Preparation of *endo*-Norbornylcarbonic–*p*-Methoxybenzoic Anhydride.—To a mixture of 3 g (0.017 mol) of *endo*-norbornyl chlorocarbonate and 2.61 g (0.017 mol) of *p*-anisic acid in 100 ml of dry ether at 0° was added, dropwise with stirring, 1.73 g (0.017 mol) of triethylamine in dry ether. The reaction mixture was stirred for 1 hr. The amine hydrochloride was filtered off and the ether solution was washed with dilute HCl, $NaHCO_3$, and water, and then dried over anhydrous magnesium sulfate. Upon evaporation of the ether an oil was obtained. Attempts to induce the oil to crystallize met with failure.

Anal. Calcd for $C_{16}H_{18}O_5$: C, 66.19; H, 6.25. Found: C, 66.04; H, 6.38.

The infrared spectrum (CCl_4) showed a double carbonyl band at 1805 and 1745 cm^{-1}, a separation of 60 cm^{-1}.

Preparation of *exo*-Norbornylcarbonic–*p*-Methoxybenzoic Anhydride.—This compound was prepared in the same manner as the endo isomer described above. An oil was obtained from the reaction mixture which crystallized upon cooling, mp 50.5–51.5°, yield, 94%.

Anal. Calcd for $C_{16}H_{18}O_5$: C, 66.19; H, 6.25. Found: C, 66.03; H, 6.36.

The infrared spectrum (CCl_4) showed a double carbonyl band at 1785 and 1727 cm^{-1}.

Registry No.—1 (exo), 35042-30-9; 2 (endo), 35042-31-0; *exo*-norbornyl carbonate, 35042-32-1; *endo*-norbornyl carbonate, 35042-33-2; *exo*-norbornyl *p*-nitrobenzoate, 10472-43-2; *endo*-norbornylcarbonic–*p*-methoxybenzoic anhydride, 35042-35-4; *exo*-norbornylcarbonic–*p*-methoxybenzoic anhydride, 35042-36-5.

Acknowledgments.—The authors are grateful to the University of Nebraska Research Council for financial support of this research.

Azaindolizines. 2. N-5 and C-1 and C-3 Protonation of 1,3-Disubstituted 5-Azaindolizines

MARTIN FRASER

Department of Chemistry, Robert Gordon's Institute of Technology, Aberdeen, Scotland, U. K.

Received November 23, 1971

1,2,3,6-Tetramethyl-5-azaindolizine (**2e**) and 1,3,6-trimethyl-2-phenyl-5-azaindolizine (**2f**) have been shown by pmr studies in trifluoroacetic acid to protonate solely at C-3. The di-5-azaindolizinylmethane (**6**) in trifluoroacetic acid diprotonates to give the di C-3 cation (**7**, 32%) and the C-3/N-5′ dication (**8**, 68%). The perchlorates of **2e** and **2f**, when examined in trifluoroacetic acid, show protonation at N-5. Equilibration in solution leads to the formation of the 1-H (**4c** and **4d**) and 3-H cations (**3c** and **3d**) at the expense of the N-5 cations (**5a** and **5b**). The 3-H cation, initially observed in low concentration is eventually the sole cation established in solution.

Carbon protonation of heteroaromatic systems containing a π-equivalent nitrogen is exceptional and is shown solely by the 2*H*-cyclopenta[*d*]pyridazine and 5-azaindolizine structures **1a–c**[1] and **2a–d**.[2] Both these systems can be considered to be nitrogen heteroanalogs of azulene which contain a π-excessive and a π-equivalent nitrogen.[3] Protonation of these compounds occurs at carbon with the establishment of a 6-π cation in the six-membered ring; other similarly structured nitrogen heteroanalogs of azulene do not protonate at carbon but at the π-equivalent nitrogen with the formation of a 10-π cation.[2,4,5]

Previous pmr studies of 5-azaindolizines (**2a–d**) and their perchlorates[6] showed protonation of **2a** and **2b** to occur at C-3 to give the 3-H cations **3a** and **3b** whereas their corresponding 3-methyl derivatives **2c** and **2d** protonated solely and predominantly at C-1 to give the 1-H cations **4a** and **4b**. This suggests that the 3-methyl group sterically inhibits protonation at C-3 in a manner akin to that found in 3-alkylindolizines.[7,8] None of the 5-azaindolizines (**2a–d**) or their perchlorates in trifluoroacetic acid[9] showed signals which could be attributed to the presence of a N-5 protonated cation. This suggests that if the N-5 cation is formed it is either too transient or in concentrations too low to be detected by pmr spectroscopy. 1,3-Disubstituted 5-azaindolizines (**2e**, **2f**, and **6**) were synthesized to test whether this steric factor would sufficiently suppress C-1 and or C-3 protonation to cause protonation at the π-equivalent N-5 site with the formation of the corresponding 10-π cations.

