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A NOVEL SYNTHESIS OF BENZO[b]OXEPINES

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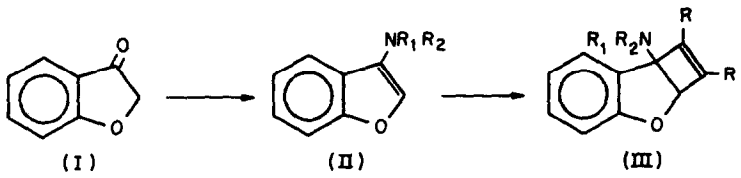
Previously (1,2) we described the reactions of 3-pyrrolidinobenzo[b]thiophene and 3-pyrrolidinothiophenes with dimethyl acetylenedicarboxylate yielding benzo[b]thiepines and thiepines, as an example of "enamine-like" cycloaddition reactions of N-heteroaryl pyrrolidines (3).

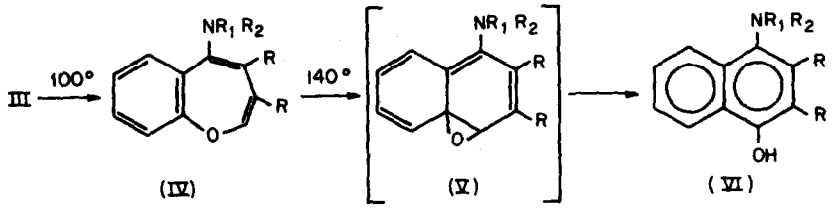
On the basis of the same type of reaction we now report on a novel synthesis of benzo[b]oxepines starting from dihydrobenzofuran-3-one (I) (4). At room temperature, the pyrrolidine enamine of I, prepared in refluxing benzene, reacted quantitatively with one equivalent of dimethyl acetylenedicarboxylate in diethyl ether to give the crystalline tricyclic adduct (III):



(I) (II) (III)

R=$COOCH_3$ AND NR_1R_2 = PYRROLIDINO

The structure of III, m.p. 107-108°, was proved by its PMR spectrum - δ_{H_1} 5.60 ppm(s), δ_{CH_3COO} 3.74 and 3.79 ppm and δ_{CH_2N} 2.63 ppm - and its IR spectrum - $\nu_{C=C}$ 1643 cm^{-1}. These data are in good agreement with those of the sulphur analogue of III (1) and with those reported by Hofmann and Hofmann (6) for a similar tricyclic product, the photo-isomer of 3,5-diacetoxy-4-phenylbenzo[b]oxepine. Upon being heated for 2 hours in dioxane at 100° III was isomerized quantitatively by opening of the cyclobutene ring into the corresponding benzo[b]oxepine (IV), m.p. 159-160°. The structure of IV was assigned on the basis of PMR spectroscopical data - δ_{H_2} 7.18 ppm(s), $\delta_{(CH_3COO)_2}$ 3.64 ppm and δ_{CH_2N} 3.25 ppm - which are in line with the expected values (1,7,8).



R = $COOCH_3$ AND NR_1R_2 = PYRROLIDINO

So far two syntheses of benzo[b]oxepines, a class of formal antiaromatic 12 π-electron heterocycles, have been reported. One comprises the isomerization of 1,6-oxido[10]annulene (7) and the other a multi-step preparation published by Hofmann and Westernacher (8). Prolonged heating (30 hours) of IV in p-xylene at 138° gave the isomeric 1-naphthol (VI), m.p. 118-119°. As with the oxepine-phenol isomerization we assume that this rearrangement takes place via the corresponding arene oxide. On treatment with a mixture of hydrochloric acid and methanol benzo[b]oxepine (IV) gave 3,4-dimethoxycarbonyl-5-hydroxybenzo[b]oxepine, m.p. 55-56° - δ_{OH} 12.00 ppm, δ_{H_2} 7.12 ppm and δ_{CH_3COO} 3.76 and 3.66 ppm - by hydrolysis of the dienamine moiety.

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3. The reported synthesis of benzazepines from 1-acetyl 3-piperidinoindole (4) may be regarded as another example of such a reaction, although no data on the degree of aromaticity of 1-acetylindole are available.

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