Alkyl Nitrate Nitration of Active Methylene Compounds. IX. The Nitration of Alkyl Substituted Heterocyclic Compounds[1]

H. FEUER* AND J. P. LAWRENCE

Department of Chemistry, Purdue University, Lafayette, Indiana 47907

Received March 23, 1972

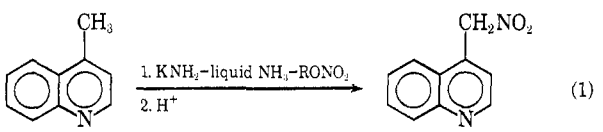
π-Deficient heterocyclic compounds such as 2-picoline (1) and 4-methylpyrimidine (2) and π-excessive heterocyclics such as 2-methylbenzoxazole (3) and 2-methylbenzothiazole (4) are readily converted to the corresponding α-nitroalkyl heterocyclics on treatment with an alkali metal amide and an alkyl nitrate in liquid ammonia. With 2,4-lutidine (5), 2,3-lutidine (6), and *s*-collidine (7) exclusive mononitration is observed, the reactivity of the methyl groups being in the order of 4 > 2 > 3. Spectral data of the α-nitroalkyl heterocyclics indicate that the primary nitro compounds are in equilibrium with their dipolar structures. The pK_a values of the three isomeric nitromethylpyridines have been determined and the order of acidities is 3 > 4 > 2.

In continuation of our studies of the alkyl nitration we are now reporting on its application to the synthesis of α-nitroalkyl heterocyclics.[2]

Previously, the only available methods for preparing these compounds involved several steps, and in general the overall yields were quite low.[3-7]

Both sodium and potassium amides were found to be effective as bases in the nitration reaction. By employing 4-picoline (8) as a model compound, it was found that, in the sodium amide–liquid ammonia system (A), a 1.0:2.5:3.1 molar ratio of 8 to sodium amide to *n*-propyl nitrate afforded optimum yields. In the potassium amide–liquid ammonia system (B) employing 2-picoline (1), a molar ratio of 1.0:2.0:2.5 of 1 to potassium amide to nitrate ester gave the highest yield.

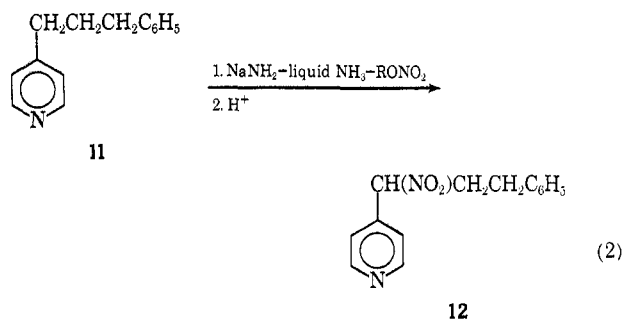
The generality of the reaction was established by its successful application to alkyl derivatives of π-deficient and π-excessive heterocyclics as well as to 2-methylthiazoline, a nonaromatic heterocyclic compound. As can be seen from the results which are summarized in Table I, systems A and B were not equally effective in providing optimum yields. For example, the nitration of lepidine (9) in systems A and B afforded 4-nitromethylquinoline (10) in 58 and 93% yields, respectively (eq 1). On the other hand,



9 10 (1)

in the nitration of 1-(4-pyridyl)-3-phenylpropane (11), the yield of 3-phenyl-1-(-4-pyridyl)nitropropane was 90% in system A and only 74% in system B (eq 2).

It is noteworthy that the nitrations of 5-ethyl-2-methylpyridine and of quinaldine (13) were only successful in system B. Moreover, as shown in Table

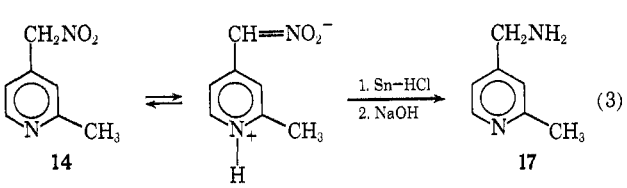


11 12 (2)

II, more concentrated reaction mixtures had to be employed to obtain potassium quinaldylnitronate (13a) in reasonable yield from 13. As indicated in Table I, the nitration of 13 in system A led only to 1-(2-quinolyl)-2-butanol. It is very likely that the alcohol formed from the base-catalyzed reaction of 13 and propanal. The latter originated by attack of base (NH_2^-) on propyl nitrate *via* α-hydrogen abstraction.

The nitrations of heterocyclics having more than one methyl group afforded only mononitration products (Table I) even though an excess of base and nitrate ester were employed. Also, further nitration was unsuccessful and resulted only in recovery of 14, when compound 14 was treated with 3.5 mol of amide and propyl nitrate. 2,4-Lutidine (5), 2,3-lutidine (6), 2,6-lutidine, and *s*-collidine (7) were converted to 2-methyl-4-nitromethylpyridine (14), 3-methyl-2-nitromethylpyridine (15), 6-methyl-2-nitromethylpyridine, and 2,6-dimethyl-4-nitromethylpyridine (16), respectively. The higher reactivities of the methyl groups in the 4 and 2 positions in compounds 5 and 6, respectively, have also been demonstrated in side-chain alkylation[8] and oximation[9] reactions.

The structure of compound 14 was confirmed by reduction to the known 4-aminomethyl-2-methylpyridine[10] (17) (eq 3) and by its nmr spectrum which



14 14a 17 (3)

(1) For previous publications see (a) H. Feuer and R. P. Monter, *J. Org. Chem.*, **34**, 991 (1969); (b) H. Feuer and M. Auerbach, *ibid.*, **35**, 2551 (1970).

(2) A preliminary announcement of this work has appeared: H. Feuer and J. P. Lawrence, *J. Amer. Chem. Soc.*, **91**, 1856 (1969).

(3) L. Zalukaev and E. Vanag, *Zh. Obshch. Khim.*, **26**, 2639 (1956); *J. Gen. Chem. USSR*, **26**, 2943 (1956).

(4) P. E. Fanta, R. A. Stein, and R. M. W. Rickett, *J. Amer. Chem. Soc.*, **80**, 4577 (1958).

(5) L. Zalukaev and E. Vanag, *Zh. Obshch. Khim.*, **29**, 1639 (1959); *J. Gen. Chem. USSR*, **29**, 1614 (1959).

(6) W. Ried and A. Sinharay, *Chem. Ber.*, **96**, 3306 (1963).

(7) L. Zalukaev and D. G. Vnenkovskaya, *Khim. Geterotsikl. Soedin.*, **3**, 515 (1967); *Chem. Abstr.*, **68**, 87112 (1968).

(8) H. Lochte and T. H. Cheavens, *J. Amer. Chem. Soc.*, **79**, 1667 (1957).

(9) S. E. Forman, *J. Org. Chem.*, **29**, 3323 (1964).

(10) E. Ochiai and T. Suzuki, *Pharm. Bull.*, **2**, 147 (1954); *Chem. Abstr.*, **50**, 1015 (1956).

TABLE I
PRODUCTS FROM REACTIONS OF SUBSTITUTED HETEROCYCLICS WITH ALKYL NITRATE IN LIQUID AMMONIA

Product[a,b]	System A,[c] yield, %[d]	System B,[e] yield, %[d]
2-Nitromethylpyridine	58	48[f]
3-Nitromethylpyridine	0[g]	0[h]
4-Nitromethylpyridine	66[f]	33
2-Methyl-4-nitromethylpyridine	69	53
6-Methyl-2-nitromethylpyridine	68	65
3-Methyl-2-nitromethylpyridine	32[i]	
5-Ethyl-2-nitromethylpyridine	0[j]	42[k]
2,6-Dimethyl-4-nitromethylpyridine	76	55
1-(4-Pyridyl)nitroethane	*l*	*l*
1-(4-Pyridyl)-3-phenylnitropropane	90	74
2-Nitromethylpyridine *N*-oxide	*m*	*n*
4-Nitromethylpyridine *N*-oxide	*o*	*o*
2-Nitromethylquinoline	0[p]	33[f]
4-Nitromethylquinoline	58	93
4-Nitromethylpyrimidine		71
1-Nitromethylisoquinoline	54	50
2-Nitromethylbenzoxazole	62	
2-Nitromethylbenzothiazole	66	
2-Nitromethylquinoxaline	55	58
4-Nitromethylcinnoline		88
2-Nitromethylthiazoline	43	

[a] Unless otherwise stated, the nitrations were carried out in *ca.* 0.5 *M* solutions of potassium amide or sodium amide in liquid ammonia and the nitro compounds were obtained directly after aqueous acidification of their crude nitronate salts with acetic acid. [b] Yields are based on starting material. [c] Sodium amide–liquid ammonia system. [d] In most cases unreacted starting material was recovered (see Experimental Section). [e] Potassium amide–liquid ammonia system. [f] Obtained after acidification of an aqueous solution of the pure salt of the nitro compound. [g] 3-Picoline was recovered in 91% yield. [h] 3-Picoline was recovered in 88% yield. [i] In another experiment 3-methyl-2-nitromethylpyridine was obtained in 52% yield when isolated as the picrate salt. [j] 5-Ethyl-2-methylpyridine was recovered in 87% yield. [k] The nitration was carried out in a 1.19 *M* solution of potassium amide in liquid ammonia. When a 0.55 *M* solution was used the yield was only 30%. [l] A mixture consisting of 1-(4-pyridyl)nitroethane and 4-acetylpyridine was obtained. [m] The product was isolated in 71% yield as the dibromo derivative, 2-(dibromonitromethyl)pyridine *N*-oxide. [n] Crude 2-nitromethylpyridine *N*-oxide was obtained in 54% yield after acidification of the crude salt with 5% hydrochloric acid. [o] The product was isolated in about 58% yield as the dibromo derivative, 4-(dibromonitromethyl)pyridine *N*-oxide. [p] The only product isolated was 26% of 1-(2-quinolyl)-2-butanol.

