The Cyanidation of Indole.
The Reaction of 5,9-Dimethylindolo[2,3-*f*]morphan with Cyanogen Bromide

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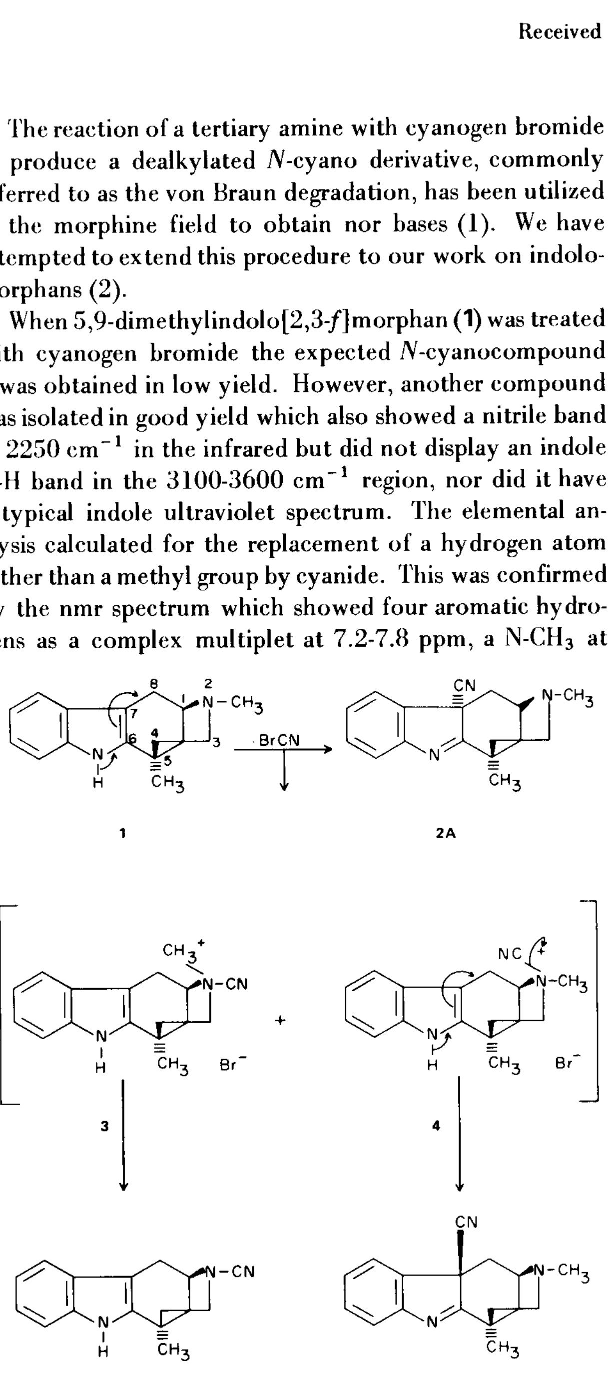
The reaction of a tertiary amine with cyanogen bromide to produce a dealkylated *N*-cyano derivative, commonly referred to as the von Braun degradation, has been utilized in the morphine field to obtain nor bases (1). We have attempted to extend this procedure to our work on indolomorphans (2).

When 5,9-dimethylindolo[2,3-*f*]morphan (**1**) was treated with cyanogen bromide the expected *N*-cyanocompound **5** was obtained in low yield. However, another compound was isolated in good yield which also showed a nitrile band at 2250 cm^{-1} in the infrared but did not display an indole N-H band in the 3100-3600 cm^{-1} region, nor did it have a typical indole ultraviolet spectrum. The elemental analysis calculated for the replacement of a hydrogen atom rather than a methyl group by cyanide. This was confirmed by the nmr spectrum which showed four aromatic hydrogens as a complex multiplet at 7.2-7.8 ppm, a N-CH$_3$ at 2.5 ppm, a C-CH$_3$ at 1.5 ppm and nine hydrogens as unresolved multiplets between 1.0 and 3.2 ppm. Infrared absorption at 1580 cm^{-1} and a plateau in the ultraviolet spectrum at 257 mμ (ϵ = 6600) suggested the presence of an indolenine system (3) such as **2**.



1 **2A**

3 **4**

5 **2B**

A 3-cyanoindolenine could arise from an electrophilic attack of cyanogen bromide on the indole 3-position in analogy to the cyanidation of an enamine (4). Presumably, the attack would be on the face of the indole opposite the bridge producing the *anti* (5) stereochemistry, shown in **2A**. However, another possible mechanism is suggested by the examination of the Drieding model of the quaternary **4**. In one of the two possible conformations of **4** the carbon atom at the indole 3-position and the carbon atom of the nitrile function are approximately two angstroms apart. Thus, there is a favorable situation for the intramolecular cyanidation of the indole 3-position by the quaternary cyanimide function. This mechanism would afford the *syn* (5) stereochemistry shown in **2B**. We have no direct evidence to support either mechanism, however, we favor the intramolecular route.

EXPERIMENTAL (6)

The melting points were determined using a Thomas Hoover apparatus which had been calibrated against known standards. The infrared spectra were recorded with a Baird Model 455 instrument on chloroform solutions. The ultraviolet spectra were determined using a Beckman DKI spectrophotometer on 95% ethanol solutions. The nmr spectra were determined with a Varian Associates A-60 spectrometer on deuteriochloroform solutions.

Reaction of a 2,5-Dimethylindolo[2,3-*f*]morphan with Cyanogen Bromide.

A solution of 2.0 g. of 2,5-dimethylindolo[2,3-*f*]morphan and 1.4 g. of cyanogen bromide in 25 ml. of chloroform was refluxed for 3 hours. The solvent was removed and the residue was chromatographed on 80 g. of alumina. The column was washed with benzene-methylene chloride (10:1). On concentration of the eluent, there was deposited 0.15 g. (7%) of 2-cyano-5-methylindolo-[2,3-*f*]morphan, m.p. 273-274°.

Anal. Calcd. for $C_{16}H_{17}N_3$: C, 76.46; H, 6.82; N, 16.72. Found: C, 76.60; H, 6.96; N, 16.85.

Removal of the solvent from the mother liquor afforded 0.86 g. (39%) of 7a-cyano-2,5-dimethylindolo[2,3-*f*]morphan, m.p. 128-129°. Recrystallization from Skelly-solve B gave an analytical sample, m.p. 133-134°.

Anal. Calcd. for $C_{17}H_{19}N_3$: C, 76.95; H, 7.21; N, 15.84. Found: C, 76.91; H, 7.25; N, 16.07.

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(5) *Syn* and *anti* refer to the relationship of the cyano function and the aminoethyl bridge.

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