TABLE I
PROTON NMR SPECTRA[a] OF SALTS OF PHOSPHOLES

Salt	Solvent	PCH δ	PCH $^2J_{PH}$, Hz	$PCH_2C_6H_5$ δ	$PCH_2C_6H_5$ $^2J_{PH}$, Hz	C=CH δ	C=CH $^2J_{PH}$, Hz	C_6CH, δ	CCH_3, δ
				A. Monomers					
1	CF_3COOH[b]			3.99	15.4	6.43	32.4		2.00
2	$CDCl_3$[c]			4.94	16.8	6.2–7.84[d]			1.85
3	$CDCl_3$[b]	3.05	15			7.53	33		2.81[e]
				B. Dimers					
4	$CDCl_3$[b]			5.3–5.7		5.9–6.3, 7.1–7.2[f]		3.8–4.1	
5	$CDCl_3$[c]			4.5–4.8		5.72–7.60[d]		3.2–3.4[g]	

[a] Taken with a Varian A-60 spectrometer. [b] External TMS as standard. [c] Internal TMS as standard. [d] Overlapped by C_6H_5 signals. [e] J_{PH} = 3 Hz. [f] Complex multiplet. [g] Overlapped by phenethyl CH_2 signals.

as well.[8] The nature of the P substituents may also play a role in preventing dimerization of phospholium ions; thus, the *P,P*-dimethyl derivative of the 3-methylphospholium ion appears to be dimeric[7] while the *P,P*-dibenzyl derivative (**2**) remains monomeric. It would seem to be necessary to consider carefully the structure assigned to a new phosphole salt in view of these results.

The two ^{31}P signals of the dimers are due to the presence of 3-phospholenium and 2-phospholenium moieties. In the dimers examined, the signals are separated by only 1–1.5 ppm. Normally, isomeric 3-phospholenium and 2-phospholenium ions have a greater spread in their ^{31}P shifts (*e.g.*, for the 1,1,3-trimethyl ions, −47.1 and −54.5 ppm, respectively). However, in the dimeric salts, the 3-phospholenium and 2-phospholenium moieties have differences in the substitution at saturated carbons. Thus, as seen in structures **4** and **5**, the 3-phospholenium moiety has carbon substituents at the two α positions, whereas the 2-phospholeniun moiety is substituted at one α and one β position. An analysis of substitution effects on ^{31}P shifts in several families of acyclic phosphorus compounds has shown the shifts to be dependent on the number of carbons in positions β and γ to the phosphorus atom.[9] As in ^{13}C nmr spectra, deshielding is associated with β carbons and shielding (a relatively weaker effect) with γ carbons. The leveling of the ^{31}P shifts for the two components of the phospholium ion dimers is a result of the different substitution patterns in the components. In particular, phosphorus in the 2-phospholenium moiety is deshielded by only one β carbon, and in the 3-phospholenium by two.

Experimental Section[10]

1,1,3-Trimethyl-2-phospholenium Iodide.—To 0.4 g of 1,3-dimethyl-2-phospholene[11] in pentane was added 1 g of methyl iodide. The salt that had precipitated after 1 day at room temperature was recrystallized from a mixture of 2-propanol and ether, mp 135–137°, δ^{31}_{P} ($CDCl_3$) −54.5 ppm.

Anal. Calcd for $C_7H_{14}IP$: C, 32.83; H, 5.51; P, 12.09. Found: C, 32.70; H, 5.52; P, 12.23.

1,1,3-Trimethyl-3-phospholenium Iodide.—This salt was prepared similarly from 1,3-dimethyl-3-phospholene;[12] it had mp 133–135° and δ^{31}_{P} ($CDCl_3$) −47.1 ppm.

Anal. Calcd for $C_7H_{14}IP$: C, 32.83; H, 5.51; P, 12.09. Found: C, 32.73; H, 5.45; P, 12.08.

Registry No.—**1**, 38864-31-2; **2**, 38857-58-8; **3**, 37737-13-6; **4**, 38863-80-8; **5**, 38863-82-0; 1,1,3-trimethyl-2-phospholenium iodide, 38857-60-2; 1,1,3-trimethyl-3-phospholenium iodide, 38857-61-3.

