal mol^{-1}, respectively. See: Streitwieser, A., Jr.; Heathcock, C. H. "Introduction to Organic Chemistry"; Macmillan: New York, 1976; p 1187.
(6) Use of excess *n*-BuLi and BTSP for this reaction may generate a small amount of *n*-BuOSiMe$_3$ (see: Brandes, D.; Blaschette, A. *J. Organomet. Chem.* **1974**, *73*, 217). However, owing to the low polarity of this byproduct, it can be easily separated from ketones or aldehydes by column chromatography.

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