prepared from **2**. For compounds **3e,f**, the reaction was run in the same manner, except that a 7:1 ratio of isocyanate to **1** was used.

3-Phenylimidazolidinetriones 4. A. By Hydrolysis of 3. Addition of 3 mL of concentrated hydrochloric acid to a mixture of 0.5 g of **3** and 5 mL of ethanol caused an exothermic reaction to occur. The resulting mixture was allowed to stand for 10–120 min and was then diluted with water and filtered to yield the product.

B. From Ureas.[9] A mixture of benzene (25–50 mL) and equal weights (5–10 g) of oxalyl chloride and the urea was refluxed for 1–6 h and then cooled, diluted with petroleum ether (bp 63–75 °C), and filtered to yield the product.

C. By Oxidation of 5. To an ice-cold mixture of 0.5 g of **5** and 3–5 mL of acetic acid was added 3 mL of 30% hydrogen peroxide, and the resulting mixture was allowed to stand at room temperature until its yellow color had essentially been discharged (1–48 h). For the slower reactions (**5c,e,f**), a further 2–3 mL of H_2O_2 was added in portions, whereas for the faster reactions the mixture was occasionally cooled to prevent overheating. The product was isolated by dilution with water and filtration.

3-Phenyl-4-thioxo-2,5-imidazolidinediones 6. Addition of 3–5 mL of concentrated hydrochloric acid to a mixture of 1 g of **5** and 10–15 mL of ethanol caused an exothermic reaction to occur. The resulting mixture was allowed to stand for about 1 h and was then diluted with water and filtered to yield the product.

5-Carbamoylimino-3-phenyl-4-thioxo-2-imidazolidinones 7. A. A mixture of 0.010 mol of **2** and 0.020 mol of isocyanate was heated on the steam bath (closed flask for **7e**) until it had essentially completely solidified. The length of the heating period seemed to affect the quality of the product. Satisfactory results were obtained after 30 min for **7a**, 2 h for **7b,c**, 1.5 h for **7e**, and 5 h for **7f**. The crude product was triturated and washed with ethanol for **7b–c** and with petroleum ether (bp 63–75 °C) for **7a,e,f**. To prepare **7d**, we refluxed a solution of 0.80 g (0.0050 mol) of **2** and 1.5 g (0.010 mol) of 4-ClC_6H_4NCO in 10 mL of benzene for 45 h and then cooled and filtered the resulting solution to yield the product.

B. A mixture of 0.50 g of **5**, 1.0 g of isocyanate, and 0.050 g of *p*-toluenesulfonic acid was heated on the steam bath (closed flask for **7e**) until it had essentially solidified (15 min for **7a,b**; 1 h for **7c,f**; 2 h for **7e**). The crude product was triturated and washed with ethanol for **7a–c** and with petroleum ether (bp 63–75 °C) for **7f**. In the case of **7e**, the crude product was dissolved in ethanol and, after filtration of the solution, reprecipitated by addition of water. For **7d**, the mixture of **5d**, isocyanate, and *p*-TsOH was heated briefly on a Bunsen flame to obtain a melt, which was allowed to solidify, and then treated with EtOH.

1*H*-Imidazo[4,5-*b*]quinoxalin-2(3*H*)-ones 8. A stirred mixture of 0.050 mol of **5**, 0.060–0.080 mol of *o*-phenylenediamine, and 10 mL of ethanol was refluxed until no more H_2S or NH_3 was evolved (24 h for **8b,c,e,f**; 48 h for **8a,d**). The product was isolated by cooling and filtration of the reaction mixture followed by washing of the precipitate with ethanol.

Acknowledgment. Financial support by the Research Allocations Committee and the Department of Chemistry of the University of New Mexico is gratefully acknowledged.