(8) F. B. Clarke, III, and F. H. Westheimer, *J. Amer. Chem. Soc.*, **93**, 4541 (1971).
(9) L. D. Quin and J. J. Breen, *Org. Magn. Resonance*, in press.
(10) All phosphole salts were available from another study.[4] Proton nmr spectra are recorded in Table I, and phosphorus spectra for **3** and **4** are in the text.
(11) D. K. Myers and L. D. Quin, *J. Org. Chem.*, **36**, 1285 (1971).
(12) L. D. Quin and D. A. Mathewes, *ibid.*, **29**, 836 (1964).

1*H*-Imidazo[1,2-*a*]imidazoles. II. The Chemistry of 1,6-Dimethyl-1*H*-imidazo[1,2-*a*]imidazole

LAIRD F. MILLER* AND RONALD E. BAMBURY

Merrell-National Laboratories, Division of Richardson-Merrell, Inc.,[1] Cincinnati, Ohio 45215

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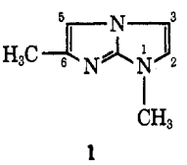
In a previous paper[2] we described the preparation of a series of 1*H*-imidazo[1,2-*a*]imidazoles which were intended as anthelmintic agents. As part of this project, the chemistry of one member of the series, 1,6-dimethyl-1*H*-imidazo[1,2-*a*]imidazole (**1**), was investigated. At



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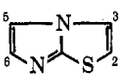
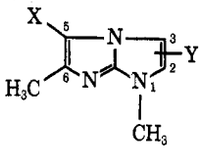


imidazo[2,1-*b*]thiazole

the time the synthetic work was carried out no unsaturated imidazo[1,2-*a*]imidazoles were reported in the literature; however, the reactions of the closely related imidazo[2,1-*b*]thiazole ring system had been studied. The investigations of Paolini[3] and Pyl[4] had revealed that in this ring system the 5 position was the most susceptible to electrophilic attack. It was, therefore, not unexpected to find similar results for the reactions of **1**.

(1) The chemical portion of this work was carried out at the Hess and Clark Division of Richardson-Merrell Inc., Ashland, Ohio, now a division of Rhodia, Inc.
(2) L. F. Miller and R. E. Bambury, *J. Med. Chem.*, **15**, 415 (1972).
(3) J. P. Paolini and L. J. Lendvay, *J. Med. Chem.*, **12**, 1031 (1969).
(4) T. Pyl, R. Giebelmann, and H. Beyer, *Justus Liebigs Ann. Chem.*, **643**, 145 (1961).

TABLE I
NMR SPECTRAL DATA (δ)



Compd	X	Y	Solvent	1 CH_3	6 CH_3	2 and/or 3 H[a]
1	H	H	$CDCl_3$	3.57	2.32	6.78 (m), 6.55 (d) (J = 2 Hz)
2[b]	Br	H	DMSO-d_6	3.89	2.35	7.74 (s, 2)
3	$C_5H_{10}N$	H	$CDCl_3$	3.40	2.28	6.83 (d), 6.52 (d) (J = 2 Hz)
4	CHO	H	$CDCl_3$	3.77	2.58	7.55 (d), 6.85 (d) (J = 2 Hz)
5	NO_2	H	DMSO-d_6	3.73	2.60	7.65 (d), 7.42 (d) (J = 2 Hz)
6	NHAc	H	$CDCl_3$	3.54	2.18	6.69 (d), 6.55 (d) (J = 2 Hz)
7	NAc_2	H	$CDCl_3$	3.67	2.18	6.73 (s, 1)
8	NO_2	NO_2	DMSO-d_6	3.85	2.60	8.85 (s, 1)

[a] Other significant nmr peaks: **1**, 5 H, δ 6.78; **2** (as HBr salt), δ 5.5 (br s, exch); **3**, δ 2.98 (m, 4), 1.58 (m, 6); **4**, δ 9.68 (s, 1); **6**, δ 2.25 (s, 3), 9.25 (br s); **7**, 2.32 (s, 6). [b] HBr salt.

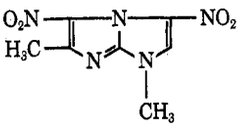
Treatment of **1** in chloroform with bromine gave 5-bromo-1,6-dimethyl-1*H*-imidazo[1,2-*a*]imidazole hydrobromide monohydrate (**2**). In most instances substitution at the 5 position was readily confirmed by the nmr spectrum which showed the 2,3 protons appearing as two doublets (Table I). However, in the case of **2** the 2,3-proton signal appeared as an apparent singlet, and it was not immediately clear where the substitution had occurred. Reaction of **2** with piperidine afforded the piperidino derivative (**3**). The nmr spectrum of this compound showed the expected pair of doublets, confirming the 5-position substitution of both **2** and **3**. Compound **2** was found to be unstable as the free base. Attempts to dibrominate **1** were unsuccessful giving only resinous material. Formylation of **1** under Vilsmeier conditions yielded the 5-formyl compound (**4**).

