

Photoaddition of Benzophenone to Azaindole,
Synthesis of the Oxetane of 7-Azaindole

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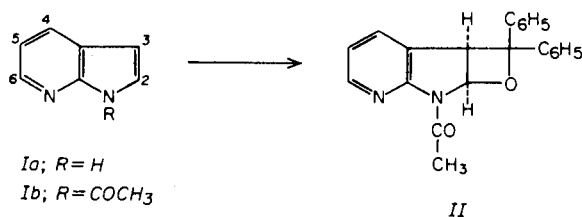
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7-Azaindole did not react with benzophenone on irradiation. However, irradiation of benzophenone in the presence of 1-acetyl-7-azaindole produced an oxetane by cycloaddition of the ketone to the 7-azaindole 2,3-double bond. The nmr and the mass spectra of the oxetane have also been studied in some detail.

J. Heterocyclic Chem., **13**, 585 (1976).

In connection with continued interest in the photocycloaddition reactions of ketones to heteroaromatic systems giving oxetanes, we have recently reported the synthesis of the oxetanes of imidazoles (1). Since the azaindoles belong to an interesting group of heterocycles from the viewpoint of their biological activity as analogs of physiologically active indoles (2), we now attempted to synthesize the oxetane of 7-azaindole (3). Although furans (4) and 2,5-dimethylthiophenes (5) form oxetanes on irradiation in the presence of benzophenone, pyrrole or imidazole itself fails to undergo such cycloaddition (6). This lack of reactivity may be due to greater electron density in the heterocyclic π -system or a quenching effect on the excited ketone by the non-bonded electrons on the nitrogen atom (7). This situation, however, has been overcome by capturing the non-bonded electrons with an electron-withdrawing protecting group, such as acetyl or benzoyl (6).

Scheme 1



Refluxing of 7-azaindole (Ia) with acetic anhydride yielded 1-acetyl-7-azaindole (Ib). Irradiation of Ib in benzene in the presence of benzophenone gave an oxetane II. As shown in the annexed Figure 1, the nmr spectrum in deuteriochloroform exhibits, besides the 1-acetyl signal at δ 2.80 ppm as a singlet, the 5-H signal at δ 6.83 ppm as a

quartet ($J_{5,4} = 8.5$ Hz and $J_{5,6} = 5$ Hz) and the 6-H signal at δ 8.30 ppm as a quartet ($J_{6,5} = 5$ Hz and $J_{6,4} = 1.5$ Hz). The 4-H signal apparently occurs around δ 7.72 ppm (8), but is not clearly separated from the benzenoid proton signals centered at δ 7.32 ppm. The 2-H proton, which is adjacent to both the oxygen and nitrogen atoms, resonates at δ 7.05 ppm and couples with the 3-H proton at δ 5.00 with $J = 6$ Hz. This was confirmed by decoupling experiments. When the δ 7.05 signal was irradiated, the δ 5.00 doublet collapsed to a singlet. Irradiation of the δ 5.00 signal also converted the δ 7.05 doublet to a singlet.

Since the mass spectrum of the oxetane II has not been reported previously, we investigated it in some detail. As outlined in the accompanying Scheme, the dominant process upon electron impact is the decomposition of the molecular ion *a* by a retro-Diels-Alder type opening of the oxetane ring to produce the original two component ions *b* and *c*. Each of these ions *b* and *c* undergoes further fragmentation. The elimination of ketene from the ion *c* may accompany hydrogen transfer from the acetyl group to the nitrogen atom of the pyridine ring to give the ion *d* as a base peak. This ion then decomposes by the loss of HCN to the *m/e* 91 ion. The spectrum also exhibits a pronounced M-1 ion (relative intensity 0.5% as compared with 0.7% of M ion), the structure of which may be formulated by *e* (9). Subsequent loss of HCN would yield the *m/e* 314 ion. The molecular ion *a* can also expel an acetyl radical to form the ion *f*, which would then lose the elements of (HCN + H) to afford the *m/e* 271 ion. The ejection of ketene from the molecular ion *a* in the same manner as in the case of the ion *c* would give rise to the ion *g*. A small but distinct ion peak appears at *m/e* 195. This ion may have structure *h*, and we assume that