TABLE II
EFFECT OF POTASSIUM AMIDE CONCENTRATION ON THE NITRATION OF QUINALDINE[a]

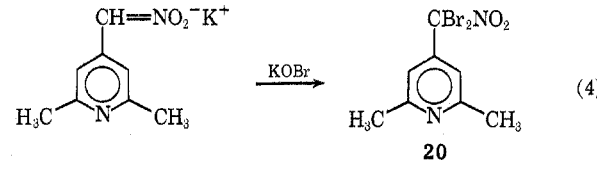
KNH_2, *M*	13a,[b] yield, %	Recovered 13, yield, %
0.35	0	88
0.59	42	42
1.58	43	43
2.84	50	37

[a] The molar ratio of **13** to KNH_2 to propyl nitrate was maintained in the ratio of 1.0:2.0:2.5. [b] Potassium quinaldylnitronate.

indicated that **14** was in equilibrium with its dipolar structure **14a**. The signal for the vinyl proton in **14a** fell at the same position (6.9 ppm) as that for the vinyl proton in sodium 4-picolylnitronate (**18**).

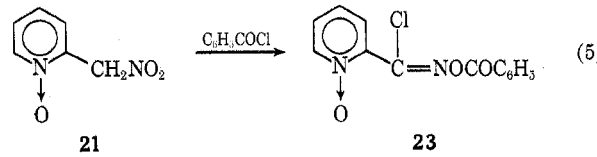
The structure of compound **15** was indicated by the 396-mμ absorption band in its ultraviolet spectrum. 3-Nitromethylpyridine (**19**) was found to absorb at 310 mμ (*vide infra*).

The structure of compound **16** was established by the fact that its dibromo derivative, 4-dibromonitromethyl-2,6-dimethylpyridine (**20**), showed in the nmr spectrum only one signal at 2.6 ppm for the two methyl groups. Compound **20** was prepared by treating the potassium salt of **16** with potassium hypobromite (eq 4).



20 (4)

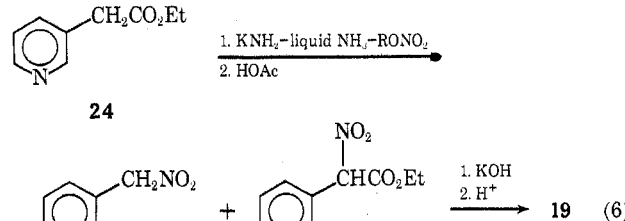
Nitrations of 2-picoline *N*-oxide and 4-picoline *N*-oxide led to the corresponding nitro salts which, however, could not be purified. A stronger acid than acetic acid, 5% hydrochloric acid was required to obtain the free nitro compounds from their salts. In this manner, 2-nitromethylpyridine *N*-oxide (**21**) was obtained in 54% yield, but it could not be purified.[11] On treatment with benzoyl chloride compound **21** was converted to the benzoyl derivative of 2-pyridylhydroxamyl chloride *N*-oxide (**23**) in 92% yield (eq 5). Similar conversions of α-nitroalkyl heterocyclics have been reported by Zalukaev.[12]



21 **23** (5)

Although the salts of the nitromethylpyridine *N*-oxides **21** and **22** could not be purified, they were converted on bromination in good yields to the stable dibromo derivatives, 2-(dibromonitromethyl)pyridine *N*-oxide and 4-(dibromonitromethyl)pyridine *N*-oxide, respectively.

Attempts to prepare 3-nitromethylpyridine (**19**) directly from 3-methylpyridine were unsuccessful and led only to recovered starting material, but it could be prepared by the nitration of ethyl 3-pyridylacetate (**24**) which afforded a mixture of compound **19** and ethyl α-nitro-3-pyridylacetate (**25**). The mixture was converted completely to **19** on treatment with base followed by acidification (eq 6).



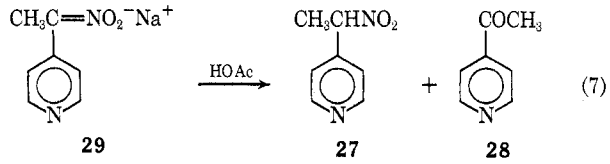
24 **19** **25** (6)

The nitration of 4-ethylpyridine (**26**) led to a mixture of 1-(4-pyridyl)nitroethane (**27**) and 4-acetylpyridine

(11) 4-Nitromethylpyridine *N*-oxide (**22**) which was obtained by acidifying the corresponding sodium or potassium salts could not be purified and decomposed on standing.

(12) L. Zalukaev and E. Vanag, *J. Gen. Chem. USSR*, **28**, 474 (1958); **30**, 529 (1960).

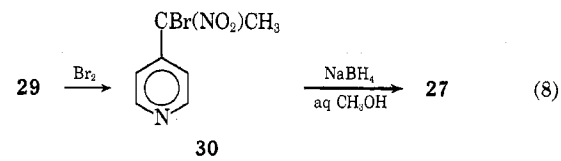
(28) after acidification of the crude nitro salt (29) (eq 7). Attempts to separate the mixture by distilla-



(7)

29 27 28

tion, column chromatography, or extraction of the nitro compound by base were unsuccessful. However, compound 27 was prepared in quantitative yield by reduction of 1-bromo-1-nitro-1-(4-pyridyl)ethane (30) with sodium borohydride. Compound 30 was prepared in 39% yield (based on 26) by bromination of crude salt 29 (eq 8). Ketone 28 was not formed dur-



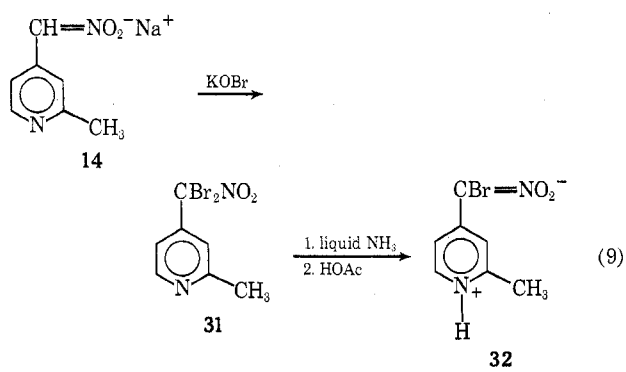
(8)

30

ing the nitration because analytically pure 27 was found to convert slowly to 28 on standing.[13]

The structures of the α-nitroalkyl heterocyclics were confirmed by ultraviolet, infrared, and nmr spectral data, and by conversion to derivatives such as picrate salts and halonitro compounds.

The halogen derivatives were prepared in good yield by treating aqueous solutions of the crude nitro salts with potassium hypobromite or hypochlorite. In the case of primary nitro compounds both acidic hydrogens were replaced by halogen. For example, bromination of the crude sodium salt of 14 afforded a 50% yield of 4-(dibromonitromethyl)-2-methylpyridine (31). It was readily converted to the monobromo compound, 4-(bromonitromethyl)-2-methylpyridine (32) in 83% yield on treatment with liquid ammonia at −33° (eq 9).[14]

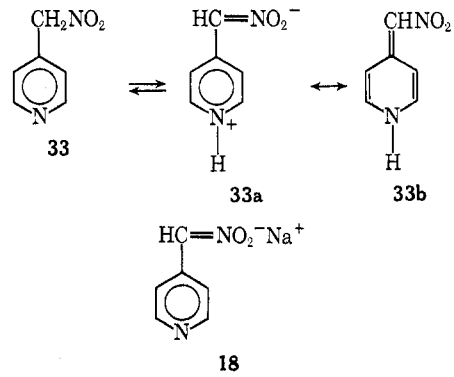


(9)

14 31 32

Spectra of α-Nitroalkyl Heterocyclics.—The ultraviolet spectra of all of the primary α-nitroalkyl heterocyclics revealed that these compounds are in equilibrium with their dipolar structures. The case of 4-nitromethylpyridine (33) is discussed somewhat in detail because its infrared and nmr spectra also confirmed the presence of the dipolar structure 33a.

In the ultraviolet spectrum of 33, there appear, in addition to the maxima at 233 and 258 mμ characteristic of the pyridine ring, absorption bands at 332 and 404 mμ. The former is attributed to the presence of the nitronate function in structure 33a because it



33 33a 33b

18

is also present in the spectrum of sodium 4-picolylnitronate (18). The band at 404 mμ which is absent in the spectrum of salt 18 might be attributed to the contribution of the higher energy structure 33b.

In the infrared spectrum, structure 33a is confirmed by a broad band at 3640–2200 cm^{-1} characteristic of the immonium group[15] and by a peak at 1502 cm^{-1} attributed to the carbon–nitrogen double-bond frequency of the nitronate group. It is shifted 77–103 cm^{-1} to lower frequencies from the normal stretching vibration of alkanenitronates[16] owing to the conjugation with the pyridine ring. In the salt 18, the peak appears at 1527 cm^{-1}.

The presence of structures 33 and 33a is also clearly demonstrated in the nmr spectrum which shows signals of both the methylene protons in 33 at 5.9 ppm and the vinyl proton in 33a at 7.0 ppm.

The presence of the dipolar tautomers of 2-nitromethylpyridine (34) and 3-nitromethylpyridine (19) are clearly indicated in their ultraviolet spectra by the absorption maxima at 325 and 398 mμ in 34 and at 310 mμ as a shoulder in 19. The absorption bands at 325 and 310 mμ are also present in the spectra of the potassium salts of 34 and 19, respectively.

The positions of the equilibria between the dipolar and neutral tautomers as calculated from the nmr data are given in Table III. They indicate that the contribution of the dipolar structures in the three isomeric nitromethylpyridines is in the order of 4 > 2 > 3. In the nitromethylquinolines the dipolar contribution is greater in the 2 isomer than in the 4 isomer. The reason for this, as suggested by molecular models might be due to steric interference to planarity in the 4 isomer between the nitro group and the peri hydrogen in the dipolar and quinoid contributions.

It should be emphasized that the ultraviolet, infrared, and nmr spectra of secondary α-nitroalkyl heterocyclics do not show the presence of dipolar structures.

Acidities of the Isomeric Nitromethylpyridines.—The pK_a values of the three isomeric nitromethylpyri-

(13) The transformation of a secondary nitro compound to a ketone was also found to occur with analytically pure diphenylnitromethane. It was converted on standing to benzophenone (unpublished results from the Ph.D. thesis of Dr. H. Friedman). It is very likely that a Nef-type reaction is involved in these transformations.