Results

The pmr spectra of 1,3-dimethyl-5-azaindolizines (**2e** and **2f**) in trifluoracetic acid[10] showed them to protonate solely at the C-3 position to give the corresponding 6-π 3-H cations **3c** and **3d**. However, the pmr spectra of the isolated perchlorates of **2e** and **2f**, prepared by the addition of perchloric acid to an ethyl acetate solution of **2e** and **2f**, gave, when dissolved in trifluoracetic acid, spectra which differed from the corresponding spectra of the 3-H cations **3c** and **3d**. These first recorded spectra of the perchlorates[10] are considered to arise from protonation of **2e** and **2f** at the respective N-5 sites to give the 10-π cations **5a** and **5b**. The spectra of the cations **5a** and **5b** gradually became more complex with time. After approximately 6 hr at 25° or 1

---

(1) A. Anderson and D. Forky, *J. Amer. Chem. Soc.*, **91**, 924 (1969).

(2) M. Fraser, *J. Org. Chem.*, **36**, 3087 (1971).

(3) A π equivalent heteroatom provides one electron and a π-excessive heteroatom provides two electrons to the π structure.

(4) K. Hofner and M. Kreuder, *Angew. Chem.*, **73**, 657 (1961).

(5) W. Armarego, *J. Chem. Soc.*, 4226 (1964).

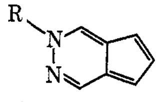
(6) Perchlorates of (**2a–d**) were prepared originally from ethanol; subsequently better yields were obtained using ethyl acetate as solvent.

(7) M. Fraser, S. McKenzie, and D. Reid, *J. Chem. Soc. B*, 44 (1966).

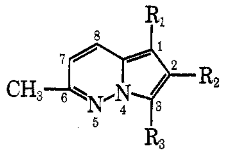
(8) W. Armarego, *ibid.*, 191 (1966).

(9) Spectra of the perchlorates of (**2a–f**) in $(CD_3)_2SO$ were identical in pattern with the spectra of (**2a–f**) in $CDCl_3$ due to the loss of perchloric acid.

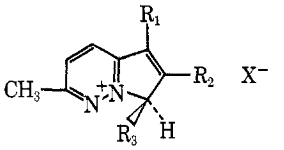
(10) Pmr spectra of **2e** in CF_3CO_2H (cation **3c**), **2e** $HClO_4$ in CF_3CO_2H (cation **5a**), **2e** $HClO_4$ in CF_3CO_2H after 15 min (**5a**, **3c**, and **4c**), and **6** in CF_3CO_2H (cations **7** and **8**), and ir spectra of **2a** $HClO_4$ and **2e** $HClO_4$ will appear following 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-37-3027. Remit check or money order for \$3.00 for photocopy or \$2.00 for microfiche.



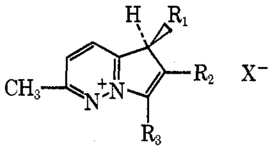
1a, $R = H$
b, $R = CH_3$
c, $R = Ph$



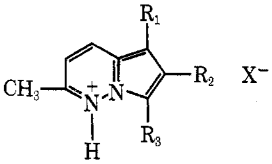
2a, $R_1 = R_3 = H; R_2 = CH_3$
b, $R_1 = R_3 = H; R_2 = Ph$
c, $R_1 = H; R_2 = R_3 = CH_3$
d, $R_1 = H; R_2 = Ph; R_3 = CH_3$
e, $R_1 = R_2 = R_3 = CH_3$
f, $R_1 = R_3 = CH_3; R_2 = Ph$
g, $R_1 = CHO; R_2 = R_3 = CH_3$
h, $R_1 = CHO; R_2 = Ph; R_3 = CH_3$



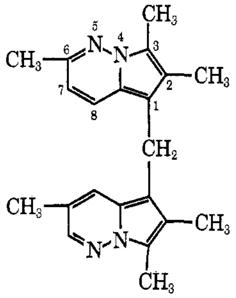
3a, $R_1 = R_3 = H; R_2 = CH_3$
b, $R_1 = R_3 = H; R_2 = Ph$
c, $R_1 = R_2 = R_3 = CH_3$
d, $R_1 = R_3 = CH_3; R_2 = Ph$



