Substituted 1-(Pyrrol-2-ylmethylene)pyrrolidinium Salts A Source of Stable 2-Azafulvenamines

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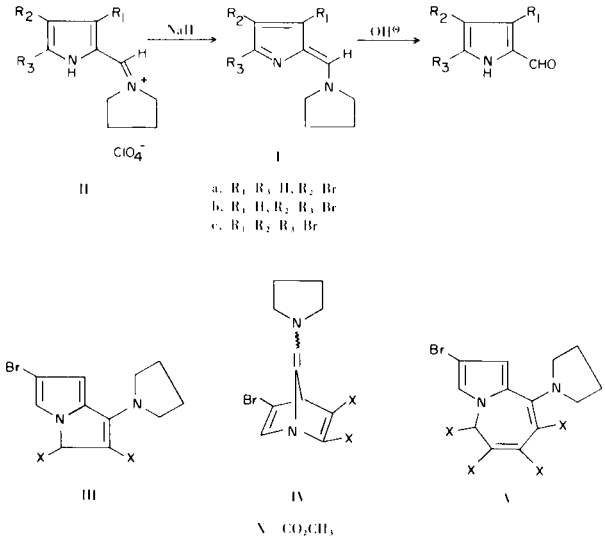
Several 2,4-disubstituted pyrroles have elicited trail-following responses from the Texas leafcutting ant, *Atta texana* (Buckley) (1). In order to generate such compounds for study, we were drawn to the possibility of employing 1-azafulvenamines, *e.g.* I, (6-amino-1-azafulvenes) as synthetic intermediates for novel pyrroles. The 1-azafulvenamines are formally available as the conjugate bases of (1-pyrrol-2-ylmethylene)pyrrolidinium salts II. These salts are readily obtained from pyrrole-2-carboxaldhydes and 2-pyrryl ketones (2) and can be useful synthetic intermediates themselves for variously ring-substituted salts.

A preparation of 6-aryl-6-dimethylamino-1-azafulvenes *via* an intermediate in the Vilsmeier-Haack benzoylation of pyrrole has been reported (3). In addition, several 6-dimethylamino-1-azafulvenes with completely substituted pyrrolenine rings have been reported from 2-pyrrolidones (4). When we treated (1-pyrrol-2-ylmethylene)pyrrolidinium perchlorate with sodium hydride in an effort to obtain the unsubstituted 6-amino-1-azafulvene, a pink oil was isolated that rapidly became a red gum. However, the 4-brominated analog, IIa, produced a stable crystalline azafulvenamine, Ia, from which 4-bromo-2-pyrrolecarboxaldehyde was regenerated with aqueous base. Similarly, 4,5-dibromo and 3,4,5-tribromo salts, IIb and IIc, respectively, provided the corresponding azafulvenamines Ib and Ic. The 4-iodo salt gave a less pure material that was much less stable.

The nmr spectra of azafulvenamines Ia-c indicated that they were *cis-trans* mixtures. The 6-proton appeared as a pair of singlets for Ia (7.28 and 7.78 ppm in deuteriochloroform) and Ib (7.55 and 8.00 in DMSO-d_6) and as a broad singlet for Ic (7.43 in deuteriochloroform). In addition, the absorptions for the *alpha* protons on the pyrrolidine ring were very broad. Addition of traces of the corresponding perchlorate salts caused the predicted collapse of the 6-proton absorption to a singlet and a pronounced contraction of the pyrrolidine absorption.

Compound Ic appeared to be the best candidate for nucleophilic additions. Attempts to displace bromine (addition-elimination) with cyanide, methoxide, or azide, or to effect addition-cyclization with dimethyl malonate ion were uniformly unsuccessful.



Compound Ia was examined for reactivity as a nucleophile and as a diene. Treatment with methyl iodide gave the product of alkylation on the pyrrolenine nitrogen proved by hydrolysis to 4-bromo-1-methyl-2-pyrrolecarboxaldehyde (ir, glc comparison) (2).