Registry No. **1**, 6784-22-1; **2**, 4955-82-2; **3a**, 10319-52-5; **3b**, 71342-18-2; **3c**, 71342-19-3; **3d**, 71342-20-6; **3e**, 54095-14-6; **3f**, 71342-21-7; **4a**, 6488-59-1; **4b**, 30592-91-7; **4c**, 71342-22-8; **4d**, 30592-92-8; **4e**, 71342-23-9; **4f**, 71342-24-0; **5a**, 71342-25-1; **5b**, 71342-26-2; **5c**, 71342-27-3; **5d**, 71342-28-4; **5e**, 71342-29-5; **5f**, 71342-30-8; **6a**, 71342-31-9; **6b**, 71342-32-0; **6c**, 71342-33-1; **6d**, 71342-34-2; **6e**, 71342-35-3; **6f**, 71342-36-4; **7a**, 71342-37-5; **7b**, 71342-38-6; **7c**, 71342-39-7; **7d**, 71342-40-0; **7e**, 71342-41-1; **7f**, 71342-42-2; **8a**, 15051-50-0; **8b**, 71342-43-3; **8c**, 71342-44-4; **8d**, 71342-45-5; **8e**, 71342-46-6; **8f**, 71342-47-7; phenyl isocyanate, 103-71-9; *p*-tolyl isocyanate, 622-58-2; *o*-tolyl isocyanate, 614-68-6; *p*-chlorophenyl isocyanate, 104-12-1; ethyl isocyanate, 109-90-0; butyl isocyanate, 111-36-4; *N,N'*-diphenylurea, 102-07-8; *N*-phenyl-*N'*-*p*-tolylurea, 4300-33-8; *N*-phenyl-*N'*-*o*-tolylurea, 13140-49-3; *N*-phenyl-*N'*-*p*-chlorophenylurea, 1967-26-6; *N*-phenyl-*N'*-ethylurea, 621-04-5; *N*-phenyl-*N'*-butylurea, 3083-88-3; *o*-phenylenediamine, 95-54-5; oxalyl chloride, 79-37-8.

Synthesis of Some 1-Azirines from α-Bromo Ketoximes via Oxazaphospholines[1]

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Received January 29, 1979

A useful route from α-bromo ketoximes **1** to azirines is described which involves protection of **1** followed by phosphine substitution and deprotection via oxazaphospholine intermediates. The mild deprotection of the oxime ethers involves intramolecular assistance by a phosphonium group. New azirines, including a ring-deuterated species, have been synthesized.

Oxazaphospholines from Protected Oxime Ethers

α-Bromo ketoximes **1** undergo a Beckmann rearrangement[2] instead of halogen substitution when treated with triphenylphosphine. However, the phosphonium products **2** can be obtained by addition of base[2] or by employing α-chloro ketoximes.[3] We now find that protection of readily available α-bromo oximes **1** in the form of ketals **3** permits clean S_N2 substitution by triphenylphosphine to produce **4** which can be deprotected under very mild conditions (trace of aqueous acid in $CHCl_3$ for 20 min at 25 °C) to generate the salts **2** (see Scheme I). These phosphonium salts **2** are readily converted to oxazaphospholines **5**,[3] which in turn can be thermolyzed to 1-azirines.[4]

Some examples of the conversion of α-bromo ketones to oxazaphospholines **5** via Scheme I are summarized in Table I. The overall sequence **1** → **5** can be carried out in one flask without isolation of intermediates (see Experimental Section). Although the yields of **5** via this route do not differ substantially from those of previous routes, the advantage of this procedure over those reported[2,3] lies

(1) Small rings. 25. Part 24: A. Hassner and V. Alexanian in "New Trends in Heterocyclic Chemistry", Elsevier, Amsterdam, 1979, pp 178-201.

(2) M. Masaki, K. Fukui, and M. Ohta, *J. Org. Chem.*, **32**, 3564 (1967).

(3) G. Guadiano, R. Mandelli, P. P. Ponti, C. Ticozzi, and A. Umani-Ronchi, *J. Org. Chem.*, **33**, 4431 (1968).

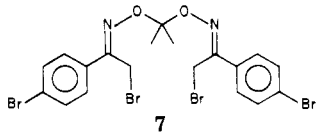
(4) (a) J. Wulff and R. Huisgen, *Chem. Ber.*, **102**, 1841 (1969); (b) H. J. Bestman and R. Kunstman, *ibid.*, **102**, 1816 (1969).

