THE REACTION OF OXINDOLES WITH β-DIKETONES

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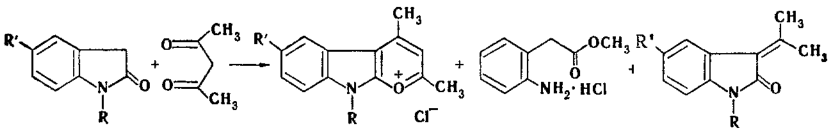
With acetylacetone in the presence of hydrogen chloride, oxindole and 1-acetyloxindole form mixtures of approximately equal amounts of 3-isopropylideneoxindole, 2,4-dimethyl-1-oxoniacarbazole chloride, and the hydrochloride of methyl o-aminophenylacetate. In the case of other 1- and 5-substituted oxindoles, the 3-isopropylidene derivatives have been isolated.

In view of the fact that oxindole and 1-methyloxindole react with hydroxymethylene ketones in the presence of hydrogen chloride to form indolo[3,2-e]pyrylium salts [1], the formation of products of similar structure could also have been expected in their reaction with β-diketones. We have shown that the treatment of equimolecular amounts of oxindole and acetylacetone in methanol with hydrogen chloride in the cold can in fact give a 33% yield of 2,4-dimethyl-1-oxoniacarbazole chloride (I) showing the IR absorption characteristic for a pyrylium ring (see Experimental). In addition to (I), this reaction gives approximately equal yields of 3-isopropylideneoxindole (II) and a crystalline substance readily soluble in water with the empirical composition $C_9H_{12}ClNO_2$ which apparently consists of the hydrochloride of methyl o-aminophenylacetate (III), formed by the hydrolytic cleavage of oxindole. The same products can be obtained by the reaction of N-acetyloxindole with acetylacetone, when deacetylation with the liberation of oxindole probably takes place first. Under these conditions, 1-methyloxindole and 6-nitro derivatives do not form pyrylium salts at all but give only the 3-isopropylidene derivatives (IV and V).



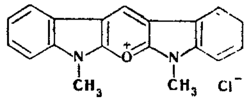
I   III   II, IV, V

II R=R'=H, IV R=CH₃, R'=H, V R=CH₃, R'=NO₂

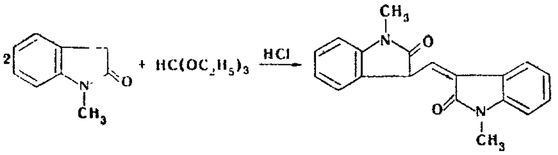
These compounds are probably formed from the oxindoles and the acetone that is obtained under the reaction conditions by the ketonic cleavage of the acetylacetone. A confirmation of this is the formation of (II), (IV), and (V) from the corresponding oxindoles and acetone under the same conditions with somewhat higher yields.

However, we have not succeeded in condensing oxindole with cyclohexanone, acetophenone, or dibenzoylmethane; in the last case, the initial diketone and (III) were recovered in full from the reaction mixture.

When a mixture of 1-methyloxindole and orthoformic ester was treated with hydrogen chloride, instead of (VI) brick-red crystals of 1-methyl-3-(1-methyloxindol-3-ylmethylene)oxindole (VII) were isolated.



VI



VII

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It appeared of interest in this connection also to consider the reaction of oxindole with analogs of β-diketones – β-keto nitriles. However, it was impossible to condense oxindole with 2-cyanocyclohexanone and α-formylbenzyl cyanide either in boiling acetic acid or on boiling for a week in ethanol in the presence of piperidine.

EXPERIMENTAL

The melting points were determined on a Kofler block and are not corrected. The UV spectra were taken on a Specord spectrophotometer in ethanol and the IR spectra on a UR-10 instrument in paraffin oil.