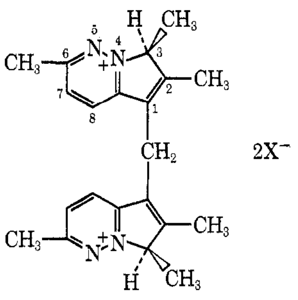
4a, $R_1 = H; R_2 = R_3 = CH_3$
b, $R_1 = H; R_2 = Ph; R_3 = CH_3$
c, $R_1 = R_2 = R_3 = CH_3$
d, $R_1 = R_3 = CH_3; R_2 = Ph$



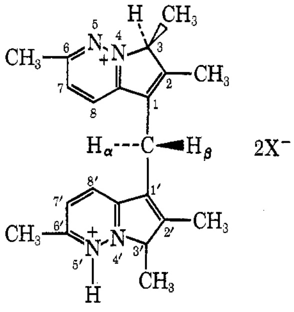
5a, $R_1 = R_2 = R_3 = CH_3$
b, $R_1 = R_3 = CH_3; R_2 = Ph$



6



7



8

hr at 50° they became identical with the spectra of the corresponding 3-H cations **3c** and **3d**. These observations show that the site of protonation of **2e** and **2f** depends upon the conditions of protonation. When trifluoroacetic acid is used as solvent and protonating agent the conditions of protonation are reversible and conducive to the selective formation of the thermodynamically more stable carbon protonated cations **3c** and **3d**.[11] On the other hand when the highly acidic medium of perchloric acid in ethyl acetate is used, the conditions of protonation are less reversible and protonation at the high-electron density[2,12] π-equivalent N-5 site is kinetically favored. In trifluoroacetic acid, proton exchange between cation and solvent is facile and the initially observed N-5 cations **5a** and **5b** of the perchlorates of **2e** and **2f** equilibrate to the more stable C-1- and C-3-protonated cations to give a complex spectra consisting of the superposed spectra of the three cations **3c**, **4c**, and **5a**[10] and **3d**, **4d**, and **5b**, respectively. The intensity of the signals of the 1-H cations **4c** and **4d**, though initially greater than those of the 3-H cations **3c** and **3d**, are transient and eventually the only cations established in trifluoroacetic acid are the 3-H cations.

The protonation of the 1,3-disubstituted 5-azaindolizine (**6**) in trifluoroacetic acid occurs with the formation of a mixture of the di C-3 protonated cation (**7**, 32%) and the C-3/N-5′ protonated dication (**8**, 68%).[10] The isolation of the perchlorates of **6** from ethyl acetate or other solvents was unsuccessful, but the percentages of the cations **7** and **8** did not materially alter either on standing or on the addition of perchloric acid to the trifluoroacetic acid solution of **6**.

Experimental Section

Melting points were determined by the capillary method and are uncorrected. Elemental analyses were performed by the analytical laboratories of Aberdeen University. Infrared spectra were measured with a Unicam SP200 spectrometer and absorption peaks were recorded in wave numbers (cm^{-1}). Ultraviolet spectra were measured with a Unicam SP800 spectrometer. Light absorption data refer to solutions in ethanol; principal maxima are italized; sh = shoulder, br = broad, and infl = inflection. Pmr 100-MHz spectra were recorded at *ca.* 25° with a Varian HA-100B spectrometer using tetramethylsilane as an internal standard. Unless otherwise stated values given on the δ scale refer to singlet absorptions, coupling constants in cycles per second (Hz), and integration values and signal assignment are in parentheses. For multiplets d = doublet, q = quartet, and t = triplet.

Procedures.—Solutions were dried over anhydrous magnesium sulfate and solvents evaporated at reduced pressure on a rotatory film evaporator. Perchloric acid refers to 70% w/w Analar perchloric acid. Petroleum ether was of boiling point range 40–60°.

The synthesis of azaindolizines (**2a–d**) has been previously reported.[2]

Formylation of 2,3,6-Trimethyl- (2c) and 3,6-Dimethyl-2-phenyl-5-azaindolizine (2d) to Give, Respectively, 1-Formyl-2,3,6-trimethyl- (2g) and 1-Formyl-3,6-dimethyl-2-phenyl-5-azaindolizine (2h).—A solution of phosphoryl oxychloride (1.69 g, 1.0 ml, 11 mmol) in dimethylformamide (10 ml) was slowly added with stirring to a solution of the 5-azaindolizines (**2c–2d**) (10 mmol) in dimethylformamide (10 ml). Once the exothermic reaction which ensued had subsided the resulting brown solution was gently warmed for 15 min, left overnight, and then poured into 2 *M* aqueous sodium hydroxide (150 ml). On cooling yellow needles of the crude aldehydes precipitated. These were filtered off, washed with water, and dried *in vacuo*. The crude aldehyde was recrystallized (benzene–petroleum ether 1:4) and then vacuum sublimed. 2,3,6-Trimethyl-5-azaindolizine (**2c**) (1.6 g) gave 1-formyl-2,3,6-trimethyl-5-azaindolizine (**2g**, 1.35 g, 72%) as long straw colored needles: mp 94°; λ_{max} 380 (br), 317 (br), 298 (br), 255 (br), 238 (infl), *232* nm (log ε 3.88, 3.92, 3.90, 4.04, 4.25, 4.27, respectively); ir (Nujol) 715, 805, 1310, 1650, (C=O) cm^{-1}; pmr ($CDCl_3$) 2.46 (3 H, 2-Me), 2.50 (3 H, 3-Me), 2.55 (3 H, 6-Me), 6.77 (d, *J* = 9.0 Hz, 1 H, H-7), 8.32 (d, *J* = 9.0 Hz, 1 H, H-8), and 10.09 (1 H, 1-formyl).