0022-3263/79/1944-3861$01.00/0

Table I. Synthesis of Oxazaphospholines 5 from Bromo Ketones $RCOCH_2Br$ via Scheme I

	R	% yield (mp, °C)				
		1	3	4	2	5
a	Ph	80	96[e]	95 (152, 230)[d,f]	90	85
b	4-ClPh	69 (124)[d]	95[e]	89 (162)[d]	94 (222)[d]	77 (141)[d]
c	4-BrPh	80 (124)[d]	38[a,e]	82	81	72 (153)[d]
d	4-MePh	73 (126)[d]	85[e]	89 (145)[d]	84	86 (139)[d]
e	4-MeOPh	66 (123)[d]	89[e]	83 (85)	97 (216)[d]	75 (134)[d]
f	*t*-Bu	96	91[e]			43[b,d]
g	Me		67[c-e]		32[b]	95 (117-119)[d]

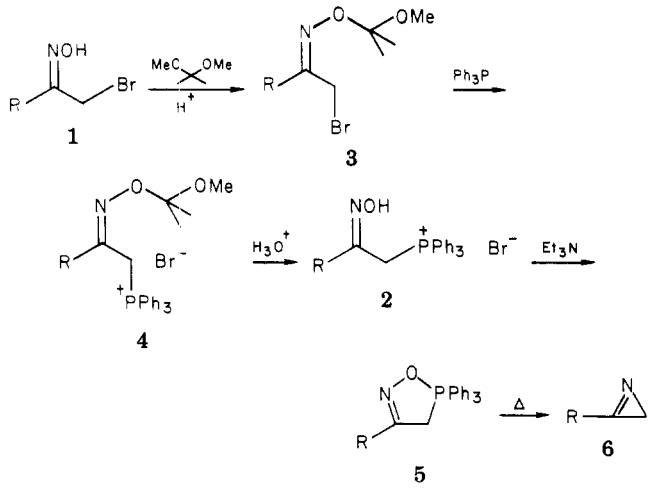
[a] Another product in this reaction was the dimer 7 which arises from 3c on heating in the presence of a trace of *p*-toluenesulfonic acid.



7

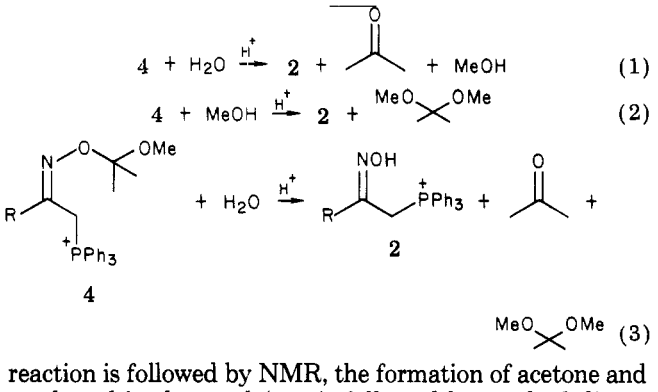
[b] Overall yield from 3. [c] Overall yield from bromo ketone. [d] Satisfactory elemental analyses were obtained. [e] The product was an oil. [f] First melt resolidifies and remelts.

Scheme I



in its consistency and generality.

It is interesting to note that the facile acid-catalyzed deprotection step (4 → 2) involves two stages (eq 1 and 2) with the overall reaction depicted by eq 3. When the

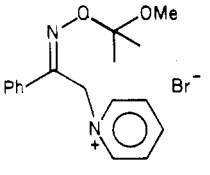


(1)

(2)

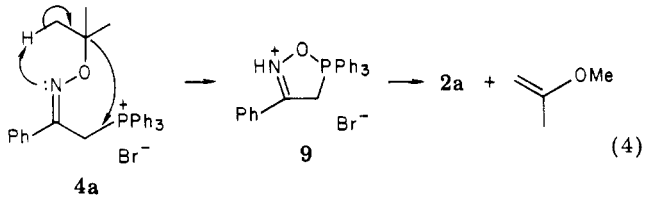
(3)

reaction is followed by NMR, the formation of acetone and methanol is observed (eq 1), followed by gradual disappearance of the methanol peak and the corresponding appearance of 2,2-dimethoxypropane signals (eq 2), with the acetone signal remaining constant. At the end of the hydrolysis the ratio of acetone to the dimethoxypropane was 1:1 as required by the stoichiometry represented in (3). The corresponding pyridinium oxime 8 is not hydrolyzed under the same conditions. The ease of hydrolysis of 4 may be due to an intramolecular electrophilic catalysis by P^+, resulting in the formation of a pentacoordinated P, as in oxazaphospholine 5. Such an interaction is not feasible in the case of 8. Furthermore, the