Reaction of IIa with dimethylacetylenedicarboxylate gave two adducts. The nmr data for these materials and for the perchlorate salt of the 1:1 adduct did not allow distinction between the two likely structures, III and IV.

Therefore, x-ray single crystal diffraction analyses were performed on the two adducts. The results showed that III was the structure of the 1:1 adduct and that the second product was a 2:1 adduct, V. Molecule III crystallizes in the triclinic space group P1 with a = 10.151 (8) A, b = 10.315 (9) A, c = 9.016 (6) A, α = 79.9 (1)°, β = 108.5 (1)°,

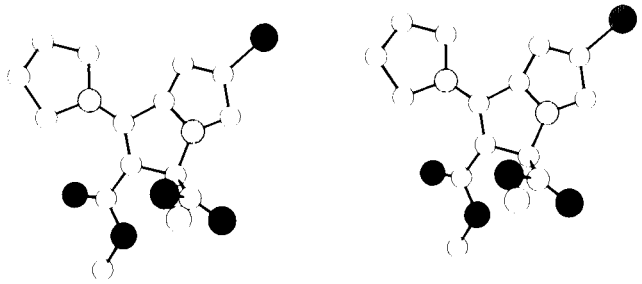


Figure 1. A stereodrawing of molecule III. The non-carbon as follows: Br. - ⊞; N - ⊜; O - ⊛.

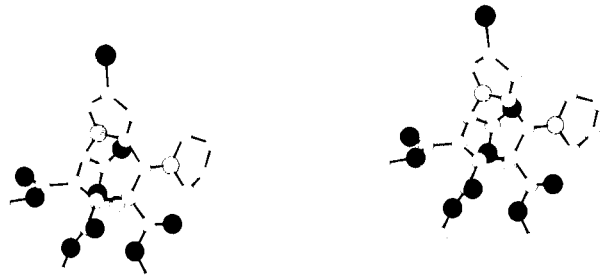


Figure 2. A sterodrawing of molecule V using the atom labelling code as in Fig 1.

and α = 119.3 (1)°. There are two molecules per unit cell corresponding to a calculated crystal density of 1.71 gm/cc. Molecule V crystallizes in the mono-clinic space group $P2_1/c$ with a = 15.511 (14) A, b = 10.314 (8) A, c = 13.820 (10) A and β = 90.2 (1)°. There are four molecules per unit cell corresponding to a density (calculated) of 1.53 gm/cc. Both structures were solved by the symbolic addition procedure for centrosymetric crystals (5). The results are illustrated in Figures 1 and 2. The figures were drawn by computer using program ORTEP (6). Atomic coordinates and thermal parameters for both molecules are being refined by full-matrix least-squares methods. Upon completion fo the refinement, full details of the structural features of III and IV will be published elsewhere (7).

These azafulvenamines apparently function as 1,3-dipoles and should find use in constructing novel heterocyclic ring systems.

EXPERIMENTAL (8)

General.

Melting points were determined on a Fisher-Johns apparatus and are uncorrected. Infrared spectra were obtained with Perkin-Elmer 137 and 457A Grating infrared spectrophotometers. Nmr spectra were obtained with a Varian T-60 instrument. The various halogenated pyrrole aldehydes could be conveniently examined by gas chromatography. We employed a Varian Aerograph 1520B instrument equipped with an SE-30 column (0.92 m. x 0.63 cm. 5% on Anakrom ABS). Ultraviolet data were obtained with a Beckman Dk-2A ratio Recording spectrophotometer. Chemical analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tennessee.

Syntheses of 4-Bromo; 3,4-Dibromo; and 3,4,5-Tribromo-2-azafulvenamines, Ia-c.