Anal. Calcd for $C_{11}H_{12}N_2O$: C, 70.2; H, 6.4; N, 14.9. Found: C, 70.3; H, 6.6; N, 14.6.

3,6-Dimethyl-2-phenyl-5-azaindolizine (**2d**, 2.02 g) gave 1-formyl-3,6-dimethyl-2-phenyl-5-azaindolizine (**2h**, 1.86 g, 78%) as bright yellow needles: mp 118°; λ_{max} 384 (br), 320 (br), 295 (br), 250 (infl), *235* (br) nm (log ε 4.93, 4.83, 4.89, 5.22, 5.35, respectively); ir (Nujol) 740, 1320, 1545, 1610, 1640 (C=O) cm^{-1}; pmr ($CDCl_3$) 2.51 (3 H, 3-Me), 2.58 (3 H, 6-Me), 6.86 (d, *J* = 9.0 Hz, 1 H, H-7), 7.43 (5 H, 2-Ph), 8.55 (d, *J* = 9.0 Hz, 1 H, H-8), and 9.83 (1 H, 1-formyl).

---

[11] Cotterall, "Strength of Chemical Bonds," Butterworths, 1954, p 272.

[12] M. Zupan, B. Stanovvick, and M. Tisler, *J. Heterocycl. Chem.*, **8**, 1 (1971).

Anal. Calcd for $C_{16}H_{14}N_2O$: C, 76.7; H, 5.6; N, 11.2. Found: C, 76.5; H, 5.7; N, 10.9.

Reduction of Aldehydes 2g and 2h to Give, Respectively, 1,2,3,6-Tetramethyl-5-azaindolizine (2e) and 1,3,6-Trimethyl-2-phenyl-5-azaindolizine (2f).—A solution of the aldehyde (**2g**–**2h**, 5 mmol) in ether (30 ml) was added dropwise during 30 min to a stirred solution of lithium aluminum hydride (1.0 g, 26 mmol) and aluminum chloride (5 g, 40 mmol) in ether (120 ml). The reaction mixture was stirred for 60 min before being poured into ice cold 0.05 *M* sulfuric acid. The acid solution was basified with potassium carbonate and extracted with ether and the ether extract washed, dried, and evaporated to leave the crude 5-azaindolizine.

1-Formyl-2,3,6-trimethyl-5-azaindolizine (**2g**, 0.94 g) gave the crude 1,2,3,6-tetramethyl-5-azaindolizine (**2e**) as a brown oil which on distillation, 155–165° (15 mm), gave **2e** as a golden oil (0.31 g, 36%): λ_{max} 400 (br), 316 (br), 304 (br), *254*, 219 nm ($\log \epsilon$ 3.51, 3.29, 3.25, 4.46, 4.37, respectively); ir (thin film) 780, 1160, 1315, 1620 cm^{-1}. The pmr ($CDCl_3$) of **2e** showed 2.21 or 2.24 (3 H, 2-Me), 2.24 or 2.21 (3 H, 1-Me), 2.43 (3 H, 3-Me), 2.48 (3 H, 6-Me), 6.18 (d, J = 8.5 Hz, 1 H, H-7), and 7.45 (d, J = 8.5 Hz, 1 H, H-8). The assignment of the H-7 and H-8 AB doublet system is substantiated by a comparative examination of the pmr ($CDCl_3$) spectra of **2e** with its precursor aldehyde **2g**. In **2g** the 1-formyl group by peri effect would be expected to cause a preponderantly greater shift in the H-8 doublet which occurs at δ 8.32, a downfield shift of 87 Hz from the position assigned to the H-8 doublet of **2e**. The H-7 doublet of **2g** is relatively less affected by the 1-formyl group and occurs at δ 6.71, a downfield shift of 59 Hz from the H-7 doublet of **2e**: pmr (CF_3COOH)[10] 1.84 (d, J = 7.8 Hz, 3 H, 3-Me), 2.27 (3 H, 2-Me), 2.32 (3 H, 1-Me), 2.83 (3 H, 6-Me), 5.27 (q, J = 7.8 Hz, 1 H, 3-methine), 8.15 (1 H, H-7), and 8.15 (1 H, H-8). The AB doublet system of **2e** in deuteriochloroform assigned to H-7 and H-8 with signals at δ 6.18 and 7.45 merge into a 2 H singlet at δ 8.15 in trifluoroacetic or deuteriotrifluoroacetic acid.