Nitrations of **1** were tried by a variety of standard methods which in most instances gave no isolable product, the ring system being quite sensitive to nitric acid. However, by dissolving **1** in cold concentrated H_2SO_4 and carefully adding *ca.* 1 equiv of nitric acid a small quantity of a mononitrated product, 1,6-dimethyl-5-nitro-1*H*-imidazo[1,2-*a*]imidazole (**5**), was obtained. These results led us to investigate several organic and inorganic nitrates as nitronium ion sources. The best yield of **5** (66%) was obtained by chilling **1** in sulfuric acid and carefully adding an equivalent amount of ethyl nitrate. Reduction of **5** in the presence of acetic anhydride gave a mixture of two products: 5-acetamido-1,6-dimethyl-1*H*-imidazo[1,2-*a*]-imidazole (**6**), whose structure was determined by its nmr spectrum, and 5-diacetylamino-1,6-dimethyl-1*H*-imidazo[1,2-*a*]imidazole (**7**).

By carefully treating **1** with 2 equiv of ethyl nitrate, a dinitrated product (**8**) was obtained. Since **8** could also be obtained by nitration of **5**, one of the $-NO_2$ groups was known to be in the 5 position; however, the location of the other group was not readily discernible. Attempts were made to determine the structure spectrally, by comparing the nmr spectrum of **8** with spectra of 1-methylnitroimidazoles of known structure, and by attempted measurement of a possible nuclear Overhauser effect (NOE). All such attempts were without success.

Reduction of **8** in the presence of acetic anhydride gave a complex mixture of products. In light of the isolation of **6** and **7** from the reduction of **5**, the mixture was probably composed of various mono- and diacetylated diamines; however, no effort was made to identify the components. The complexity of the mixture also precluded the use of the components as intermediates for structure identification.

In order to obtain at least an indication of the probable location of the second $-NO_2$ group in **8** a series of Hückel molecular orbital (HMO) calculations was made. The method of computation and parameters are discussed in the Experimental Section. Since the nitrations were electrophilic attacks carried out in strongly acidic media, the HMO derived quantities chosen for comparison were the electrophilic superdelocalizability (S^E) and the effective charge. Calculations were first made on **1** and indicated the 5 position as the favored site for electrophilic substitution, in agreement with the experimental results. Similar calculations were carried out on **5**. The S^E values calculated for the 2 and 3 positions of **5** (triprotonated model) were 1.175 and 1.234, respectively, indicating the 3 position as the favored site for electrophilic substitution.[5] We therefore feel that the most likely structure for **8** is 1,6-dimethyl-3,5-dinitro-1*H*-imidazo-[1,2-*a*]imidazole.



8

Experimental Section

Melting points were taken in open capillary tubes with a calibrated thermometer using a Thomas-Hoover melting point apparatus. Elemental analyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Mich. The nmr spectra were recorded on a Varian A-60 spectrometer by the Analytical Department of Merrell-National Laboratories. The NOE measurement was attempted on a Bruker HFX-90 spectrometer at the University of Cincinnati. HMO calculations were performed on an IBM S360/40 computer by the Biomedical Engineering

(5) A table of the calculated S^E and effective charge values will appear following these pages in the microfilm edition of this volume of the journal. Single copies may be obtained from the Business Operations Office, Books and Journals Division, American Chemical Society, 1155 Sixteenth St., N.W., Washington, D. C. 20036, by referring to code number JOC-73-1955. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche.

Department of Merrell-National Laboratories. The program used was previously described by Allen, *et al.*[6] Parameters chosen were those suggested by Streitwieser.[7]

5-Bromo-1,6-dimethyl-1*H*-imidazo[1,2-*a*]imidazole Hydrobromide Monohydrate (2).—A solution of Br_2 (1.2 g, 0.0074 mol) in $CHCl_3$ (5 ml) was slowly added to **1** (1 g, 0.0074 mol) in $CHCl_3$ (15 ml) maintained at 5°. The solution was stirred for 5 min and evaporated and the crude solid crystallized from $MeNO_2$ to give **2** (1.5 g), mp 132–133° dec. *Anal.* Calcd for $C_7H_{11}Br_2N_3O$: C, 26.86; H, 3.54; N, 13.42. Found: C, 27.07; H, 3.36; N, 13.64.