8

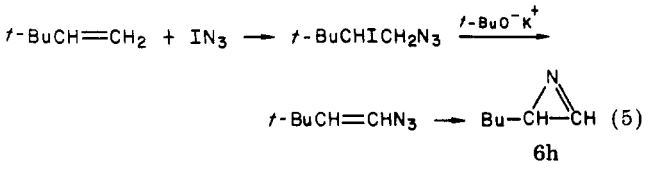
melting point behavior of **4a** supports the postulated interaction of the oxime oxygen with P^+. The protected oxime **4a** loses 2-methoxy-1-propene upon melting (160–170 °C) to generate **2a** (mp and mmp 230 °C), presumably via **9** (which as the protonated form of **5a** is in equilibrium with **2a**). The pyridinium analogue 8 does not show this behavior.



(4)

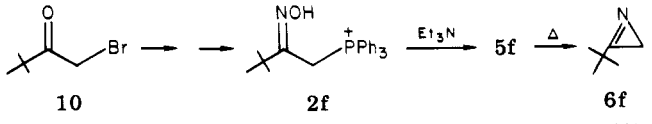
Synthesis of Some Azirines

We have applied the above procedure to the synthesis of some azirines which are not easily accessible via the more general vinyl azide route.[5] For instance, 2-*tert*-butylazirine (**6f**) is not accessible via IN_3 addition to *tert*-butylethylene; instead, the regioisomeric **6h** is formed.



(5)

Using the sequence described, we were able to convert α-bromopinacolone[6a] (**10**) into **5**, which on pyrolysis at 100–150 °C gave 2-*tert*-butylazirine (**6f**) in 57% yield; only a trace of ketenimine product was formed.[6b]

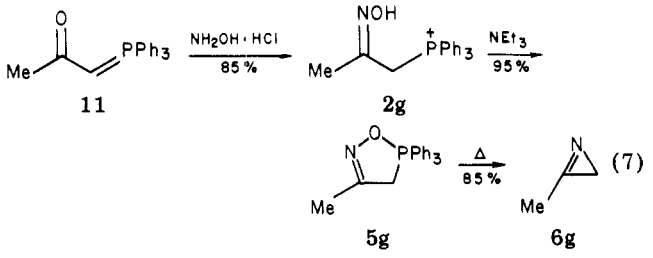


(6)

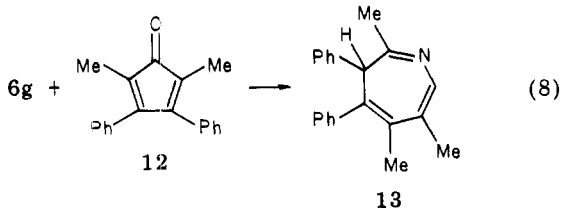
Similarly, 2-methylazirine (**6g**, R = CH_3) was obtained

(5) A. Hassner and F. W. Fowler, *J. Am. Chem. Soc.*, **90**, 2869 (1968).

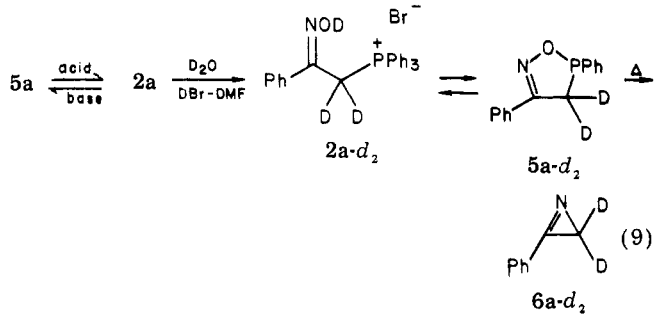
on pyrolysis of **5g** (R = CH_3). The latter[3] was accessible via the ylide **11** as shown in eq 7. **5g** was identical with the compound prepared via Scheme I.