Anal. Calcd for $C_{11}H_{14}N_2$: C, 75.8; H, 8.1; N, 16.1. Found: 75.6; H, 8.3; N, 16.0.

1-Formyl-3,6-dimethyl-2-phenyl-5-azaindolizine (**2h**, 1.13 g) gave the crude 1,3,6-trimethyl-2 phenyl 5-azaindolizine (**2f**) as a brown oil which subsequently solidified. Vacuum sublimation gave **2f** as a yellow solid (0.43 g, 38%): mp 67°; λ_{max} 395 (br), 310 (br), *262* nm ($\log \epsilon$ 4.48, 3.25, 3.17, respectively); ir (Nujol) 700, 770, 1196, 1610 cm^{-1}; pmr ($CDCl_3$) 2.28 (3 H, 1-Me), 2.44 (3 H, 3-Me), 2.51 (3 H, 6-Me), 6.26 (d, J = 8.5 Hz, 1 H, H-7), 7.37 (5 H, 2-Ph), and 7.54 (d, J = 8.5 Hz, 1-H, H-8); pmr (CF_3COOH) 1.78 (d, J = 7.0 Hz, 3 H, 3-Me), 2.47 (3 H, 1-Me), 2.89 (3 H, 6-Me), 5.40 (q, J = 7.0 Hz, 1 H, 3-methine), 7.58 (5 H, 2-Ph), 8.17 (d, J = 9.0 Hz, 1 H, H-7), and 8.33 (d, J = 9.0 Hz, 1 H, H-8).

Anal. Calcd for $C_{16}H_{16}N_2$: C, 81.1; H, 6.8; N, 11.9. Found: C, 81.4; H, 6.8; N, 11.9.

By analogy with the 1- and 3-methine and methylene resonances of indolizines[7,8,12] and 5-azaindolizines[2,14] protonation of **2e** and **2f** in trifluoroacetic acid is inferred to occur at C-3. The deuteriotrifluoroacetic acid spectra of **2e** and **2f** are similar in pattern to their spectra in trifluoroacetic acid, apart from the absence of the 1 H quartets at δ 5.27 and 5.40 assigned to the 3-methine hydrogens and the spin coupled 3 H, 3-methyl, high-field doublets at δ 1.84 and 1.78, which appear as 3 H singlets at δ 1.86 and 1.80, respectively.

1,2,3,6-Tetramethyl-5-azaindolizinium Perchlorate (3c, 4c, and 5a, X = ClO_4) and 1,3,6-Trimethyl-2-phenyl-5-azaindolizinium Perchlorate (3d, 4d, and 5b, X = ClO_4).—Perchloric acid (3.0 ml, 37% excess) was added to a solution of **2e**–**2f** (2 mmol) in ethyl acetate (5 ml). On cooling 5-azaindolizinium perchlorate precipitated and was collected.