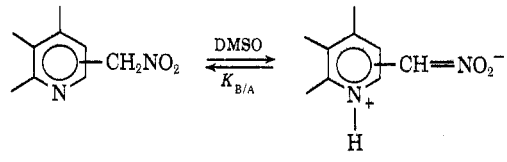
(14) Zalukaev reported that 2-(dibromonitromethyl)quinoline was converted to 2-(bromonitromethyl)quinoline on treatment with ethanolic ammonia at room temperature.[12]

(15) R. T. Conley, "Infrared Spectroscopy," Allyn and Bacon, Boston, Mass., 1966, p 136.

(16) H. Feuer, C. Savides, and C. N. R. Rao, *Spectrochim. Acta*, **19**, 431 (1963).

TABLE III

CALCULATED EQUILIBRIA BETWEEN THE TAUTOMERS OF NITROMETHYL HETEROCYCLICS FROM THEIR NMR SPECTRA

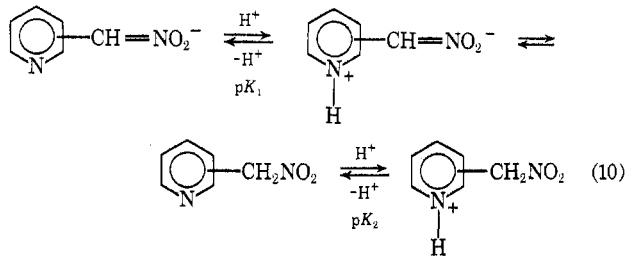


A B

Compd[a,b]	$K_{B/A}$
2-Nitromethylpyridine[c]	0.09
3-Nitromethylpyridine[c]	0.02
4-Nitromethylpyridine	0.50
2-Methyl-4-nitromethylpyridine	0.46
2,6-Dimethyl-4-nitromethylpyridine	0.67
2-Nitromethylquinoline	1.63
4-Nitromethylquinoline[c]	0.50
1-Nitromethylisoquinoline	3.56
4-Nitromethylpyrimidine	0.50
4-Nitromethylcinnoline	10.70
2-Nitrobenzothiazole	5.70

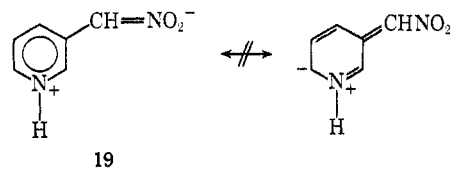
[a] Nmr data are detailed in the Experimental Section. [b] Unless otherwise stated the spectra were determined in dimethyl sulfoxide on a Varian A-60 spectrometer. [c] Spectra were determined on a Varian XL-100.

dines were determined by titrating aqueous solutions of their pure salts with dilute hydrochloric acid and by plotting the pH *vs.* the volume of titrant added. Two pK_a values were obtained because both the nitronate function and ring nitrogen are protonated in this process (eq 10). The salts employed in this study were



(10)

potassium 2-picolylnitronate (**35**), potassium 3-picolylnitronate (**36**), and **18**. The results which are summarized in Table IV, show that the order of acidity in the nitromethylpyridine series is 3 > 4 > 2. This order parallels that reported for the three isomeric hydroxypyridines.[17] The higher acidity of 3-hydroxypyridine has been explained by the lack of resonance stabilization of the dipolar structure. A similar rationale can be advanced to explain the higher acidity of 3-nitromethylpyridine (**19**).



19

Experimental Section

Equipment.—All infrared spectra were taken with a Perkin-Elmer recording spectrophotometer, Models 21 and 421. Nuclear magnetic resonance spectra were determined on a Varian Model A-60 analytical nmr spectrometer using tetramethylsilane as an internal standard. Ultraviolet spectra were obtained with a Bausch and Lomb Spectronic 505 UV spectrometer. Gas chromatographic analyses were performed on an Aerograph A-90-s using a 4 ft SF-96 on Chromosorb P or Chromosorb W column. Solvents were evaporated on a Buchler flash evaporator.

(17) A. Albert and J. N. Phillips, *J. Chem. Soc.*, 1294 (1956).

TABLE IV

pK_a VALUES OF THE ISOMERIC NITROMETHYLPYRIDINES AT 25°

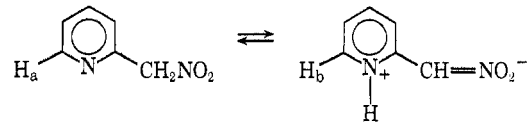
Nitromethylpyridine	pK_1	pK_2
2	7.21	3.92
3	5.55 (5.75)[a]	3.50
4	6.60	3.35

[a] This value was obtained by titrating an aqueous solution of 3-nitromethylpyridine with dilute aqueous potassium hydroxide.

Materials.—Ethyl nitrate and propyl nitrate of Eastman White Label grade were used as received. 4-Methylpyrimidine[18] and 4-methylcinnoline[19] were prepared by methods described in the literature. 1-Methylisoquinoline was prepared by catalytic dehydrogenation of 1-methyl-3,4-dihydroisoquinoline[20] with palladium on carbon in refluxing decalin. The remaining alkyl substituted heterocyclics were obtained from commercial sources and were distilled prior to use.

2-Nitromethylpyridine (34).—The following experiment is typical of the procedure employed in the sodium amide–liquid ammonia system (A). To a freshly prepared solution of sodium amide (0.23 mol) in 300 ml of liquid ammonia was added 8.4 g (0.09 mol) of 2-picoline (1) rapidly at −33°. After stirring for 10 min, 29.6 g (0.28 mol) of *n*-propyl nitrate was added as rapidly as possible while the temperature was kept below −33°.[21] The mixture was stirred an additional 5 min, the ammonia gradually replaced with absolute ether, and the reaction mixture filtered after room temperature was reached (3–5 hr).

The crude sodium 2-picolylnitronate[22] was dried *in vacuo*, dissolved in 20 ml of water, and acidified with 11.0 g of glacial acetic acid at room temperature. Extracting the solution with chloroform, drying (Na_2SO_4), concentrating the extract *in vacuo*, and distilling the residue afforded 7.3 g (58%) of **2-nitromethylpyridine**: bp 70° (0.2 mm); $n^{20}D$ 1.5519; uv max (95% C_2H_5OH) 253 mμ (sh), 259 (log ε 3.46), 265 (sh), 325 (3.23), and 398 (2.40); ir (neat) 1568 cm^{-1} (NO_2); nmr (DMSO-d_6) δ 8.5 (m, 0.9, H_a), 7.95 (m, 0.09, H_b), 7.4 (m, 3, N=CHCH=CHCH), 6.91 (s, 0.09, CH) and 5.5 (s, 2, CH_2).



Anal. Calcd for $C_6H_6N_2O_2$: C, 52.17; H, 4.38; N, 20.28. Found: C, 51.84; H, 4.41; N, 19.97.

The ethereal filtrate was concentrated *in vacuo* and the residue treated with excess ethanolic picric acid solution. The precipitate was recrystallized from 95% ethanol to yield 2.6 g (9%) of **2-picolinium picrate**: mp 167° (lit.[23] mp 165°).

2-Nitromethylpyridinium picrate was prepared in the usual manner:[24] mp 152° (95% ethanol) (lit.[25] mp 152–153°).

4-Nitromethylpyridine (33).—The experimental procedure was similar to that described for the preparation of **34**, except that 0.205 mol of sodium amide, 7.6 g (0.082 mol) of 4-picoline, and 26.9 g (0.256 mol) of *n*-propyl nitrate were employed.

Recrystallization of the crude salt from 95% ethanol afforded 12.1 g (92%) of **sodium 4-picolylnitronate**[22] (**18**): mp 255–257°;

(18) V. E. Smith and B. E. Christensen, *J. Org. Chem.*, **20**, 829 (1955).

(19) T. L. Jacobs, S. Winstein, R. B. Henderson, and E. C. Spaeth, *J. Amer. Chem. Soc.*, **69**, 1310 (1946).

(20) W. M. Whaley and W. H. Hartung, *J. Org. Chem.*, **14**, 650 (1949)

(21) *CAUTION!* The first few drops of alkyl nitrate should be added slowly because a considerable exotherm develops.

(22) *CAUTION!* The dry nitro salts exhibit a high heat of hydration and may decompose violently on exposure to the atmosphere.

(23) A. Ladenburg, *Justus Liebigs Ann. Chem.*, **247**, 1 (1888).

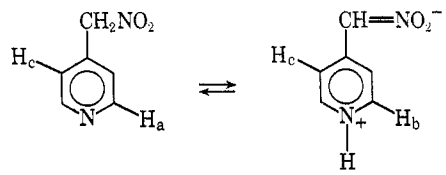
(24) R. Shriner, R. Fuson, and D. Curtin, "The Systematic Identification of Organic Compounds," 4th ed, Wiley, New York, N. Y., 1957, p 229.

(25) L. Zalukaev and E. Vanag, *J. Gen. Chem. USSR*, **27**, 3314 (1957).

uv max (95% C_2H_5OH) 332 mμ (log ε 4.13); ir (KBr) 1527 cm^{-1} ($C{=}NO_2^-$); nmr (D_2O) δ 8.3 (m, 2, N=CH), 7.6 (m, 2, N=CHCH), and 7.0 (s, 1, CH).

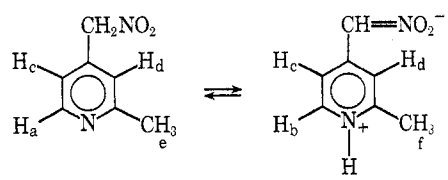
Anal. Calcd for $C_6H_5N_2NaO_2$: C, 45.00; H, 3.12; N, 17.50; Na, 14.37. Found: C, 44.99; H, 3.22; N, 17.36; Na, 14.32.