2-Methylazirine (**6g**), the lowest molecular weight azirine isolated, is a volatile liquid [bp 42 °C (1 atm)] with an unpleasant odor and a C–N stretching frequency at 1772 cm^{-1} characteristic of azirines. Its NMR spectrum[6b] showed a methyl singlet at δ 2.50 and a singlet for the ring protons at δ 1.35. The mass spectrum showed a parent ion peak at *m/e* 55 and the base peak at *m/e* 54, corresponding to the methylazirinium cation. **6g** decomposed on standing at room temperature within 24 h. It was trapped, however, with dimethyldiphenylcyclopentadienone **12**[7] to produce the azepine **13**.



Previous attempts to directly exchange the ring protons in azirines have not been successful.[8] By taking advantage of the reversible ring opening of oxazaphospholines **5** (as shown below), we have succeeded in exchanging the now very acidic methylene protons in **2**. Thus, **5**-d_2 was obtained in >95% (d_2) isotopic purity in a single exchange. Pyrolysis of **5**-d_2 gave the dideuterated azirine **6a**-d_2[6b] in 44% yield: *m/e* 119 (100) $(M)^+$.



This azirine synthesis complements the well-established azide route of Hassner and Fowler[5] and, in low molecular weight systems, obviates the necessity of handling potentially explosive low molecular weight vinyl azides.

Experimental Section

Oxazaphospholines 5 via Protected Oxime α-Phosphonium Salts 4. General Procedure. A solution of hydroxylamine sulfate (0.60 mL) in water (100 mL) was added to a solution of the various α-bromo ketones (0.50 mol) in a mixture of methanol (800 mL) and water (300 mL) at room temperature. After 12 h of stirring at room temperature, water (400 mL) was added and the *syn*-α-bromo ketoximes **1a–f**[9] were collected and dried at room temperature. A solution of the dry oxime (0.10 mol), excess 2,2-dimethoxypropane (0.5 mol), and *p*-toluenesulfonic acid monohydrate (0.4 g) in methylene chloride (400 mL) was allowed to stand at room temperature overnight. After extraction with a 1 M sodium bicarbonate solution (3 × 50 mL) and drying ($MgSO_4$), the solvent was evaporated in vacuo at room temperature to give (2-methoxy-2-propyl)-α-bromo syn-*O*-ketoximes **3a–f**. Pure samples were prepared by stirring the protected oximes with neutral alumina (Woelm) in pentane, followed by evaporation of the solvent to dryness in vacuo at room temperature. In the case of **3c**, evaporation of the reaction mixture to dryness produced *O,O'*-[2,2-propanediyl]bis[*O*-4-α-dibromoacetophenone oxime] (**7**): mp 83 °C; NMR ($CDCl_3$) δ 7.60 (m, 8 H), 4.30 (s, 4 H), 1.80 (s, 6 H).

Anal. Calcd for $C_{19}H_{18}Br_4N_2O_2$: C, 36.45; H, 2.90. Found: C, 36.54; H, 2.94.

A solution of the protected oxime (**3a–f**) (0.10 mol) and triphenylphosphine (0.11 mol) in dry ether (300 mL, stirred with neutral alumina)[10] was allowed to stand at room temperature. After 72 h, the precipitate was collected and recrystallized from a mixture of chloroform and ether (1:4 (v/v)) to give (2-methoxy-2-propyl)phenacyltriphenylphosphonium bromide *syn-O*-oximes (**4a–e**).

Hydrogen bromide (48%, 1.0 mL) was added dropwise to a solution of **4a–f** (0.10 mol) in reagent grade chloroform (200 mL). After 2 h of stirring at room temperature, anhydrous ether was added and the crystals were collected and recrystallized from a mixture of absolute methanol and acetone (1:4 (v/v)) to give phenacyltriphenylphosphonium bromide oximes (**2a–e**) as colorless crystals.