Reaction of 2 with Piperidine.—A mixture of **2** (3.1 g, 0.01 mol) and piperidine (2.5 g, 0.03 mol) in C_6H_6 (50 ml) was refluxed for 4 hr and cooled. The solution was extracted with H_2O (discarded), and the organic phase was dried ($MgSO_4$) and evaporated. The residue (1.6 g) was not readily purified either as the free base or as a salt; however, the nmr spectrum of the crude material confirmed the structure as 1,6-dimethyl-5-piperidino-1*H*-imidazo[1,2-*a*]imidazole (**3**).

1,6-Dimethyl-5-formyl-1*H*-imidazo[1,2-*a*]imidazole (4).—**1** (50 g, 0.37 mol) in DMF (100 ml) was slowly added to a formylation complex prepared as described by James, *et al.*,[8] from DMF (250 ml) and $POCl_3$ (80 g, 0.52 mol). The solution was stirred 1 hr at 25°, chilled for 16 hr, and then treated with H_2O (300 ml) and sufficient $NaHCO_3$ to bring the pH to 8. The solution was heated to reflux, cooled, and extracted with $CHCl_3$. The organic phase was extracted with 10% HCl which was then basified with 10% NaOH and extracted with $CHCl_3$. The $CHCl_3$ was evaporated to give a crude solid (50 g) which was crystallized from petroleum ether (bp 90–100°) yielding **4** (29 g), mp 130–135° (oxime mp 280° dec). *Anal.* Calcd for $C_8H_9N_3O$: C, 58.88; H, 5.56; N, 25.75. Found: C, 58.82; H, 5.54; N, 25.79.

1,6-Dimethyl-5-nitro-1*H*-imidazo[1,2-*a*]imidazole (5).—To concentrated H_2SO_4 (5 ml) chilled to −10° was slowly added **1** (1.3 g, 0.01 mol). The temperature was lowered to −20° and ethyl nitrate (0.9 g, 0.01 mol) was added dropwise. After stirring 5–10 min, the acid solution was poured on crushed ice and the pH adjusted to 4–5 with aqueous NaOH. The aqueous phase was extracted with $CHCl_3$ which was evaporated to give crude **5** (1.2 g). Crystallization from C_6H_6 gave pure **5**, mp 181–184°. *Anal.* Calcd for $C_7H_8N_4O_2$: C, 46.66; H, 4.47; N, 31.10. Found: C, 46.81; H, 4.44; N, 31.19.

Reduction of 5 in Acetic Anhydride Solution.—A solution of **5** (4 g, 0.02 mol) in Ac_2O (50 ml) was reduced under 1.5 atm of H_2 pressure for 16 hr in the presence of Raney nickel catalyst.[9] The catalyst was filtered off, the Ac_2O was evaporated, and the residue was taken up in $CHCl_3$. After stirring vigorously for several hours with aqueous $NaHCO_3$, the $CHCl_3$ was separated and evaporated to an oil (3.8 g) which crystallized on standing. A tlc showed two components, one predominant. By careful crystallization from EtOAc a small amount of the minor constituent was obtained, mp 133–137°. It was unsuitable for elemental analysis, but was shown by its nmr spectrum to be principally 5-acetamido-1,6-dimethyl-1*H*-imidazo[1,2-*a*]imidazole (**6**). The mother liquors were evaporated and carefully treated with *i*-PrOH–Et_2O to give a white solid, mp 124–127°, which was shown by its elemental analysis and nmr spectrum to be 5-diacetylamino-1,6-dimethyl-1*H*-imidazo[1,2-*a*]imidazole (**7**). *Anal.* Calcd for $C_{11}H_{14}N_4O_2$: C, 56.40; H, 6.02; N, 23.91. Found: C, 56.02; H, 6.10; N, 24.09.

1,6-Dimethyl-2(or 3),5-dinitro-1*H*-imidazo[1,2-*a*]imidazole (8).—In a manner similar to the preparation of **5**, **1** (16.2 g, 0.12 mol) in H_2SO_4 (150 ml) was treated with 1 equiv of ethyl nitrate (10.9 g, 0.12 mol) at −20°. After addition was complete the temperature was adjusted to −15° and a second equivalent of ethyl nitrate was added. The acid solution was stirred at −5° for 20 min and poured on crushed ice. The resulting solution was extracted with $CHCl_3$ which on evaporation gave crude **8**. Recrystallization from H_2O gave pure **8** (3.2 g), mp 190–192°. *Anal.* Calcd for $C_7H_7N_5O_4$: C, 37.34; H, 3.14; N, 31.11. Found: C, 37.41; H, 3.10; N, 31.24.