A solution of 5.0 g (0.031 mol) **18** in 25 ml of water was acidified at 0–5° with 3.8 g of glacial acetic acid. Filtering, drying *in vacuo*, and recrystallizing the precipitate from warm (~50°) 95% ethanol afforded 3.1 g (72%) of **4-nitromethylpyridine (33)**: mp 97° dec; uv max (95% C_2H_5OH) 233 mμ (log ε 3.28), 258 (3.23), 332 (3.47), and 4.0 (3.20); ir (KBr) 3640–2200 (=N^+H) and 1502 cm^{-1} ($C{=}NO_2^-$); nmr (DMSO-d_6) δ 8.9 (m, 1.33, H_a), 8.0 (m, 0.67, H_b), 7.6 (m, 2, H_c), 7.0 (s, 0.33, CH), and 5.9 (s, 1.33, CH_2).



Anal. Calcd for $C_6H_6N_2O_2$: C, 52.17; H, 4.38; N, 20.28. Found: C, 52.16; H, 4.43; N, 19.99.

2-Methyl-4-nitromethylpyridine (14).—From 0.21 mol of sodium amide, 9.1 g (0.08 mol) of 2,4-lutidine (**5**) and 28.0 g (0.27 mol) of *n*-propyl nitrate there was obtained 22.4 g of crude salt, dried *in vacuo*.[22] A 17.4-g portion was dissolved in 25 ml of water and acidified with 8.0 g of glacial acetic acid at 0–5°. Filtering, drying *in vacuo*, and recrystallizing the precipitate from warm (~50°) acetone–water (1:1) gave 6.9 g (69%) of **2-methyl-4-nitromethylpyridine**: mp 120°; uv max (95% C_2H_5OH) 241 mμ (log ε 3.18), 262 (3.28), 331 (3.48), and 394 (3.44); ir (KBr) 3640–2191 (=N^+H) and 1497 cm^{-1} ($C{=}NO_2^-$); nmr (DMSO-d_6) δ 8.6 (m, 0.68, H_a), 7.9 (m, 0.32, H_b), 7.4 (m, 2, H_c + H_d), 6.9 (s, 0.32, CH), 5.8 (s, 1.37, CH_2), 2.5 (s, 2.06, H_e), and 2.4 (s, 0.94, H_f).



Anal. Calcd for $C_7H_8N_2O_2$: C, 55.25; H, 5.30; N, 18.41. Found: C, 55.40; H, 5.49; N, 18.17.

The ethereal filtrate was concentrated *in vacuo* and the residue treated with excess picric acid solution to yield 2.9 g (11%) of **2,4-lutidinium picrate**: mp 180° (lit.[23] mp 179°).

Reduction of 2-Methyl-4-nitromethylpyridine (14).—Granulated tin (12.0 g) was added in two portions over a 10-min period to a solution of 4.0 g (0.03 mol) **14** in 200 ml of 6 *N* hydrochloric acid. After refluxing for 2 hr, the colorless solution was cooled and made basic to litmus with 6 *N* sodium hydroxide. The filtrate was extracted with ether and dried (Na_2SO_4), and the ethereal extract concentrated *in vacuo* to give a colorless oil which was divided into two portions.

Treating one portion with ethanolic picric acid gave **4-aminomethyl-2-picolinium picrate**: mp 198° dec (95% EtOH) (lit.[10] mp 195–196°).

The second portion was taken up in absolute ether and saturated with hydrogen chloride to give **4-aminomethyl-2-picolinium chloride**: mp 272° (MeOH) (lit.[10] mp 274°).

6-Methyl-2-nitromethylpyridine (37).—The general procedure was followed except that the acidified solution was extracted with chloroform, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was eluted with benzene on an aluminum oxide (alumina, acid washed) column. 2,6-Lutidine (10.0 g, 0.094 mol) gave 9.7 g (68%) of **6-methyl-2-nitromethylpyridine**: $n^{20}D$ 1.5487; uv max (95% C_2H_5OH) 258 mμ (sh), 263 (log ε 3.49), 270 (sh), 310 (2.67), and 396 (2.83); ir (neat) 1553 cm^{-1} (NO_2); nmr (CCl_4) δ 7.2–7.9 (m, 3, ring H), 5.6 (s, 2, CH_2), and 2.6 (s, 3, CH_3).

Anal. Calcd for $C_7H_8N_2O_2$: C, 55.25; H, 5.30; N, 18.41. Found: C, 55.04; H, 5.54; N, 18.48.

6-Methyl-2-nitromethylpyridinium picrate was prepared in the usual manner:[24] mp 122–124° dec (95% ethanol).

Anal. Calcd for $C_{13}H_{11}N_5O_9$: C, 40.94; H, 2.89; N, 18.37. Found: C, 41.03; H, 3.00; N, 18.08.

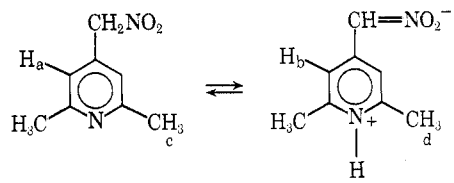
3-Methyl-2-nitromethylpyridine (15).—The work-up procedure was similar to that described for the preparation of **37**. 2,3-Lutidine (9.9 g, 0.092 mol) gave 4.5 g (32%) of **3-methyl-2-nitromethylpyridine**: mp 79°; uv max (95% C_2H_5OH) 256 mμ (sh), 263 (log ε 4.01), 279 (sh), 302 (3.32), and 396 (3.87); ir (KBr) 1551 cm^{-1} (NO_2); nmr ($CDCl_3$) δ 8.7 (m, 2, N=CHCH=CH), 7.6 (m, 1, N=CHCH), 5.7 (s, 2, CH_2), and 2.5 (s, 3, CH_3).

Anal. Calcd for $C_7H_8N_2O_2$: C, 55.25; H, 5.30; N, 18.41. Found: C, 54.99; H, 5.08; N, 18.55.

3-Methyl-2-nitromethylpyridinium picrate was prepared in the usual manner:[24] mp 157° (95% ethanol).

Anal. Calcd for $C_{13}H_{11}N_5O_9$: C, 40.94; H, 2.97; N, 18.37. Found: C, 40.92; H, 3.08; N, 18.10.

2,6-Dimethyl-4-nitromethylpyridine (16) (76%): mp 129° dec (H_2O); uv max (95% C_2H_5OH) 258 mμ (sh), 266 (log ε 3.49), 279 (sh), and 401 (3.92); ir (KBr) 3640–2078 (=N^+H) and 1475 cm^{-1} ($C{=}NO_2^-$); nmr (DMSO-d_6) δ 7.4 (s, 2, H_a + H_b), 6.9 (s, 0.4, CH), 5.9 (s, 1.2, CH_2), 2.5 (s, 3.6, H_c), and 2.4 (s, 2.4, H_d).

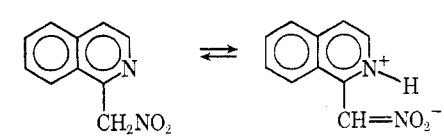


Anal. Calcd for $C_8H_{10}N_2O_2$: C, 57.83; H, 6.02; N, 16.87. Found: C, 58.07; H, 6.28; N, 17.13.

1-(4-Pyridyl)-3-phenylnitropropane (12) (90%): mp 58° (EtOH); uv max (95% C_2H_5OH) 260 mμ (log ε 3.22); ir (KBr) 1551 cm^{-1} (NO_2); nmr ($CDCl_3$) δ 8.9 (m, 2, N=CH), 7.4 (m, 7, N=CHCH + C_6H_5), 5.5 (m, 1, CH), and 2.8 [m, 4, $(CH_2)_2$].

Anal. Calcd for $C_{14}H_{14}N_2O_2$: C, 69.40; H, 5.83; N, 11.56. Found: C, 69.47; H, 5.89; N, 11.33.

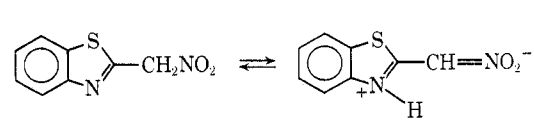
1-Nitromethylisoquinoline (54%): mp 167° dec (95% EtOH); uv max (95% C_2H_5OH) 230 mμ (log ε 4.20), 253 (3.57), 262 (3.59), 305 (3.85), 380 (sh), 410 (4.28), and 432 (4.34); ir (KBr) 1538 cm^{-1} (NO_2); nmr[26] (DMSO-d_6) δ 14.0 (s, NH), 6.8–8.5 (m, ring H), 7.2 (s, CH), nad 6.4 (s, CH_2).



Anal. Calcd for $C_{10}H_8N_2O_2$: C, 63.82; H, 4.26; N, 14.89. Found: C, 63.82; H, 4.14; N, 15.10.

2-Nitromethylbenzoxazole (3) (62%): mp 76° (lit.[6] mp 78°) (EtOH); uv max (95% C_2H_5OH) 236 mμ (log ε 3.79), 265 (3.39), 272 (3.43), 280 (3.29), and 348 (3.45); ir (KBr) 1558 cm^{-1} (NO_2); nmr ($CDCl_3$) δ 7.2–7.9 (m, 4, ring H) and 5.8 (s, 2, CH_2).

2-Nitromethylbenzothiazole (4).—The general procedure was followed except crude **4** was purified by dissolving it in 200 ml of 5% aqueous sodium bicarbonate, precipitating with glacial acetic acid and recrystallizing from warm (~50°) 95% ethanol. 2-Methylbenzothiazole (10.6 g, 0.071 mol) gave 9.1 g (66%) **2-nitromethylbenzothiazole**: mp 144° dec (lit.[6] mp 125–126° dec); uv max (95% C_2H_5OH) 383 mμ (log ε 4.21); ir (KBr) 3599–2162 (=N^+H) and 1473 cm^{-1} ($C{=}NO_2^-$); nmr[26] (DMSO-d_6) δ 9.1 (s, NH), 7.0–8.2 (m, ring H + CH), and 6.3 (s, CH_2).

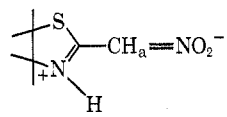


Anal. Calcd for $C_8H_6N_2O_2S$: C, 49.48; H, 3.02; N, 14.43, S, 16.49. Found: C, 49.20; H, 2.89; N, 14.15; S, 16.30.

