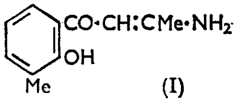
662. *The Reaction of* 3-*Bromo*-4-*chromanone and of* 4-*Chromone with Diethylamine and other Bases*

By I. M. Lockhart and (Miss) E. M. Tanner

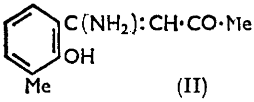
It is shown that reaction of 3-bromo-4-chromanone or of 4-chromone with diethylamine yields 2-diethylaminovinyl *o*-hydroxyphenyl ketone (IV).

Colonge and Guyot[1] showed that 3-bromo-4-chromanone (III) reacts with diethylamine in aqueous suspension at room temperature to give a bright yellow crystalline solid which they formulated as 3-diethylamino-4-chromanone. On refluxing with 6N-hydrochloric acid for one hour, the product was converted into 4-chromone.

We have repeated this work and concluded from examination of the yellow product that the attributed chromanone structure was not consistent with the infrared spectrum (a band at 1628 cm.$^{-1}$, but no band at 1690 cm.$^{-1}$ typical of the carbonyl group in a 4-chromanone), with the ultraviolet spectrum [$\lambda_{max.}$ 362 mμ (ε 29,900) in contrast with 4-chromanone, $\lambda_{max.}$ 322 mμ (ε 3417)], or with the potentiometric titration (weak base, p$K_a < 3$). The product was readily decomposed by hydrogen chloride to give 4-chromone (V) and diethylamine hydrochloride.



(I)



(II)

The same yellow crystalline product was obtained when 4-chromone (V) was treated with diethylamine under conditions similar to those used with 3-bromo-4-chromanone. This indicated that the first step in the reaction with 3-bromo-4-chromanone was almost

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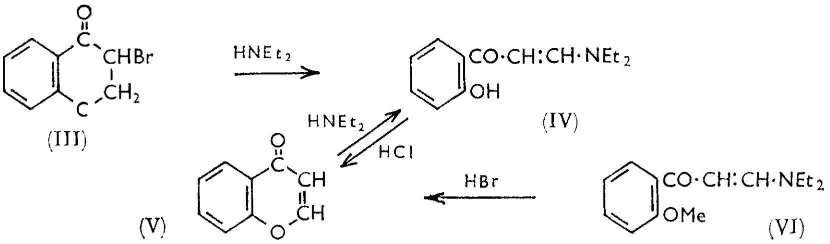
[1] J. Colonge and A. Guyot, *Bull. Soc. chim. France*, 1958, 329.

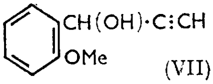
certainly elimination of hydrogen bromide. If subsequent addition of the amine occurred across the resulting double bond, 2-diethylamino-4-chromanone would have been the likely product but such a structure was equally incompatible with the physical chemistry data.

Wittig and Blumenthal [2] suggested that 2,8-dimethyl-4-chromone reacted with ammonia to give a product which had structure (I) or (II), and it seemed probable that a similar reaction was occurring in the present case. We suggest that the structure of the product from reaction of 3-bromo-4-chromanone (III) with diethylamine is the vinyl ketone (IV). Such a structure was consistent with the infrared spectrum (the band at 1628 cm.$^{-1}$ being attributed to a carbonyl involved in conjugate chelation), the high-intensity long-wavelength ultraviolet band, and the behaviour of the compound as a weak base. The nuclear magnetic resonance spectrum confirmed the correctness of the structure assigned; the magnitude of the spin–spin splitting (about 12 c./sec.) indicated that the compound had a *trans*-configuration of hydrogen around the double bond.

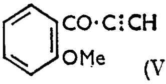


(III) (IV) (V) (VI)

Although we have not synthesised 2-diethylaminovinyl *o*-hydroxyphenyl ketone (IV) by an unequivocal route, the corresponding methoxy-compound (VI) has been prepared. *o*-Methoxybenzaldehyde was treated with acetylene in the presence of sodamide and the resulting carbinol (VII) oxidised with chromium trioxide. Addition of diethylamine to the ethynyl ketone (VIII) gave the diethylamino-compound (VI). After allowance had been made for replacement of hydroxyl by methoxyl, a comparison of the infrared spectrum (carbonyl band at 1633 cm.$^{-1}$), ultraviolet spectrum [$\lambda_{max.}$ 339 mμ (ε 17,150)], and potentiometric titration (weak base, pK_a ~3) of the methoxy-compound (VI) with the corresponding data for the product of the reaction of 3-bromo-4-chromanone with diethylamine was consistent with this latter having the structure (IV).