A slurry of 10.1 mmoles of hexane-washed sodium hydride in 80 ml. of tetrahydrofuran (THF) was prepared under nitrogen. The salt, II, (2) was added at one time (10 mmoles). After the mixture had been stirred for 15 minutes it was diluted with 80 ml. of hexane and suction-filtered. Recrystallization from THF-ethylacetate or aqueous ethanol afforded 68-81% yields of I. Treatment of II with a two phase system of ether and aqueous base was only partially successful since it caused partial conversion of I to aldehyde, m.p. 160-165° dec.; ir (chloroform): 1618 cm^{-1}, uv (ethanol): λ max 200 (11,700), 250 (3400), sh 297 (8300), 345 (17,200).

Anal. Calcd. for $C_9H_{11}BrN_2$: C, 47.59; H, 4.88; Br, 35.18; N, 12.34. Found: C, 47.53; H, 4.94; Br, 35.33; N, 12.26.

Compound Ib, m.p. 123-124.5°; ir (chloroform): 1620 cm^{-1}.

Anal. Calcd. for $C_9H_{10}Br_2N_2$: C, 35.32; H, 3.30; Br, 52.23; N, 9.16. Found: C, 35.44; H, 3.30; Br. 52.27; N. 9.13.

Compound Ic, m.p. 175-178°, ir (chloroform): 1625 cm^{-1}, uv (ethanol): λ max 200 (16,000), 348 (22,700).

Anal. Calcd. for $C_9H_9Br_3N_2$: C, 28.08; H, 2.36; Br, 62.28; N, 7.28. Found: C, 28.12; H, 2.47; Br, 62.33; N, 7.12.

Reaction of Ia with Dimethyl Acetylenedicarboxylate. Isolation of 3*H*-Pyrrolizine-2,3-dicarboxylic Acid, 6-Bromo-1-(1-pyrrolidinyl)-, Dimethyl Ester and 5*H*-Pyrrolo[1,2-*a*]azepine-5,6,7,8-Tetracarboxylic Acid, 2-Bromo-9-(1-pyrrolidinyl)-, Tetramethyl Ester.

The azafulvenamine, Ia, (5.0 mmoles) and 1 ml. (10 mmoles) of dimethyl acetylenedicarboxylate were dissolved in 40 ml. of dichloromethane. After 18 hours the mixture was concentrated on the flash evaporator, and residual azafulvanamine was hydrolyzed in 10 ml. each of methanol and water with 0.5 g. of sodium bicarbonate vigorously stirred at room temperature for 2 hours. The mixture was diluted with water and extracted with ether. The organic phase was now washed with 30 ml. of 1.5 *N* hydrochloric acid in 2 portions. The 1:1 adduct was recovered from the aqueous phase by basification (sodium carbonate) and extraction (ether) to give 700 mg. (38%) light yellow powder. The less basic 2:1 adduct was recovered from the mother liquor; 430 mg. (43%).

Compound III: m.p. 115-116° (ether); ir (chloroform): 1675, 1740 cm^{-1}; nmr (chloroform) 3.65 (s, 3, CH_3), 3.75 (s, 3, CH_3), 5.42 (bs, 1, benzylic H), 6.28 (bd, 1, aryl H), 6.95 (bt, 1, aryl H) ppm; uv (ethanol): λ max 235 (17500), 281 (21000), 348 (15000).

Anal. Calcd. for $C_{15}H_{17}BrN_2O_4$: C, 48.79; H, 4.64; Br, 21.64; N, 7.59. Found: C, 48.82; H, 4.63; Br, 21.87; N, 7.55.

Compound IV: m.p. 207° dec. (ether); ir (chloroform): 1675, 1740 cm^{-1}.

Anal. Calcd. for $C_{21}H_{23}BrN_2O_8$: C, 49.31; H, 4.54; Br, 15.63; N, 5.48. Found: C, 49.18; H, 4.33; Br, 15.37; N, 5.28.

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(8) Mention of a proprietary product does not constitute an endorsement by the USDA.