Triethylamine (0.20 mol) was added to a solution of **2a–e** (0.10 mol) in absolute methanol (150 mL) at 0 °C to give colorless crystals of oxazaphospholines (**5a–e**), recrystallized from methanol.[11]

(2-Methoxy-2-propyl)-1-phenacylpyridinium Bromide *syn-O*-Oxime (8). A solution of **3a** (5.72 g, 0.020 mol) and pyridine (1.738 g, 0.022 mol) in dry acetone (100 mL) was boiled under reflux for 2 h and the solution was filtered and concentrated to a final volume of 25 mL. After an additional 1 h of boiling, anhydrous ether (200 mL) was added and the crystals were collected and recrystallized from a mixture of acetone and ether (4:1) to give **8** (5.85 g, 80%) as colorless crystals: mp 101 °C; NMR ($CDCl_3$) δ 9.60 (dd, 2 H, *J* = 7, 2 Hz), 8.80 (t, 1 H, *J* = 7 Hz), 8.30 (t, 2 H, *J* = 7, 7 Hz), 8.10 (m, 2 H), 6.50 (s, 2 H), 3.23 (s, 3 H), 1.53 (s, 6 H).

3-*tert*-Butyl-5,5,5-triphenyl-4,5-dihydro-1,2,5-oxazaphosphole (5f). A solution of **3f** (26.6 g, 0.100 mol) and triphenylphosphine (26.2 g, 0.100 mol) and triethylamine (5 drops) in ether (400 mL) was allowed to stand at room temperature for 1 week. The amorphous precipitate was isolated by decanting the solvent. Addition of chloroform (200 mL) and 48% hydrobromic acid (1.0 mL) and stirring for 2 h at room temperature followed by addition of anhydrous ether (400 mL) gave a brown oil. Triethylamine (10.1 g, 0.100 mol) was added to a solution of the oil in methanol (100 mL) at 0 °C, and after 10 min, ice (40 g) was added to give **5f** (16.0 g, 43%) as colorless crystals: NMR ($CDCl_3$) δ 7.6–7.1 (m, 15 H), 3.06 (d, 2 H, J_{HP} = 11 Hz), 1.17 (s, 9 H).

Anal. Calcd for $C_{24}H_{26}NOP$: C, 76.78; H, 6.98; N, 3.73. Found: C, 76.67; H, 7.02; N, 3.82.

2-*tert*-Butylazirine (6f). Solid **5f** (7.50 g, 0.020 mol) in a round-bottomed flask mounted with a distillation head and a condenser was pyrolyzed by heating in an oil bath to 120 °C. The product distilled into a cooled flask at −78 °C to give **6f** (1.10 g, 57%) as a colorless liquid: bp 80 °C (1 atm); NMR ($CDCl_3$) δ 1.40 (s, 2 H), 1.27 (s, 9 H).

(6) (a) J. H. Boyer and D. Straw, *J. Am. Chem. Soc.*, **74**, 4506 (1952). (b) No efforts were made to isolate the trace amounts of the ketenimines[4,5] present in the pyrolysate.

(7) D. J. Anderson and A. Hassner, *Synthesis*, 483 (1975); A. Hassner and D. J. Anderson, *J. Org. Chem.*, **39**, 3070 (1974).

(8) R. J. Isbister and A. Hassner, unpublished results.

(9) (a) J. H. Smith, J. H. Heidema, E. T. Kaiser, J. B. Wetherington, and J. W. Moncrief, *J. Am. Chem. Soc.*, **94**, 9274 (1972); (b) J. H. Smith and E. T. Kaiser, *J. Org. Chem.*, **39**, 718 (1974).

(10) Alternatively, one drop of triethylamine added to the solvent system effectively prevents the acid-catalyzed hydrolysis of **4a–e**.

(11) Excessive heating should be avoided since it causes partial decomposition of the oxazaphospholines.