(VII)



(VIII)

Treatment of the methoxy-compound (VI) with hydrobromic acid afforded 4-chromone (V). Demethylation with hydrobromic acid would first be expected to yield the hydroxy-compound (IV). If structure (IV) was correct for the product of reaction of 3-bromo-4-chromanone with diethylamine (which is converted into 4-chromone by hydrochloric acid), then the demethylated product from compound (VI) would be expected to react further in the presence of hydrobromic acid to yield 4-chromone (V).

We similarly believe that the compound obtained by reaction of 3-bromo-4-chromanone with piperidine [1] is not a piperidino-chromanone but the piperidino-analogue of compound (IV).* The dimethylamino-analogue of compound (IV) has also been prepared.

EXPERIMENTAL

Unless otherwise stated, infrared spectra were measured on Nujol mulls using a Grubb–Parsons DB1/S3A spectrometer with sodium chloride optics. Ultraviolet spectra were measured

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* *Note added in Proof.*—Since this Paper was submitted for publication, P. W. Feit (*Acta Chem. Scand.*, 1964, **18**, 2401) has reached the same conclusion.

[2] G. Wittig and H. Blumenthal, *Ber.*, 1927, **60***B*, 1085.

in solution in ethanol with a Unicam S.P. 700 spectrophotometer; pK_a measurements were made by potentiometric titration in 50% ethanol using a Radiometer automatic titrator.

Reaction of 3-*Bromo*-4-*chromanones with Bases.*—3-Bromo-4-chromanone [3] was treated with diethylamine and piperidine as described by Colonge and Guyot.[1] The former yielded 2-*diethylaminovinyl* o-*hydroxyphenyl ketone* as yellow prisms, m. p. 76—76·5° (Found: C, 70·85; H, 7·5; N, 6·6. $C_{13}H_{17}NO_2$ requires C, 71·2; H, 7·8; N, 6·4%); $\nu_{max.}$ 1618, 1581, 1544 and 1628, 1577, 1537, 1487 cm.$^{-1}$ (chloroform); $\lambda_{max.}$ 214, 226, 248, 256, 262, 362 mμ (ε 12,490, 11,180, 6850, 7610, 7570, 29,900); pK_a <3, and the latter afforded *o*-hydroxyphenyl 2-piperidinovinyl ketone as yellow prisms, m. p. 119—120° (lit.,[4] 123—124°) (Found: C, 73·1; H, 7·35; N, 6·2. Calc. for $C_{14}H_{17}NO_2$: C, 72·7; H, 7·4; N, 6·1%); $\nu_{max.}$ 1615, 1577, 1530 cm.$^{-1}$; $\lambda_{max.}$ 213, 227, 249, 256, 262, 362 mμ (ε 14,000, 12,300, 7640, 8430, 8410, 31,500). Treatment of 3-bromo-4-chromanone with aqueous dimethylamine under similar conditions afforded 2-*dimethylaminovinyl* o-*hydroxyphenyl ketone* as yellow prisms, m. p. 129—130° [from benzene–light petroleum (b. p. 60—80°)] (Found: C, 69·55; H, 6·7; N, 7·15. $C_{11}H_{13}NO_2$ requires C, 69·1; H, 6·85; N, 7·4%); $\nu_{max.}$ 1624, 1587, 1540 cm.$^{-1}$; $\lambda_{max.}$ 214, 227, 246, 255, 261, 360 mμ (ε 12,780, 12,700, 6850, 7620, 7500, 28,000).