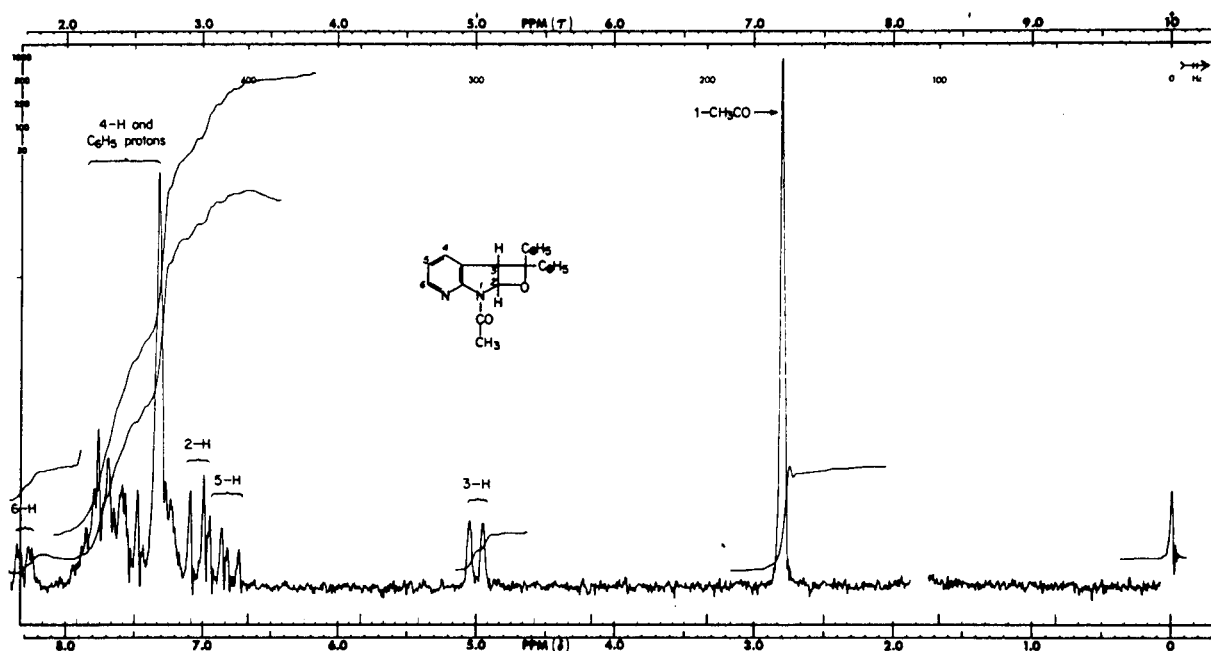
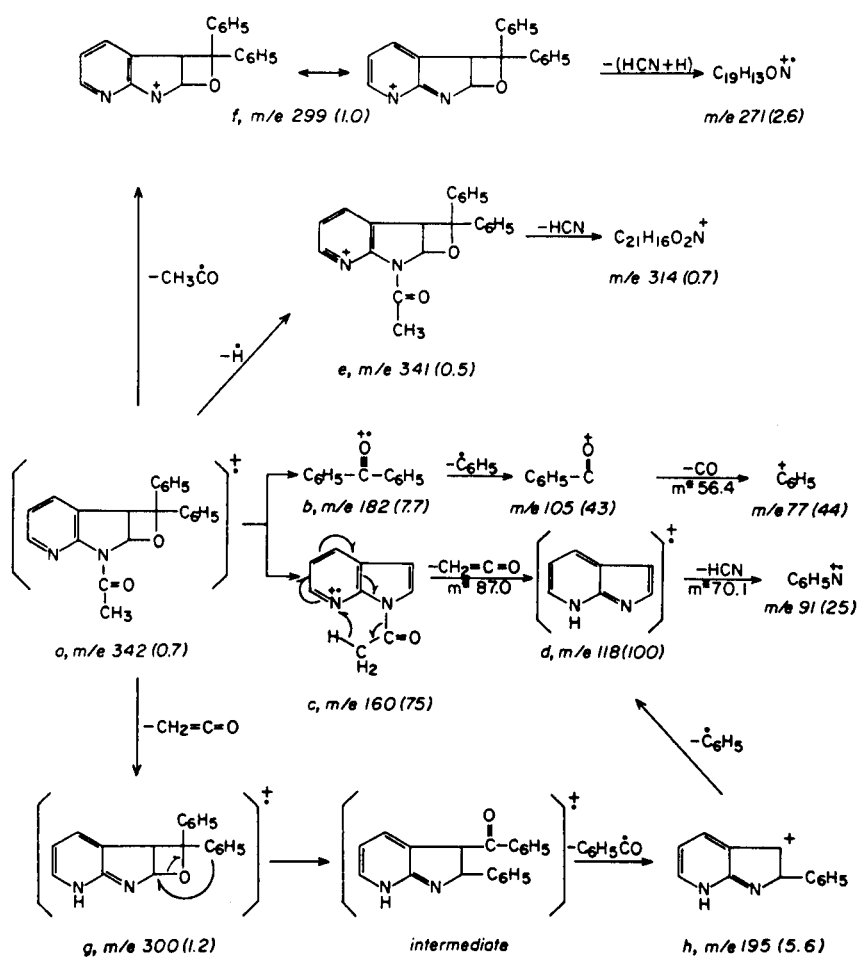