Acetone Oxime α-Triphenylphosphonium Bromide (2g). A solution of chloroacetone (9.25 g, 0.100 mol) and hydroxylamine hydrochloride (10.42 g, 0.150 mol) was allowed to stand at room temperature for 12 h. After the solution was extracted with methylene chloride (3 × 50 mL), 2,2-dimethoxypropane (10.4 g, 0.100 mol) and *p*-toluenesulfonic acid monohydrate (0.050 g) were added. The resulting solution was boiled under reflux for 24 h. The acid was neutralized by washing the solution with 1% sodium bicarbonate (3 × 100 mL). After the mixture was dried, the product was distilled to give (2-methoxy-2-propyl)-α-chloroacetone *syn*-*O*-oxime (**3g**) (12.10 g, 67%) as a colorless oil: bp 40 °C (0.10 mm); NMR ($CDCl_4$) δ 4.07 (s, 2 H), 3.12 (s, 3 H), 1.95 (s, 3 H), 1.40 (s, 6 H); *m/e* 148 (5), 147 (8), 92 (10), 91 (30), 72 (50), 71 (15).

Anal. Calcd for $C_7H_{14}ClNO_2$: C, 46.80; H, 7.86. Found: C, 46.88; H, 7.83.

3g (1.805 g, 0.010 mol) and triphenylphosphine (2.623 g, 0.010 mol) in dry acetone (10 mL) were boiled under reflux in the presence of triethylamine (1 drop) for 75 h. Addition of ether gave an oil which was dissolved in 95% ethanol (10 mL), and concentrated hydrochloric acid (10 drops) was added. Addition of ether after 5 h gave a colorless solid which was recrystallized from a mixture of absolute ethanol and ether (1:4 (v/v)) to give **2g** (1.2 g, 32.4%): mp 223 °C (lit.[3] mp 223 °C).

3-Methyl-5,5,5-triphenyl-4,5-dihydro-1,2,5-oxazaphosphole (5g). Triethylamine (10.1 g, 0.100 mol) was added at once to a suspension of a pure sample of **2g** (36.98 g, 0.100 mol) at 0 °C with vigorous stirring. The suspended **2g** dissolved and within a few minutes **5g** precipitated (31.5 g, 95%) as pale yellow crystals. An analytical sample[12] was prepared by rapid recrystallization from a mixture of methylene chloride and ether (1:4) to give **5g** as tan crystals: mp 117–119 °C dec; NMR ($CDCl_3$) δ 7.35 (m, 15 H), 3.08 (d, 2 H, J_{HP} = 11 Hz), 2.12 (s, 3 H); *m/e* 278 (84), 277 (100).

Anal. Calcd for $C_{21}H_{20}NOP$: C, 75.66; H, 6.05. Found: C, 75.76; H, 6.07.

2-Methylazirine (6g). **5g** (3.33 g, 0.010 mol) was pyrolyzed as in the case of **6f** to give 2-methylazirine (**6g**) (0.35 g, 63.6%). Redistillation gave a pure sample as a colorless liquid: bp 42–43 °C (1 atm); IR (NaCl) 1772 ($\nu_{C=N}$); NMR ($CDCl_3$) δ 2.50 (s, 3 H), 1.35 (s, 2 H); *m/e* (70 eV) 55 (84), 54 (100), 53 (7), 52 (22), 51 (15), 41 (18), 40 (30), 39 (15), 38 (11); *m/e* (15 eV) 55 (100), 54 (88).

2,5,6-Trimethyl-3,4-diphenyl-3*H*-azepine (13). A solution of 2-methylazirine (**6g**) (0.220 g, 0.0040 mol) and 2,5-dimethyl-3,4-diphenylcyclopentadienone dimer (**12**) (0.520 g, 0.0010 mol) in chloroform (25 mL) was heated in a Fischer–Porter tube at 100 °C for 48 h. Evaporation of the solvent, followed, by addition of pentane (50 mL) gave **12** (0.031 g, 6%). Concentration of the filtrate to a final volume of 10 mL and cooling gave the azepine **13** (0.14 g, 22%) as a pale yellow solid: NMR ($CDCl_3$) δ 7.50–6.90 (m, 10 H), 6.66 (s, 1 H), 5.10 (s, 1 H), 2.16 (s, 3 H), 1.90 (s, 3 H), 1.67 (s, 3 H); *m/e* 288 (22), 278 (70), 286 (100), 272 (17), 260 (12), 246 (16).