1,2,3,6-Tetramethyl-5-azaindolizine (**2e**, 0.35 g) gave 1,2,3,6-tetramethyl-5-azaindolizinium perchlorate (0.32 g, 73%) as orange colored needles: mp 105–108°; ir (Nujol) 1100 (ClO_4), 1260, 1315, 1405, 1520, 1640, 3500 cm^{-1}; pmr (CF_3COOH), the first recorded spectrum was attributed to the N-5 cation **5a**,[10] 2.37 or 2.44 (3 H, 1-Me), 2.44 or 2.37 (3 H, 2-Me), 2.69 (3 H, 3-Me), 2.80 (3 H, 6-Me), 6.64 (d, J = 8.5 Hz, 1 H, H-7), and 8.15 (d, J = 8.5 Hz, 1 H, H-8). A broad singlet or triplet which would be expected to arise from the proton bonded to nitrogen was not discernible, though it may be obscured by the broad acid–solvent peak below δ 9.50. The pmr spectrum of other azaindolizines, for which N-protonation has previously been established, have also characteristically shown the absence of a signal attributable to a proton bonded to nitrogen and other incidences of the nonappearance of a proton bonded to nitrogen have been cited.[1,2,15,16] The first recorded spectrum of 1,2,3,6-tetramethyl-5-azaindolizinium perchlorate in deuteriotrifluoroacetic acid was identical in pattern with its first spectrum in trifluoroacetic acid showing that the nitrogen-protonated cation **5a** is formed rather than a carbon-protonated cation. When the first spectrum of 1,2,3,6-tetramethyl-5-azaindolizinium perchlorate in trifluoroacetic acid is retraced after approximately 15 min, a complex spectrum constituted of the three superposed spectra of the three cations **5a** (15%), **3c** (35%), and **4c** (50%) is obtained.[10] The signals of the transient 1-H-cation **4c** were located as the residual signals in this spectrum after assignment of the signals of the 3-H and N-5 cations **3c** and **5a**; they occurred at (CF_3COOH) 1.67 (d, J = 8.0 Hz, 3 H, 1-Me), 2.31 (3 H, 2-Me), 2.52 (3 H, 3-Me), 2.93 (3 H, 6-Me), 4.10 (q, J = 8.0 Hz, 1 H, 1-methine), 8.14 (d, J = 9.0 Hz, 1 H, H-7), and 8.44 (d, J = 9.0 Hz, 1 H, H-8); (CF_3COOD) 1.66 (3 H, 1-Me), 2.32 (3 H, 2-Me), 2.53 (3 H, 3-Me), 2.94 (3 H, 6-Me), 8.14 (d, J = 9.0 Hz, 1 H, H-7), and 8.44 (d, J = 9.0 Hz, 1 H, H-8). After approximately 6 hr the only signals remaining were identical in pattern with those of the spectrum of **2e** in trifluoroacetic acid, due to the presence of the 3-H cation **3c**.

Anal. Calcd for $C_{11}H_{15}ClN_2O_4$: C, 48.1; H, 5.1; N, 10.2; Cl, 12.9. Found: C, 47.8; H, 5.3; N, 10.4; Cl, 12.7.

1,3,6-Trimethyl-2-phenyl-5-azaindolizine (**2f**, 0.43 g) gave 1,3,6-trimethyl-2-phenyl-5-azaindolizinium perchlorate (0.38 g, 72%) as orange colored needles: mp 187°; ir (Nujol) 775, 1060 (ClO_4), 1100 (ClO_4), 1190, 1260, 1320, 1410, 1520, 1650, 3300 cm^{-1}. The first recorded spectrum, taken 15 min after dissolving the perchlorate in trifluoroacetic acid, showed a proponderance of the N-5-protonated cation **5b** (80%) whose signals occur at 2.43 (3 H, 1-Me), 2.65 (3 H, 3-Me), 2.82 (3 H, 6-Me), 6.67 (d, J = 8.5 Hz, 1 H, H-7), 7.52 (5 H, 2-Ph), and 8.22 (d, J = 8.5 Hz, 1 H, H-8). The 1-H cation **4d** was also present (on average *ca.* 20%, its low-field signals being recorded first were weaker than the high-field signals): 1.57 (d, J = 7.0 Hz, 3 H, 1-Me), 2.69 (3 H, 3-Me), 2.96 (3 H, 6-Me), 4.05 (q, J = 7.0 Hz, 1 H, 1-methine), 7.57 (5 H, 2-Ph), 8.16 (d, J = 9.0 Hz, 1 H, H-7), and 8.54 (d, J = 9.0 Hz, 1 H, H-8); pmr (CF_3COOD) 1.56 (3 H, 1-Me), 2.69 (3 H, 3-Me), 2.96 (3 H, 6-Me), 5.75 (5 H, 2-Ph), 8.16 (d, J = 9.0 Hz, 1 H, H-7), and 8.54 (d, J = 9.0 Hz, 1 H, H-8). This first recorded spectrum of the perchlorate of **2f**, when retraced after a further 5 min, showed a marked increase in the concentration of the 1-H cation **4d** (55%) and the emergence of the 3-H cation **3d** (20%). After 1 hr the ratio of the three cations **3d**, **4d**, and **5b** was approximately 82, 12, and 6%, respectively. Finally after about 6 hr the spectrum of 1,3,6-trimethyl-2-phenyl-5-azaindolizinium perchlorate became identical in pattern with the spectrum of **2f** in trifluoroacetic acid which showed solely the presence of the 3-H cation **3d**.

Anal. Calcd for $C_{16}H_{17}ClN_2O_4$: C, 56.8; H, 5.1; N, 8.3; Cl, 10.3. Found: C, 56.8; H, 5.0; N, 8.6; Cl, 10.5.