(6) R. C. Allen, G. L. Carlson, and C. J. Cavallito, *J. Med. Chem.*, **13**, 909 (1970).

(7) A. Streitwieser, "Molecular Orbital Theory for Organic Chemists," Wiley, New York, N. Y., 1961.

(8) P. N. James and H. R. Snyder in "Organic Synthesis," Collect. Vol. IV, Norman Rabjohn, Ed., Wiley, New York, N. Y., 1963, pp 539–541.

(9) Raney nickel was obtained from Pfaltz and Bauer, Inc., New York, N. Y.

Registry No.—**1**, 38739-75-2; **2**, 38739-94-5; **3**, 38739-95-6; **4**, 38739-96-7; **5**, 38739-97-8; **6**, 38739-98-9; **7**, 38739-99-0; **8**, 38740-00-0; piperidine, 110-89-4.

Acknowledgments.—The authors wish to thank Drs. Fred Kaplan and David Lankin of the University of Cincinnati for attempting the NOE determination. We also wish to express our thanks to Dr. Michael Randall for supervising the HMO calculations and Dr. Michael Edwards for his invaluable suggestions and assistance.

Internal Strain in Benzylic Radical Formation. The Effect of Ring Size in the Reaction of Trichloromethyl Radicals with Benzocycloalkenes

ROSY H.-W. WONG AND GERALD JAY GLEICHER*

Department of Chemistry, Oregon State University, Corvallis, Oregon 97331

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The degree of importance of steric factors in the formation of organic free radicals has not received full elucidation. Part of this is due to the complexity of the situation and the need to assess both intramolecular and intermolecular effects. The former can qualitatively be considered in terms of I strain as originally proposed by Brown.[1] Overberger, in describing the extension of this generalized approach to radical-forming reactions, has equated changes in activation energy with strain changes in cyclic systems.[2] Intermolecular interactions between attacking radicals and substrates can also greatly influence the course and extent of reaction. Such bulky species as the dialkylamino radical cation[3] and the trichloromethyl radical[4] show unexpectedly increased selectivity in hydrogen-abstraction processes because of this form of steric control.

The relation of internal strain to radical formation has been studied by several groups of workers. Relative rates of hydrogen atom abstraction from cycloalkanes in both the liquid and vapor phases have been obtained using chlorine atom,[5] bromine atom,[6] methyl radical,[7] trichloromethyl radical,[8] and trichloromethylsulfonyl radical,[5] among others. It was noted that ring size did, indeed, affect the relative rates of reaction. With few exceptions the order of reactivity was cyclobutane ≪ cyclopentane < cyclohexane < cycloheptane < cyclooctane. This order clearly shows that the ground-state strain of the cycloalkane cannot be the cause of the effect.

(1) (a) H. C. Brown and M. Gerstein, *J. Amer. Chem. Soc.*, **72**, 2926 (1950); (b) H. C. Brown and R. B. Johannessen, *ibid.*, **73**, 212 (1951).

(2) C. G. Overberger, H. Biletch, A. B. Finestone, J. Lilker, and J. Herbert, *ibid.*, **75**, 2078 (1953).

(3) R. Bernardi, R. Galli, and F. Minischi, *J. Chem. Soc. B*, 324 (1968).

(4) (a) G. J. Gleicher, *J. Org. Chem.*, **33**, 332 (1968); (b) W. D. Totherow and G. J. Gleicher, *J. Amer. Chem. Soc.*, **91**, 7150 (1969).

(5) G. A. Russell, *ibid.*, **80**, 4997 (1958).

(6) K. C. Ferguson and E. Whittle, *Trans. Faraday Soc.*, **67**, 2618 (1971).

(7) W. A. Pryor, D. L. Fuller, and J. P. Stanley, *J. Amer. Chem. Soc.*, **94**, 1632 (1972).

(8) (a) E. S. Huyser, E. Schimcke, and R. L. Burham, *J. Org. Chem.*, **28**, 2141 (1963); (b) F. B. Wampler and R. K. Kuntz, *Int. J. Chem. Kinet.*, **3**, 283 (1971).