4,4-Dideuterio-3,5,5,5-tetraphenyl-4,5-dihydro-1,2,5-oxazaphosphole (5a-d_2). Deuterium bromide (47%) in deuterium oxide (17.5 g) was added to a suspension of **5a** (39.5 g, 0.100 mol) in a mixture of dry dimethylformamide (100 mL) and deuterium oxide (50 mL) at 0 °C over a period of 10 min with stirring. The reaction mixture was warmed to dissolve the solid, filtered, and cooled to 0 °C. Dry triethylamine (ca. 30 mL) was then added to the cold solution and the colorless precipitate was collected and washed with methanol-*d*. Rapid recrystallization of the product from a mixture of methylene chloride and ether (1:4) gave **5a**-d_2 (26.5 g, 67%) containing 5% monodeuterated **5a**-*d* (by NMR).

2-Phenyl-3,3-dideuterioazirine (6a-d_2). **5a**-d_2 (3.97 g, 0.0100 mol) was pyrolyzed as in **6f** to give 2-phenyl-3,3-dideuterioazirine (**6a**-d_2) (0.52 g, 44%) containing 6% **6a**-*d* (by NMR): *m/e* (15 eV) 119 (100%).

Acknowledgment. Support of this research by NCI Grant CA 19203 from DHEW is gratefully acknowledged.

Registry No. 1a, 17082-13-2; **1b**, 71426-50-1; **1c**, 71426-51-2; **1d**, 71426-52-3; **1e**, 71426-53-4; **1f**, 71426-54-5; **2a**, 71426-55-6; **2b**, 71426-56-7; **2c**, 71426-57-8; **2d**, 71426-58-9; **2e**, 71426-59-0; **2g**, 71426-60-3; **3a**, 50314-87-9; **3b**, 71426-61-4; **3c**, 71426-62-5; **3d**, 71426-63-6; **3e**, 71426-64-7; **3f**, 71426-65-8; **3g**, 71426-66-9; **4a**, 71426-67-0; **4b**, 71426-68-1; **4c**, 71426-69-2; **4d**, 71486-17-4; **4e**, 71426-70-5; **5a**, 14264-70-1; **5a**-d_2, 71426-71-6; **5b**, 71426-72-7; **5c**, 17631-19-5; **5d**, 71426-73-8; **5e**, 71426-74-9; **5f**, 71426-75-0; **5g**, 17631-21-9; **6a**-d_2, 71426-76-1; **6f**, 71426-77-2; **6g**, 71426-78-3; **7**, 71463-33-7; **8**, 71426-79-4; **12**, 26307-17-5; **13**, 71426-80-7; hydroxylamine sulfate, 10039-54-0; triphenylphosphine, 603-35-0; 2,2-dimethoxypropane, 77-76-9; α-bromoacetophenone, 70-11-1; α-bromo-*p*-chloroacetophenone, 536-38-9; α,*p*-dibromoacetophenone, 99-73-0; α-bromo-*p*-methylacetophenone, 619-41-0; α-bromo-*p*-methoxyacetophenone, 2632-13-5; 1-bromo-3,3-dimethyl-2-butanone, 5469-26-1; 1-bromo-2-propanone, 598-31-2.

Supplementary Material Available: Analytical data on compounds **1b–e** → **5b–e** and **4a** (4 pages). Ordering information is given on any current masthead page.

(12) A previous attempt[3] to obtain **5g** in pure form has been unsuccessful.

Nitrogen-15 Nuclear Magnetic Resonance Spectroscopy. Effects of Hydrogen Bonding and Protonation on Nitrogen Chemical Shifts in Imidazoles[1a]

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Received May 8, 1979

The ^{15}N chemical shifts of imidazoles, *N*-methylimidazole and 4-methylimidazole, have been measured in acidic and neutral nonaqueous media. Both hydrogen bonding and protonation of the imidazoles result in upfield shifts of the average of the nitrogen resonances, but the magnitudes of the protonation shifts far exceed those associated with hydrogen bonding. The less-than-normal shifts of the imidazolium ions in nonaqueous media suggest ion-pair formation resulting from interion hydrogen bonding. Such effects diminish in solvents of higher dielectric constant and greater solvating power for salts.

The imidazole unit in the histidyl residues of several enzymes plays a major role in hydrolytic bond cleavage in peptides. A study of the behavior of free imidazole and its derivatives toward hydrogen-bonding and protonating

0022-3263/79/1944-3864$01.00/0