2-Nitromethylthiazoline (43%): mp 128–130° dec; ir (KBr)

(26) The relative proton values could not be determined because the signals for the aromatic and vinyl protons fell in the same range.

3636–2439 (=N⁺H) and 1575 cm⁻¹ (C=NO₂⁻); nmr (DMSO-d_6) δ 9.1 (s, 0.42, NH),[27] 7.0 (s, 1, H_a), and 3.1–4.1 (m, 4, CH_2).

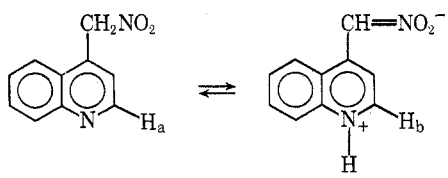


Anal. Calcd for $C_4H_6N_2O_2S$: C, 32.88; H, 4.11; N, 19.18; S, 21.92. Found: C, 33.48; H, 4.40; N, 18.56; S, 22.21.

Attempts to further purify the crude product by recrystallization or sublimation resulted in decomposition.

4-Nitromethylquinoline (**10**).—The following experiment is typical of the procedure employed in the potassium amide–liquid ammonia system (B). To a freshly prepared solution of potassium amide (0.13 mol) in 300 ml of liquid ammonia was added rapidly 9.3 g (0.06 mol) of lepidine (**9**) at −33°. After the mixture stirred for 3 min, 17.2 g (0.16 mol) of *n*-propyl nitrate was added as rapidly as possible while the temperature was kept below −33°.[21] The mixture was stirred an additional 5 min, the ammonia gradually replaced with absolute ether, and the reaction mixture was filtered after room temperature was reached (3–4 hr).

The crude salt[22] was dried *in vacuo*, dissolved in 100 ml of water, and acidified with 7.9 g of glacial acetic acid at room temperature. The precipitate was filtered, dried *in vacuo*, and recrystallized from warm (~50°) 95% ethanol to yield 11.3 g (93%) of **4-nitromethylquinoline**: mp 136° dec; uv max (95% C_2H_5OH) 304 mμ (log ε 3.50), 317 (3.51), 370 (3.42), 440 (sh), and 456 (3.44); ir (KBr) 3640–2213 (=N⁺H) and 1470 cm⁻¹ (C=NO₂⁻); nmr (100 MHz) (DMSO-d_6) δ 9.06 (d, 0.66, H_a), 8.47 (d, 0.34, H_b), 8.35–7.45 (m, 5.7, NH + CH + ring H), and 6.42 (s, 1.32, CH_2).



Anal. Calcd for $C_{10}H_8N_2O_2$: C, 63.82; H, 4.26; N, 14.89. Found: C, 63.67; H, 4.73; N, 14.54.

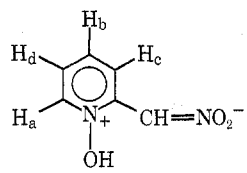
5-Ethyl-2-nitromethylpyridine.—The experimental procedure was similar to that described for the preparation of **10**, except that 0.179 mol of potassium amide in 150 ml of liquid ammonia, 10.8 g (0.089 mol) of 5-ethyl-2-methylpyridine, and 23.5 g (0.224 mol) of *n*-propyl nitrate were employed. Work-up as described in the preparation of compound **37** gave 6.2 g (42%) of 5-ethyl-2-nitromethylpyridine: $n^{20}D$ 1.5378; uv max (95% C_2H_5OH) 259 mμ (sh), 264 (log ε 3.28), 270 (3.27), 322 (2.67), and 400 (2.84); ir (neat) 1555 cm⁻¹ (NO_2); nmr (CCl_4) δ 8.6 (m, 1, N=CH), 7.4–7.9 (m, 2, CH=CH), 5.6 (s, 2, CH_2NO_2), 2.7 (q, 2, CH_2), and 1.3 (t, 3, CH_3).

Anal. Calcd for $C_8H_{10}N_2O_2$: C, 57.83; H, 6.02; N, 16.87. Found: C, 57.58; H, 5.86; N, 16.64.

5-Ethyl-2-nitromethylpyridinium picrate was prepared in the usual manner:[24] mp 115°.

Anal. Calcd for $C_{14}H_{13}N_5O_9$: C, 42.53; H, 3.29; N, 17.72. Found: C, 42.76; H, 3.57; N, 17.68.

2-Nitromethylpyridine *N*-Oxide (**21**).—The experimental procedure was similar to that described for the preparation of compound **10** except that the crude dry salt[22] was dissolved in 20 ml of water and carefully acidified with 5% hydrochloric acid at 0–5° to pH 2. The precipitate was filtered, washed with a little cold water, and recrystallized repeatedly from 95% ethanol to give 2.4 g (54%) of analytically impure 2-nitromethylpyridine *N*-oxide: mp 120° dec; ir (KBr) 3636–1681 (OH), 1546 (C=NO₂⁻), and 1220–1205 cm⁻¹ (N–O); nmr (DMSO-d_6) δ 11.4 (s, 1, OH), 8.0–8.4 (m, 1, H_a), and 7.2–8.0 (m, 4, H_b + H_c + H_d + CH).



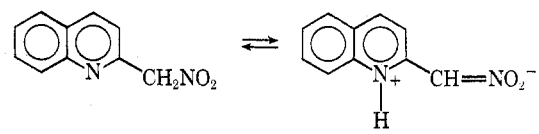
(27) This value was determined by comparing the integrated area with that for H_a considered to be 1.0. The low integration is probably due to the broadness of the signal.

2-Nitromethylquinoline.—The experimental procedure was similar to that described for the preparation of compound **10** except that 0.284 mol of potassium amide in 100 ml of ammonia, 20.3 g (0.142 mol) of quinaldine (**13**), and 37.4 g (0.356 mol) of *n*-propyl nitrate were employed.

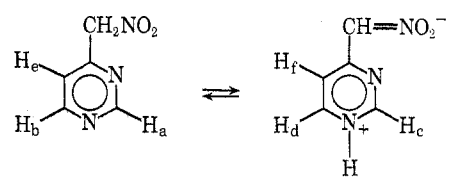
The crude salt was recrystallized from 95% ethanol to give 16.0 g (50%) of **potassium 2-quinaldylnitronate**:[22] mp 290° dec; uv max (95% C_2H_5OH) 283 mμ (sh), 290 (log ε 4.02), 323 (4.09), and 337 (4.09); ir (KBr) 1531 cm⁻¹ (C=NO₂⁻); nmr (D_2O) δ 6.9–8.4 (m, 6, ring H) and 6.9 (s, 1, CH).

Anal. Calcd for $C_{10}H_7KN_2O_2$: C, 53.10; H, 3.10; K, 17.30; N, 12.39. Found: C, 53.01; H, 3.23; K, 17.04; N, 12.54.

Concentrating the ethereal filtrate *in vacuo* afforded 7.4 g (37%) of unreacted **13**. Potassium 2-quinaldylnitronate (16.0 g, 0.07 mol) gave (67%) of **2-nitromethylquinoline**: mp 122° (95% EtOH) (lit.[3] mp 121–122°); uv max (95% C_2H_5OH) 302 mμ (log ε 3.67), 395 (sh), 416 (4.27), and 439 (4.37); ir (KBr) 1538 cm⁻¹ (NO_2); nmr (DMSO-d_6) δ 13.2 (s, 0.38, NH), 6.8–8.4 (m, 6, ring H), 7.0 (s, 0.62, CH), and 5.9 (s, 0.76, CH_2).



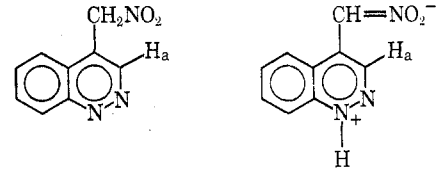
4-Nitromethylpyrimidine (71%): mp 125° dec (CH_3OH); uv max (95% C_2H_5OH) 244 mμ (log ε 3.45), 362 (3.58), and 402 (sh); ir (KBr) 1575 cm⁻¹ (NO_2); nmr (DMSO-d_6) δ 9.1 (m, 0.78, H_a), 8.8 (m, 0.78, H_b), 8.4 (s, 0.33, H_c), 7.8 (m, 0.33, H_d), 7.6 (m, 0.78, H_e), 7.2 (m, 0.33, H_f), 6.8 (s, 0.33, CH), and 5.9 (s, 1.33, CH_2).



Anal. Calcd for $C_5H_5N_3O_2$: C, 43.17; H, 3.59; N, 30.22. Found: C, 43.38; H, 3.70; N, 30.10.

4-Nitromethylquinoxaline. (58%): mp 121° (purified by sublimation at 100°, 0.03 mm) (lit.[4] mp 122–123°); uv max (95% C_2H_5OH) 235 mμ (log ε 4.27), 302 (sh), 317 (3.77), 407 (3.62), 435 (sh), and 462 (sh); ir (KBr) 1537 cm⁻¹ (NO_2); nmr (DMSO-d_6) δ 9.0 (s, 1, N=CH), 7.7–8.3 (m, 4, C_6H_4), and 5.8 (s, 2, CH_2).

4-Nitromethylcinnoline (88%): mp 152° dec (95% EtOH); uv max (95% C_2H_5OH) 260 mμ (log ε 3.69), 282 (sh), 322 (3.27), 430 (sh), 450 (4.13), and 479 (4.17); ir (KBr) 1515 cm⁻¹ (C=NO₂⁻); nmr (DMSO-d_6) δ 13.6 (s, 0.52, NH),[27] 9.3 (s, 1, H_a), 7.1–8.0 (m, 4, C_6H_4), 7.4 (s, 0.91, CH), and 6.4 (s, 0.17, CH_2).



Anal. Calcd for $C_9H_7N_3O_2$: C, 57.14; H, 3.65; N, 22.22. Found: C, 57.24; H, 3.85; N, 22.19.