2,2′,3,3′,6,6′-Hexamethylmethylene-1,1′-di-5-azaindolizine (6).—Addition of 40% aqueous formaldehyde (2.0 ml) to a solution of 2,3,6-trimethyl-5-azaindolizine (**2c**, 0.8 g, 5 mmol) in ethanol (3 ml) gave on warming a cloudy solution. This solution, when heated a further 10 min and then cooled, precipitated brilliant yellow needles of the symmetrical di-5-azaindolizinylmethane (**6**, 0.81 g, 98%); recrystallization from ethyl acetate gave mp 158–159°; λ_{max} 397 (br), 315 (br), 303 (br), *251*, 238 (infl) nm ($\log \epsilon$ 4.76, 4.54, 4.54, 5.62, 5.44, respectively), ir (Nujol) 700, 785, 800, 1150, 1260, 1290, 1310, 1325, 1530, 1550, 1620 cm^{-1}; pmr ($CDCl_3$) 2.13 (6 H, 2-Me), 2.39 (6 H, 3-Me), 2.46 (6 H, 6-Me), 4.11 (2 H, bridge methylene), 6.07 (d, J = 9.0 Hz, 2 H, H-7), and 7.10 (d, J = 9.0 Hz, 2 H, H-8); pmr (CF_3COOH)[10] cation **7** (32%), 1.92 (d, J = 7.5 Hz,

---

(13) M. Fraser, A. Malera, B. Malloy, and D. Reid, *J. Chem. Soc.*, 3288 (1962).

(14) W. Flitsch and U. Kramer, *Justus Liebigs Ann. Chem.*, **735**, 35 (1970).

(15) R. Himman and E. Whipple, *J. Amer. Chem. Soc.*, **84**, 2539 (1962).

(16) Pmr studies failed to reveal the presence of a proton bonded to nitrogen in trifluoroacetic acid solution possibly due to a rapid rate of exchange with solvent. However, the ir spectra of the perchlorates of **2e** and **2f** had in common with other N-protonated azaindolizinium perchlorates and in contrast to the perchlorates of **2a**, **2b**, and **2d**, a broad, medium strong absorption in the 3300–3500-cm^{-1} region attributable to a proton bonded to nitrogen.

6 H, 3-Me), 2.42 (6 H, 2-Me), 2.80 (6 H, 6-Me), 4.25 (2 H, bridge methylene), 5.52 (q, J = 7.5 Hz, 2 H, 3-methine), 8.16 (2 H, H-7), and 8.16 (2 H, H-8); cation **8** (68%), 1.93 (d, J = 7.5 Hz, 3 H, 3-Me), 2.30 (3 H, 2′-Me), 2.40 (3 H, 2-Me), 2.67 (3 H, 3′-Me), 2.80 (3 H, 6-Me), 2.85 (3 H, 6′-Me), 4.36 (t, J = 14 Hz, 2 H, $H_\alpha H_\beta$ bridge methylene), 5.44 (q, J = 7.5 Hz, 1-H, 3-methine), 6.82 (d, J = 8.5 Hz, 1 H, H-7′), 7.77 (d, J = 8.5 Hz, 1 H, H-7), 7.97 (d, J = 8.5 Hz, 1 H, H-8), and 8.32 (d, J = 8.5 Hz, H-8′). Cation **8** showed no signal arising from a proton bonded to nitrogen; the two hydrogens H_α and H_β of the bridging methylene though magnetically nonequivalent would appear to experience a similar magnetic environment since the anticipated AB quartet is observed rather as a broad singlet at δ 4.36 with small wings at δ 4.50 and 4.24, the latter wing being obscured by the bridging methylene signal of the cation **7**.

Anal. Calcd for $C_{21}H_{24}N_4$: C, 75.9; H, 7.3; N, 16.8. Found: C, 75.8; H, 7.2; N, 16.8.

Registry No.—**2e**, 34876-65-8; **2f**, 34876-66-9; **2g**, 34876-67-0; **2h**, 34876-68-1; **3c**, 34876-69-2; **3d**, 34876-70-5; **4c**, 34876-71-6; **4d**, 34876-72-7; **5a**, 34876-73-8; **5b**, 34876-74-9; **6**, 34876-75-0.

Acknowledgments.—The author wishes to thank Mr. N. Faulkes for operating the Varian HA-100B spectrometer and to record thanks to Drs. Buchan, Reid, Watson, Webster, and Youngson for helpful suggestions.