Condensation of Oxindole with Acetylacetone. With ice cooling, a solution of 0.67 g (5 mmoles) of oxindole and 1 g (10 mmoles) of acetylacetone in 10 ml of methanol was saturated with dry hydrogen chloride. After 1-2 h, the reaction mixture was diluted with a small volume of absolute ether until a slight turbidity appeared and was left for crystallization. The yellow acicular crystals of 2,4-dimethyl-1-oxoniacarbazole chloride that deposited were filtered off and carefully washed with ether. Yield 0.39 g (33%). mp 206°C (from methanol). Found, %: C 66.8; H 5.1; N 6.1. $C_{13}H_{12}ClNO$. Calculated, %: C 66.8; H 5.1; N 6.0. IR spectrum: 1640, 1590, 1560 cm^{-1}. UV spectrum, λ_{max} (log ε): 204 (4.28), 255 (4.31), 260 (4.35), 335 (3.96) nm. The filtrate was evaporated to approximately one fifth of its initial volume, and then 20 ml of water was added and it was extracted with small portions of ether. The aqueous layer deposited 0.30 g (30%) of the hydrochloride of methyl o-aminophenylacetate (III), mp 125°C. Found, %: C 54.0; H 6.0; N 6.8; Cl 17.6. $C_9H_{11}NO_2 \cdot HCl$. Calculated, %: C 53.6; H 5.9; N 6.9; Cl 17.6. IR spectrum: 1720, 1620, 1605, 1565 cm^{-1}. UV spectrum, λ_{max} (log ε): 207 (4.11), 234 (3.78), 290 (3.11) nm. The ethereal extract was concentrated and the light yellow crystals of 3-isopropylideneoxindole that deposited were filtered off and crystallized from methanol. Yield 0.28 g (33%). mp 185°C (literature [2] 186°C). IR spectrum: 1690, 1620 cm^{-1}. UV spectrum, λ_{max}, nm (log ε): 202 (4.11), 219 (3.51) 250 (4.33), 254 (4.33), 259 (4.42), 292 (3.43).

Similarly, 0.87 g (5 mmoles) of 1-acetyloxindole and 1 g (10 mmoles) of acetylacetone gave 0.5 g (36%) of 2,4-dimethyl-1-oxoniacarbazole chloride and 0.35 g (38%) of 3-isopropylideneoxindole.

3-Isopropylidene-1-methyloxindole (IV). a) A methanolic solution of 0.75 g (5 mmoles) of 1-methyloxindole and 1 g (10 mmoles) of acetylacetone was saturated with hydrogen chloride and gave 0.4 g (43%) of yellow crystals with mp 82-84°C (from petroleum ether). Found, %: C 77.5; H 7.1; N 7.6. $C_{12}H_{13}NO$. Calculated, %: C 77.0; H 7.0; N 7.5. IR spectrum: 1690, 1624, 1600 cm^{-1}. UV spectrum, λ_{max}, nm (log ε): 201 (4.72), 256 (4.72), 262 (4.80), 294 (4.02).

b) Similarly, 0.75 g (5 mmoles) of 1-methyloxindole and 0.60 g (10 mmoles) of acetone gave 0.51 g (54%) of 3-isopropylidene-1-methyloxindole.

3-Isopropylidene-1-methyl-5-nitrooxindole (V). a) From 0.97 g (5 mmoles) of 1-methyl-5-nitrooxindole and 1.0 g (10 mmoles) of acetylacetone was obtained 0.77 g (66%) of light brown acicular crystals with mp 184°C (from methanol). Found, %: C 62.1; H 5.2; N 11.7. $C_{12}H_{12}N_2O_3$. Calculated, %: C 62.1; H 5.2; N 12.1. IR spectrum: 1690, 1610 cm^{-1}. UV spectrum, λ_{max}, nm (log ε): 254 (4.30), 297 (4.06), 350 (3.98).

b) From 0.97 g (5 mmoles) of 1-methyl-5-nitrooxindole and 0.60 g (10 mmoles) of acetone was obtained 0.94 g (78%) of 3-isopropylidene-1-methyl-5-nitrooxindole with mp 184°C.

Reaction of Oxindole with Dibenzoylmethane. A solution of 0.67 g (5 mmoles) of oxindole and 1.12 g (5 mmoles) of dibenzoylmethane in 10 ml of methanol was saturated in the cold with hydrogen chloride. On standing, the reaction mixture deposited 0.85 g of orange crystals of dibenzoylmethane with mp 78°C. The filtrate deposited 0.65 g of (III) with mp 125°C (from ethanol).

1-Methyl-3-(1-methyloxindol-3-ylmethylene)oxindole (VII). A solution of 1.47 g (10 mmoles) of 1-methyloxindole in 7 ml of orthoformic ester was saturated in the cold with hydrogen chloride and was left at 20°C for several days. This gave 1.3 g (43%) of red acicular crystals with mp 236°C (from chloroform). Found, %: C 75.0; H 5.3. $C_{19}H_{16}N_2O_2$. Calculated, %: C 75.0; H 5.3. IR spectrum: 1620, 1600, 1465, 1380 cm^{-1}. UV spectrum, λ_{max}, nm (log ε): 263 (4.09), 278 (4.13), 271 (4.49).

LITERATURE CITED

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2. A. Wahl and V. Livovschi, Bull. Soc. Chim. France, 5, 653 (1938).