Potassium 2-picolylnitronate (**35**) (67%): mp 294–296° dec (95% EtOH); uv max (95% C_2H_5OH) 327 mμ (log ε 3.77); ir (KBr) 1538 cm⁻¹ (C=NO₂⁻); nmr (D_2O) δ 8.4 (m, 2, N=CHCH=CHCH), 7.8 (m, 1, N=CHCH=CH), 7.2 (m, 1, N=CHCH), and 7.2 (s, 1, CH).

Anal. Calcd for $C_6H_5KN_2O_2$: C, 40.91; H, 2.84; K, 22.21; N, 15.91. Found: C, 40.87; H, 2.93; K, 21.94; N, 16.10.

3-Nitromethylpyridine (**19**).—To a freshly prepared solution of potassium amide (0.085 mol) in 300 ml of liquid ammonia was added rapidly at −33° 12.7 g (0.077 mol) of ethyl 3-pyridylacetate (**24**). After the mixture stirred for 3 min, 10.5 g (0.115 mol) of ethyl nitrate was added as rapidly as possible while the temperature was kept below −33°. The mixture was stirred an additional hour, the ammonia gradually replaced with absolute ether, and after attaining room temperature (3–4 hr) the reaction mixture was filtered. The solid as dissolved in 100 ml of water and acidified with glacial acetic acid to pH 5. The solution was ex-

tracted with chloroform and dried ($MgSO_4$), and the extract concentrated *in vacuo* to yield 9.6 g of a pale yellow oil. An nmr spectrum of this material indicated that it was a mixture consisting of 65% **19** and 35% **ethyl α-nitro-3-pyridylacetate (25)**: nmr ($CDCl_3$) δ 8.6 (m, 2, N=CH), 7.8 (m, 1, N=CHCH=CH), 7.3 (m, 1, N=CHCH), 6.3 (s, 0.32, CH), 5.5 (s, 1.28, CH_2NO_2), 4.2 (q, 0.67, CH_2), and 1.2 (t, 1.07, CH_3).

The mixture was dissolved in 25 ml of 40% aqueous sodium hydroxide (the temperature rose to 60°), 20 ml of water was added, and the solution heated to 80°. After cooling to 10–15°, the mixture was diluted with a little water, acidified to pH 4–5 with aqueous oxalic acid, and sodium oxalate removed by filtration. The filtrate was extracted with chloroform, dried ($MgSO_4$), and concentrated *in vacuo*. Eluting the residue with chloroform on an aluminum oxide (alumina, acid washed) column gave 7.0 g (66%) of pure **3 nitromethylpyridine**: $n^{20}D$ 1.5338; uv max (95% C_2H_5OH) 310 mμ (log ε 2.66); ir (neat) 1563 cm^{-1} (NO_2); nmr (DMSO-d_6) δ 8.3 (m, 2, N=CH), 7.5 (m, 1, N=CHCH=CH), 7.0 (m, 1, N=CHCH), and 5.4 (s, 2, CH_2).

Anal. Calcd for $C_6H_6N_2O_2$: C, 52.17; H, 4.38; N, 20.28. Found: C, 52.18; H, 4.58; N, 20.40.

3-Nitromethylpyridinium picrate was prepared in the usual manner:[24] mp 150–151° (95% EtOH).

Anal. Calcd for $C_{12}H_9N_5O_9$: C, 39.24; H, 2.47; N, 19.07. Found: C, 39.35; H, 2.41; N, 19.37.

1-(4-Pyridyl)nitroethane (27).—To a solution of 1.5 g (39.0 mmol) sodium borohydride in 20 ml of 75% aqueous methanol (by volume) was added 2.0 g (8.7 mmol) of 1-bromo-1-(4-pyridyl)-nitroethane (**30**) (*vide infra* for preparation) at such a rate as to maintain a gentle reflux. After the addition was completed the reaction mixture was cooled to room temperature, diluted with 50 ml of water, and acidified to pH 1–2 with 30% sulfuric acid. The solution was then concentrated to 50 ml *in vacuo* and the residue neutralized with 5% aqueous sodium bicarbonate. The solution was extracted with methylene chloride and dried ($MgSO_4$), and the extract concentrated *in vacuo* to yield 1.3 g (100%) of **1-(4-pyridyl)nitroethane**: $n^{25}D$ 1.5255; uv max (95% C_2H_5OH) 258 mμ (log ε 3.25); ir (neat) 1555 cm^{-1} (NO_2); nmr (CCl_4) δ 8.6 (m, 2, N=CH), 7.4 (m, 2, N=CHCH), 5.7 (q, 1, CH), and 1.8 (d, 3, CH_3).

Anal. Calcd for $C_7H_8N_2O_2$: C, 55.25; H, 5.30; N, 18.41. Found: C, 55.35; H, 5.26; N, 18.61.

4-(1-Nitroethyl)pyridinium picrate was prepared in the usual manner:[24] mp 118–120° dec (95% EtOH).

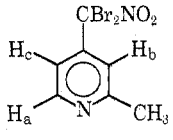
Anal. Calcd for $C_{13}H_{11}N_5O_9$: C, 40.94; H, 2.89; N, 18.37. Found: C, 41.11; H, 3.06; N, 18.27.

2-(Dibromonitromethyl)pyridine.—The following experiment is typical of the procedure employed for the bromination of the salts of α-nitroalkyl heterocyclics. Crude sodium 2-picolylnitronate obtained from the nitration of 7.8 g (0.08 mol) 2-picoline (**1**) was dissolved in 100 ml of water and added in one portion to 0.17 mol of aqueous potassium hypobromite (prepared from 26.9 g of bromine and 22.2 g of 85% assay potassium hydroxide in 100 ml of water) at 0–5°. The solution was extracted with chloroform and dried (Na_2SO_4). The extract was concentrated *in vacuo* and the residue recrystallized from ether–petroleum ether (bp 30–60°) (1:1) to yield 14.2 g (57%) of **2-(dibromonitromethyl)-pyridine**: mp 43° (lit.[7] mp 42–43°); ir (KBr) 1575 cm^{-1} (NO_2); nmr (CCl_4) δ 8.5 (m, 1, N=CH), 7.9 (m, 2, N=CHCH=CHCH), and 7.3 (m, 1, N=CHCH).

4-(Dibromonitromethyl)pyridine (61%): mp 94–97° (95% EtOH); ir (KBr) 1587 cm^{-1} (NO_2); nmr ($CDCl_3$) δ 8.8 (m, 2, N=CH) and 7.6 (m, 2, N=CHCH).

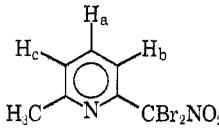
Anal. Calcd for $C_6H_4Br_2N_2O_2$: C, 24.32; H, 1.35; Br, 54.05; N, 9.46. Found: C, 24.59; H, 1.58; Br, 54.15; N, 9.49.

4-(Dibromonitromethyl-2-methylpyridine (31) (50%): mp 107° (95% EtOH); ir (KBr) 1575 cm^{-1} (NO_2); nmr ($CDCl_3$) δ 8.6 (m, 1, H_a), 7.4 (m, 2, $H_b + H_c$), and 2.7 (s, 3, CH_3).



Anal. Calcd for $C_7H_6Br_2N_2O_2$: C, 27.10; H, 1.94; Br, 51.45; N, 9.03. Found: C, 27.30; H, 2.09; Br, 51.59; N, 8.98.

2-(Dibromonitromethyl)-6-methylpyridine (54%): mp 56–57° (95% EtOH); ir (KBr) 1580 cm^{-1} (NO_2); nmr ($CDCl_3$) δ 7.9 (m, 2, $H_a + H_b$), 7.3 (m, 1, H_c), and 2.5 (s, 3, CH_3).



Anal. Calcd for $C_7H_6Br_2N_2O_2$: C, 27.10; H, 1.94; Br, 51.45; N, 9.03. Found: C, 26.90; H, 2.07; Br, 51.59; N, 8.75.

2-(Dibromonitromethyl)-3-methylpyridine (49%): mp 97° (95% EtOH); ir (KBr) 1590 cm^{-1} (NO_2); nmr ($CDCl_3$) δ 8.5 (m, 1, N=CH), 7.3–7.9 (m, 3, N=CHCH=CHCH), and 2.6 (s, 3, CH_3).

Anal. Calcd for $C_7H_6Br_2N_2O_2$: C, 27.10; H, 1.94; Br, 51.45; N, 9.03. Found: C, 26.82; H, 1.70; Br, 51.70; N, 8.77.

4-(Dibromonitromethyl)-2,6-dimethylpyridine (20) (41%): mp 90–94° (chloroform–hexane, 1:1); ir (KBr) 1575 cm^{-1} (NO_2); nmr ($CDCl_3$) δ 7.4 (s, 2, ring H) and 2.6 (s, 6, CH_3).

Anal. Calcd for $C_8H_8Br_2N_2O_2$: C, 29.63; H, 2.47; Br, 49.39; N, 8.64. Found: C, 29.74; H, 2.58; Br, 49.20; N, 8.48.

1-Bromo-1-(4-pyridyl)nitroethane) (30) (39%): bp 80–82° (0.13 mm); $n^{20}D$ 1.5693; ir (neat) 1575 cm^{-1} (NO_2); nmr (CCl_4) δ 8.7 (m, 2, N=CH), 7.5 (m, 2, N=CHCH), and 2.6 (s, 3, CH_3).

Anal. Calcd for $C_7H_7BrN_2O_2$: C, 36.36; H, 3.03; Br, 34.63; N, 12.12. Found: C, 36.40; H, 3.07; Br, 34.52; N, 12.25.

1-Bromo-1-(4-pyridyl)-3-phenylnitropropane (62%): mp 64–66° (95% EtOH); ir (KBr) 1567 cm^{-1} (NO_2); nmr ($CDCl_3$) δ 8.9 (m, 2, N=CH), 7.6 (m, 2, N=CHCH), 7.4 (m, 5, C_6H_5), and 2.7–3.3 (m, 4, CH_2CH_2).

Anal. Calcd for $C_{14}H_{13}BrN_2O_2$: C, 52.34; H, 4.36; Br, 24.92; N, 8.97. Found: C, 52.19; H, 4.28; Br, 25.03; N, 8.69.