Synthesis of β-Cyano-α,β-Unsaturated Isocyanates and Their Reactions with Hydrogen Chloride

MASATAKA OHOKA,* SHOZO YANAGIDA, AND SABURO KOMORI

Department of Applied Chemistry, Faculty of Engineering, Osaka University, Yamadakami, Suita, Osaka, Japan

Received March 13, 1972

When enaminonitriles with a primary nitrogen atom were allowed to react with phosgene in refluxing ethyl acetate, N-acylation occurred to give the corresponding β-cyano-α,β-unsaturated isocyanates in 37–79% yield. The reaction of thus obtained isocyanates with hydrogen chloride in dioxane at 100° for 24 hr gave 5,6-disubstituted uracils in good yields. Reaction of isocyanate **2c** with hydrogen chloride at 60° for 6 hr afforded 6-chloro-5-methyl-4-phenyl-2(3*H*)-pyrimidinone in 74% yield.

The reactions of enaminonitriles having a primary or a secondary nitrogen atom with acylating agents such as carboxylic acid chlorides and carboxylic acid anhydrides have been reported.[1–3] In these reactions C-acylation or N-acylation products were obtained, depending on the nature of enaminonitriles and acylating agents.

Recently, Samaraj, *et al.*,[4] have reported the synthesis of α,β-unsaturated isocyanates from ketimine and phosgene. However, the reaction of primary enamines (tautomers of ketimines) with phosgene has not been reported yet.

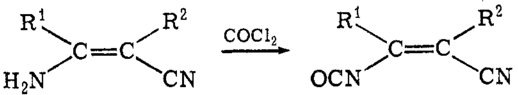
In addition, recently N-acylations of nitriles in the presence of hydrogen halide with acylating agents have been reported to yield various heterocycles. Simchen, *et al.*, have widely investigated the intramolecular cyclization reactions of various acid chlorides[5–9] or isocyanates[10] having a cyano group in the same molecule in the presence of hydrogen halide; for instance, they obtained quinazolones from *o*-cyanophenyl isocyanates.[10] In view of these studies intramolecular cyclization of β-cyano-α,β-unsaturated isocyanates is synthetically of interest.

We have now attempted the synthesis of β-cyano-α,β-unsaturated isocyanates by reacting phosgene with enaminonitriles, easily obtainable by condensation of nitriles in the presence of sodium.[11,12] In addition, the cyclization reaction of isocyanates thus obtained was carried out.

Results and Discussion

Synthesis of Unsaturated Isocyanates.—All the enaminonitriles used in this study were shown to exist predominantly as enamine tautomer in $CDCl_3$ by nmr analysis.

When enaminonitriles **1a–d** were allowed to react with phosgene in refluxing ethyl acetate, the expected N-acylation occurred to give the corresponding β-cyano-α,β-unsaturated isocyanates **2a–d** in 37–79% yield.



1 **2**

a, $R^1 = CH_3CH_2$; $R^2 = CH_3$

b, $R^1 = CH_3CH_2CH_2$; $R^2 = CH_3CH_2$

c, $R^1 = C_6H_5$; $R^2 = CH_3$

d, $R^1, R^2 = -(CH_2)_4-$

In the cases of **1a** and **1b**, considerable amounts of resinous substances were formed. They may be formed by polymerization of once-formed isocyanates or may be derived from C-phosgenated intermediates; this is not clear at present.

The structures of **2a–d** were established on the basis of ir and nmr spectra and elemental analysis. Yields and spectra are listed in Table I. Nmr spectra of **2a–c** showed that they are mixtures of the cis and trans isomer.

---

[1] E. Benary and M. Schmidt, *Chem. Ber.*, **54**, 2157 (1921).

[2] E. Benary and W. Lau, *ibid.*, **56**, 591 (1923).

[3] H. E. Schroeder and G. W. Rigby, *J. Amer. Chem. Soc.*, **71**, 2205 (1949).

[4] L. I. Samaraj, O. W. Wischenewski, and G. I. Derkatsch, *Angew. Chem.*, **80**, 620 (1968).

[5] G. Simchen, *ibid.*, **78**, 674 (1966).

[6] G. Simchen and W. Krämer, *Chem. Ber.*, **102**, 3656 (1969).

[7] G. Simchen, *ibid.*, **103**, 389 (1970).

[8] G. Simchen, *ibid.*, **103**, 407 (1970).

[9] G. Simchen and J. Wenzelburger, *ibid.*, **103**, 413 (1970).

[10] G. Simchen, G. Entenmann, and R. Zondler, *Angew. Chem.*, **82**, 548 (1970).

[11] H. Adkins and G. M. Whitman, *J. Amer. Chem. Soc.*, **64**, 150 (1942).

[12] G. A. Reynolds, W. J. Humphlett, R. W. Swamer, and C. R. Hauser, *J. Org. Chem.*, **16**, 165 (1951).