Figure 1



Scheme 2

it may be formed from the ion *g* by migration of a phenyl group with concomitant opening of the oxetane ring and by subsequent loss of a benzoyl radical, as depicted in the Scheme 2.

The pharmacological activity of the oxetane II is being studied and will be published elsewhere.

EXPERIMENTAL

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. Nmr spectra were obtained on a Varian A-60 instrument in deuteriochloroform and chemical shifts are reported in parts per million downfield from internal TMS (δ scale). Abbreviations s = singlet, d = doublet, and q = quartet. Mass spectra were recorded on a Hitachi Perkin-Elmer RMU-6H at 70 ev using a direct inlet system. The relative intensities of the ions are indicated in parentheses as a percentage of the base peak. 7-Aza-indole was purchased from Aldrich Chemical Co. Microanalyses were carried out by A. Bernhardt Microanalytical Laboratory, 5521 Elbach über Engelskirchen, West Germany.

1-Acetyl-7-azaindole (Ib).

The acetylation of 7-azaindole (Ia) was carried out as reported previously (10). 7-Azaindole (1.0 g.) was heated under reflux with acetic anhydride (5.5 ml.) for 2 hours. Acetic anhydride was distilled under reduced pressure, water (3 ml.) was added, and the solution was basified with sodium carbonate. Extraction with chloroform yielded a solid, m.p. 62-63° (1.0 g.); nmr: 3.11 (3H, s, 1-CH₃CO), 6.73 (1H, d, J_{3,2} = 4 Hz, 3-H), 7.35 (1H, q, J_{5,4} = 8 Hz and J_{5,6} = 5 Hz, 5-H), 8.06 (1H, q, J_{4,5} = 8 Hz and J_{4,6} = 2 Hz, 4-H), 8.20 (1H, d, J_{2,3} = 4 Hz, 2-H), and 8.73 (1H, q, J_{6,5} = 5 Hz and J_{6,4} = 2 Hz, 6-H).

Photoreaction of Benzophenone with 1-Acetyl-7-azaindole (Ib).

A solution of 1-acetyl-7-azaindole (Ib) (1.3 g.) and benzophenone (4.6 g.) in dry benzene (70 ml.) was placed in a vessel into which a quartz immersion well containing a Pyrex filter sleeve and a Hanovia 450W medium pressure mercury lamp was fitted. The double-walled immersion well containing the light source was cooled with water and the solution was irradiated while nitrogen

was bubbled through the solution before and during the irradiation. After 18 hours, the irradiation was discontinued and the solution was evaporated under reduced pressure. Upon addition of benzene-hexane, the crude oxetane (0.27 g.) was crystallized out, which was further purified by chromatography over Merck silica gel 60 (35-70 mesh ASTM). Elution with benzene-chloroform (1:3) yielded the pure oxetane II, m.p. 210-211° (0.11 g.).

Anal. Calcd. for C₂₂H₁₈O₂N₂: C, 77.17; H, 5.30; N, 8.18. Found: C, 77.45; H, 5.11; N, 7.98.

Acknowledgment.

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REFERENCES AND NOTES

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