2-(Dibromonitromethyl)pyridine *N*-oxide (71%): mp 181–183° dec (acetone–95% ethanol, 2:1); ir (KBr) 1575 cm^{-1} (NO_2); nmr (DMSO-d_6) δ 8.3 (m, 2, N=CHCH=CHCH) and 7.4 (m, 2, N=CHCH=CH).

Anal. Calcd for $C_6H_4Br_2N_2O_3$: C, 23.08; H, 1.28; Br, 51.28; N, 8.97. Found: C, 23.35; H, 1.46; Br, 51.00; N, 8.75.

4-(Dibromonitromethyl)pyridine *N*-oxide (59%): mp 103–104° dec (chloroform); ir (Nujol) 1577 cm^{-1} (NO_2); nmr ($CDCl_3$) δ 8.2 (m, 2, N=CH) and 7.7 (m, 2, N=CHCH).

Anal. Calcd for $C_6H_4Br_2N_2O_3$: C, 23.08; H, 1.28; Br, 51.28; N, 8.97. Found: C, 23.09; H, 1.21; Br, 51.35; N, 9.18.

4-(Dibromonitromethyl)quinoline (75%): mp 159° (95% ethanol); ir (KBr) 1575 cm^{-1} (NO_2); nmr ($CDCl_3$) δ 9.2 and 7.7–8.4 (m, aromatic H).

Anal. Calcd for $C_{10}H_6Br_2N_2O_2$: C, 34.68; H, 1.73; Br, 46.24; N, 8.09. Found: C, 34.65; H, 1.79; Br, 46.03; N, 7.80.

2-(Dibromonitromethyl)benzoxazole (53%): mp 79° (95% ethanol); ir (KBr) 1553 cm^{-1} (NO_2); nmr ($CDCl_3$) δ 7.2–8.0 (m, C_6H_4).

Anal. Calcd for $C_8H_4Br_2N_2O_3$: C, 28.57; H, 1.19; Br, 47.62; N, 8.33. Found: C, 28.79; H, 1.42; Br, 47.52; N, 8.36.

2-(Dibromonitromethyl)benzothiazole (61%): mp 70° (95% ethanol); ir (KBr) 1575 cm^{-1} (NO_2); nmr ($CDCl_3$) δ 7.3–8.2 (m, C_6H_4).

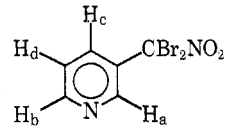
Anal. Calcd for $C_8H_4Br_2N_2O_2S$: C, 27.27; H, 1.14; Br, 45.45; N, 7.97; S, 9.23. Found: C, 27.24; H, 1.20; Br, 45.42; N, 7.97; S, 9.22.

2-(Dibromonitromethyl)quinoxaline (55%): mp 88° (95% ethanol); ir (KBr) 1587 cm^{-1} (NO_2); nmr ($CDCl_3$) δ 9.4 (s, 1, N=CH) and 7.7–8.3 (m, 4, C_6H_4).

Anal. Calcd for $C_9H_5Br_2N_3O_2$: C, 31.12; H, 1.44; Br, 46.11; N, 12.10. Found: C, 31.32; H, 1.48; Br, 46.38; N, 11.84.

3-(Dibromonitromethyl)pyridine.—The following experiment is typical of the procedure employed for the bromination of α-nitroalkyl heterocyclics. Pure 3-nitromethylpyridine (1.4 g, 0.01 mol) was dissolved in 10 ml of 10% aqueous sodium hydroxide and added in one portion to an aqueous solution of 0.05 mol

potassium hypobromite at 0–5°. The precipitate was filtered and recrystallized from ethanol–water (1:1) to give 3.0 g (100%) of **3-(dibromonitromethyl)pyridine**: mp 74–75°; ir (KBr) 1570 cm^{-1} (NO_2); nmr ($CDCl_3$) δ 9.1 (m, 1, H_a), 8.7 (m, 1, H_b), 8.1 (m, 1, H_c), and 7.4 (m, 1, H_d).



Anal. Calcd for $C_6H_4Br_2N_2O_2$: C, 24.32; H, 1.35; Br, 54.05; N, 9.46. Found: C, 24.28; H, 1.54; Br, 54.30; N, 9.46.

4-(Dibromonitromethyl)pyrimidine (85%): mp 73–74° (ethanol–water, 1:1); ir (KBr) 1572 cm^{-1} (NO_2); nmr ($CDCl_3$) δ 9.1 (s, 1, N=CHN), 8.9 (d, 1, N=CH), and 7.9 (d, 1, N=CH-CH).

Anal. Calcd for $C_5H_3Br_2N_3O_2$: C, 20.20; H, 1.01; Br, 53.87; N, 14.14. Found: C, 20.28; H, 0.86; Br, 54.12; N, 14.17.

1-(Dibromonitromethyl)isoquinoline (100%): mp 135–136° (95% ethanol); ir (KBr) 1587 cm^{-1} (NO_2); nmr ($CDCl_3$) δ 7.5–8.0 and 8.3–8.6 (m, ring H).

Anal. Calcd for $C_{10}H_6Br_2N_2O_2$: C, 34.68; H, 1.73; Br, 46.24; N, 8.09. Found: C, 34.71; H, 1.71; Br, 46.23; N, 8.00.

4-(Dibromonitromethyl)cinnoline (98%): mp 134° dec (95% ethanol); ir (KBr) 1587 cm^{-1} (NO_2); nmr ($CDCl_3$) δ 9.8 (s, 1, N=CH), 8.6–8.9, and 7.8–8.0 (m, 4, C_6H_4).

Anal. Calcd for $C_9H_5Br_2N_3O_2$: C, 31.12; H, 1.44; Br, 46.11; N, 12.10. Found: C, 31.22; H, 1.65; Br, 46.06; N, 11.82.

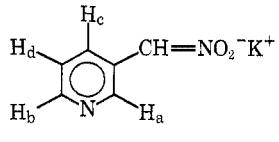
2-(Dichloronitromethyl)pyridine.—A solution of 5.4 g (0.03 mol) of pure potassium 2-picolylnitronate (**35**) in 50 ml of water was added in one portion to 51 ml of aqueous potasssium hypochlorite[28] (prepared from 125 g of 70% calcium hypochlorite (HTH), 87.5 g of potassium carbonate, and 25 g of 85% assay potassium hydroxide) at room temperature. The mixture was extracted with ether and dried (Na_2SO_4), and the extract concentrated *in vacuo*. Distillation of the residue afforded 3.0 g (48%) of **2-(dichloronitromethyl)pyridine**: bp 62° (0.05 mm); $n^{20}D$ 1.5519; ir (neat) 1587 cm^{-1} (NO_2); nmr (CCl_4) δ 8.6 (m, 1, N=CH), 8.0 (m, 2, N=CHCH=CHCH), and 7.4 (m, 1, N=CHCH=CH).

Anal. Calcd for $C_6H_4Cl_2N_2O_2$: C, 34.80; H, 1.93; Cl, 34.27; N, 13.53. Found: C, 34.93; H, 2.15; Cl, 34.48; N, 13.58.

1-Chloro-1-(4-pyridyl)nitroethane.—Crude potassium 1-(4-pyridyl)ethanenitronate prepared from 17.8 g (0.17 mol) of 4-ethylpyridine was dissolved in 300 ml of water and the solution saturated with chlorine at −10°. The solution was basified with 10% sodium hydroxide solution and extracted with chloroform. The extract was dried ($MgSO_4$) and concentrated *in vacuo*. The residue was distilled to give 19.5 g (63%) of **1-chloro-1-(4-pyridyl)-nitroethane**: bp 65–67° (10^{-3} mm); $n^{20}D$ 1.5393; ir (neat) 1575 cm^{-1} (NO_2); nmr (CCl_4) δ 8.7 (m, 2, N=CH), 7.5 (m, 2, N=CHCH), and 2.5 (s, 3, CH_3).

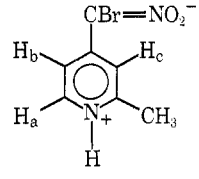
Anal. Calcd for $C_7H_7ClN_2O_2$: C, 45.16; H, 3.76; Cl, 19.06; N, 15.05. Found: C, 45.39; H, 3.79; Cl, 19.08; N, 15.23.

Potassium 3-Picolylnitronate (36).—A solution of 2.3 g (0.017 mol) of pure 3-nitromethylpyridine in 10 ml of absolute ethanol was added in one portion to a solution of 0.018 mol of potassium ethoxide in 50 ml of absolute ethanol. The solution was poured into 200 ml of absolute ether and the precipitate filtered to give 2.6 g (89%) of **potassium 3-picolylnitronate**: mp 235° dec (isopropyl alcohol); uv max (95% C_2H_5OH) 315 mμ (log ϵ 4.36); ir (KBr) 1543 cm^{-1} ($C=NO_2^-$); nmr (D_2O) δ 8.6 (m, 1, H_a), 8.2 (m, 2, $H_b + H_c$), 7.3 (m, 1, H_d), and 7.0 (s, 1, CH).



Anal. Calcd for $C_6H_5KN_2O_2$: C, 40.91; H, 2.84; K, 22.21; N, 15.91. Found: C, 40.64; H, 3.11; K, 22.02; N, 15.77.

4-(Bromonitromethyl)-2-methylpyridine (32).—4-(Dibromonitromethyl)-2-methylpyridine (**31**) (5.0 g, 0.016 mol) was dissolved in 300 ml of liquid ammonia at −33°. After 10 min the ammonia was gradually replaced with absolute ether and the mixture filtered after room temperature was attained. Then the solid was dissolved in 50 ml of water and acidified with 1.0 g of glacial acetic acid at room temperature. Filtering the precipitate afforded 3.1 g (83%) of 4-(bromonitromethyl)-2-methylpyridine: mp 116–117° dec (95% ethanol); uv max (95% C_2H_5OH) 271 mμ (log ϵ 3.44) and 419 (3.18); ir (KBr) 3636–1818 ($=N^+H$) and 1481 cm^{-1} ($C=NO_2^-$); nmr (DMSO-d_6) δ 8.6 (s, 1, NH), 7.8 (m, 1, H_a), 7.5 (m, 2, $H_b + H_c$), and 2.5 (s, 3, CH_3)



Anal. Calcd for $C_7H_7BrN_2O_2$: C, 36.36; H, 3.03; Br, 34.63; N, 12.12. Found: C, 36.60; H, 3.08; Br, 34.80; N, 11.89.

2-Pyridylhydroxamyl Chloride *N*-Oxide (23).—Crude 2-nitromethylpyridine *N*-oxide (**21**) (1.1 g, 0.007 mol) was covered with 7.5 ml of benzoyl chloride and the mixture warmed gently on a steam bath. The white precipitate was slurried in ether, filtered and washed with water to yield 1.8 g (92%) of **2-pyridylhydroxamyl chloride *N*-oxide**: mp 187–188° (95% ethanol); ir (KBr) 1764 cm^{-1} (C=O); nmr ($CDCl_3$) δ 8.0–8.4 and 7.2–7.7 (m, ring H).

Anal. Calcd for $C_{13}H_9ClN_2O_3$: C, 56.52; H, 3.26; Cl, 12.84; N, 10.14. Found: C, 56.43; H, 3.53; Cl, 13.05; N, 9.92.

Determination of Acidity Constants.—Samples (0.1 g) of nitronate salt were dissolved in 20 ml of carbon dioxide free water and titrated under nitrogen with 0.04 *M* hydrochloric acid. The pK_a values were determined by plotting the volume of titrant against the pH which was read directly from a Beckman Zeromatic pH meter. The pK_a values are tabulated in Table IV.

Registry No.—**4**, 22918-12-3; **10**, 22918-11-2; **12**, 22918-10-1; **14**, 22918-07-6; **15**, 35624-30-7; **15** picrate, 35624-31-8; **16**, 22918-09-8; **18**, 35624-32-9; **19**, 35589-59-4; **19** picrate, 35589-60-7; **20**, 35624-33-0; **21**, 35624-34-1; **23**, 35624-35-2; **25**, 35624-36-3; **27**, 35624-37-4; **27** picrate, 35624-38-5; **30**, 35624-39-6; **32**, 35624-40-9; **33**, 22918-06-5; **34**, 3243-07-0; **35**, 35624-43-2; **36**, 35624-44-3; **37**, 22918-08-7; **37** picrate, 35624-46-5; 1-nitromethylisoquinoline, 35624-47-6; 2-nitromethylthiazoline, 35624-48-7; 5-ethyl-2-nitromethylpyridine, 24998-78-5; 5-ethyl-2-nitromethylpyridinium picrate, 35624-50-1; potassium 2-quinaldylnitronate, 35624-51-2; 4-nitromethylpyrimidine, 35624-52-3; 4-nitromethylquinoxaline, 35624-53-4; 4-nitromethylcinnoline, 35624-54-5; 4-(dibromonitromethyl)pyridine, 35624-55-6; 2-(dibromonitromethyl)-6-methylpyridine, 35624-56-7; 2-(dibromonitromethyl)-3-methylpyridine, 35624-43-2; 1-bromo-1-(4-pyridyl)-3-phenylnitropropane, 35624-58-9; 2-(dibromonitromethyl)pyridine *N*-oxide, 22918-13-4; 4-(dibromonitromethyl)pyridine *N*-oxide, 35624-60-3; 4-(dibromonitromethyl)quinoline, 35619-67-1; 2-(dibromonitromethyl)benzoxazole, 35619-68-2; 2-(dibromonitromethyl)benzothiazole, 35619-69-3; 2-(dibromonitromethyl)quinoxaline, 35619-70-6; 3-(dibromonitromethyl)pyridine, 35619-71-7; 4-(dibromonitromethyl)pyrimidine, 35619-72-8; 1-

(28) A. I. Vogel, "A Textbook of Practical Organic Chemistry," 3rd ed, Wiley, New York, N. Y., 1962, p 461.

(dibromonitromethylisoquinoline, 35619-73-9; 4-(dibromonitromethyl)cinnoline, 35619-74-0; 2-(dichloronitromethyl)pyridine, 35619-75-1; 1-chloro-1-(4-pyridyl)nitroethane, 35619-76-2; 4-(bromonitromethyl)-2-methylpyridine, 35619-77-3.

Acknowledgments.—Financial support of this work by the Office of Naval Research is gratefully acknowledged. We would like to thank Dr. John B. Grützner for helpful discussions of the nmr data during the preparation of the manuscript.

The Free-Radical Addition of *tert*-Butyl Hypochlorite to Some Bridged Polycyclic Olefins

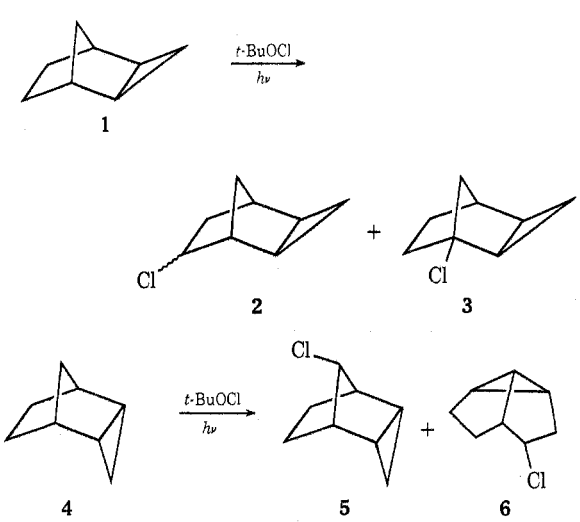
PETER K. FREEMAN* AND R. S. RAGHAVAN

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

Received February 24, 1972

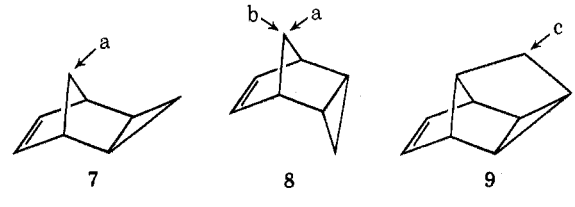
Irradiation of *tert*-butyl hypochlorite and *endo*-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene in carbon tetrachloride at 40° produces a 59% yield of *exo*-6-*tert*-butoxy-*endo*-7-chloro-*endo*-tricyclo[3.2.1.$0^{2,4}$]octane and *exo*-6-*tert*-butoxy-*exo*-7-chloro-*endo*-tricyclo[3.2.1.$0^{2,4}$]octane in a ratio of 43:57, while similar treatment of *tert*-butyl hypochlorite and *exo*-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene results in a 56% yield of trans adduct, *exo*-6-*tert*-butoxy-*endo*-7-chloro-*exo*-tricyclo[3.2.1.$0^{2,4}$]octane, and cis adduct, *exo*-6-*tert*-butoxy-*exo*-7-chloro-*exo*-tricyclo[3.2.1.$0^{2,4}$]octane, in a ratio of 78:22. Similar photolytic treatment of *tert*-butyl hypochlorite and deltacyclene generates *exo*-8-*tert*-butoxy-*endo*-9-chlorodeltacyclane and *exo*-8-*tert*-butoxy-*exo*-9-chlorodeltacyclane in a ratio of 85:15 in an overall yield of 37%. The stereochemistry of the chain transfer step of the intermediate *tert*-butoxycycloalkyl radicals and the lack of cyclopropylethyl radical rearrangement are rationalized as a result of predominant 1,2 addition taking place by way of classical *tert*-butoxycycloalkyl intermediates.

Recently we have reported that radical chlorination of *exo*-tricyclo[3.2.1.$0^{2,4}$]octane with *tert*-butyl hypochlorite results in abstraction of hydrogen from C-6 and C-1 to generate *exo*- and *endo*-6-chloro-*exo*-tricyclo[3.2.1.$0^{2,4}$]octane (**2**) and 1-chloro-*exo*-tricyclo[3.2.1.$0^{2,4}$]octane (**3**), while, in contrast, radical chlorination of *endo*-tricyclooctane **4** results in 93% or greater



abstraction of hydrogen at C-8, leading to *anti*-8-chlorotricyclooctane **5** and *endo*-2-chlorotricyclo[3.3.0.$0^{4,6}$]octane (**6**).[1]

Since several unique aspects of *tert*-butoxy abstraction in these tricyclooctane ring systems have been at least partially revealed, it appeared to be of some interest to pursue a complementary line of research to gain additional insight into the nature of related radical intermediates. Tobler and coworkers[2] have shown that the radical reaction of *tert*-butyl hypochlorite with norbornene results in both addition and substitution, addition predominating. Therefore, we chose to investigate the analogous reaction of *tert*-butyl hypochlorite with *exo*-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (**7**), *endo*-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (**8**), and deltacyclene (**9**). Abstraction reactions are of interest in each case, since there is the potential for anchimeric assistance to abstraction of the bishomocyclopropenyl (abstraction at a in **7** and **8**) and trishomocyclopropenyl type (abstraction at b in **8**), while abstraction at c in **9** could produce an interesting degenerate 5-deltacyclenyl radical. Addition of *tert*-butoxy to the double bond of **7** or **9** would generate a radical intermediate analogous to the major intermediate in the abstraction reaction of **1**, while addition to *endo*-tricyclooctene **8** would yield a radical we have been unable to characterize in the radical chlorination of **4**, due to the predominance of C-8 abstraction.



Results

When *endo*-tricyclooctene **8** was irradiated with *tert*-butyl hypochlorite using a 2:1 molar ratio of olefin to *tert*-butyl hypochlorite in carbon tetrachloride solution at 40°, the products on vpc analysis were found to consist of two components in a ratio of 43:57 in the order of increasing retention times, in an overall yield of 59%. The retention times of the two components were much longer than expected for monochlorides, suggesting the possibility that free-radical adducts had been formed. Since the monochloride region in the chromatogram was conspicuously free of peaks, hydrogen abstraction did not compete with addition.

(1) P. K. Freeman, R. S. Raghavan, and G. L. Fenwick, *J. Amer. Chem. Soc.*, **94**, 5101 (1972).

(2) E. Tobler, D. E. Battin, and D. J. Foster, *J. Org. Chem.*, **29**, 2834 (1964).