Reaction of 2-*Diethylaminovinyl* o-*Hydroxyphenyl Ketone with Hydrogen Chloride.*—Ethereal hydrogen chloride was added to the ketone (12·6 g.) in anhydrous ether (250 ml.) until no more precipitation occurred. The product was recrystallised from ethyl methyl ketone (30 ml.) and afforded white plates (5·3 g.), m. p. 220—222°, which were identified as diethylamine hydrochloride. The mother-liquors were evaporated *in vacuo* and the residual brown oil crystallised on standing. Recrystallisation from light petroleum (b. p. 60—80°) afforded white needles (5·25 g.), m. p. 54·5—55·5° (lit.,[1] 57°) which were identified as 4-chromone and characterised as the oxime which crystallised from ethanol–water with m. p. 184—185° (lit.,[1] 184°).

Reaction of 4-*Chromone with Diethylamine.*—4-Chromone (1·0 g., from above experiment) was shaken with diethylamine (0·5 g.) in water (5 ml.) for 3 hr. The solid was filtered off, washed with water, and dried. Recrystallisation from light petroleum (b. p. 60—80°) afforded yellow prisms (1·1 g.) of m. p. 74—75·5°. Mixed m. p. and the infrared spectrum showed that the product was identical with that from treatment of 3-bromo-4-chromanone with diethylamine and was 2-diethylaminovinyl *o*-hydroxyphenyl ketone.

Ethynyl o-*Methoxyphenyl Ketone* (VIII).—Acetylene was added to *o*-methoxybenzaldehyde (68 g.) in the presence of sodamide in liquid ammonia by a method similar to that of Jones and McCombie.[5] o-*Methoxyphenylethylcarbinol* (VII) was obtained as a pale yellow liquid (59 g.) of b. p. 123—125°/2 mm. and having n_D^{21} 1·5550 (Found: C, 73·8; H, 6·3. $C_{10}H_{10}O_2$ requires C, 74·05; H, 6·2%). Oxidation of the carbinol (VII) with chromium trioxide in the manner described by Bowden *et al.*[6] afforded *ethynyl* o-*methoxyphenyl ketone* (39·5 g.) as a pale yellow oil, b. p. 106°/0·8 mm., with n_D^{20} 1·5777 (Found: C, 74·8; H, 5·45. $C_{10}H_8O_2$ requires C, 75·0; H, 5·0%).

2-*Diethylaminovinyl* o-*Methoxyphenyl Ketone* (VI).—Diethylamine (2·3 g., 1 mole) in methanol (20 ml.) was added dropwise with stirring to an ice-cold solution of ethynyl *o*-methoxyphenyl ketone (5 g.) in methanol (20 ml.). The mixture was set aside at room temperature for 3 hr. and evaporated *in vacuo*. The residue, in ether (20 ml.), was extracted with 2N-hydrochloric acid, the acid extracts basified with 10N-sodium hydroxide, and the alkaline solution extracted with ether. The ether extracts were dried ($MgSO_4$) and evaporated *in vacuo*. Recrystallisation from light petroleum (b. p. 60—80°) afforded 2-*diethylaminovinyl* o-*methoxyphenyl ketone* (4·1 g.) as pale yellow prisms. An analytical sample had m. p. 50—51° (Found: C, 71·8; H, 8·05; N, 6·2. $C_{14}H_{19}NO_2$ requires C, 72·1; H, 8·2; N, 6·0%); $\nu_{max.}$ 1633, 1596, 1579, 1534 and 1633, 1592, 1575, 1544, 1482 cm.$^{-1}$ (chloroform); $\lambda_{max.}$ 256, 308, 339 mμ (ε 4360, 17,650, 17,150); pK_a ~3.

Reaction of 2-*Diethylaminovinyl* o-*Methoxyphenyl Ketone with Hydrobromic Acid.*—The ketone (VI) (2·5 g.) was heated under reflux with hydrobromic acid (25 ml.; 48—50% w/w) for 1½ hr. The solution was evaporated *in vacuo* and re-evaporated twice from water. The residue in water (50 ml.) was extracted with ether, the ether extracts dried ($MgSO_4$), and evaporated *in vacuo*. The crystalline residue (1·0 g.) was recrystallised from light petroleum

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[3] F. Arndt and G. Källner, *Ber.*, 1924, **57**, 202.

[4] C. W. Winter and C. S. Hamilton, *J. Amer. Chem. Soc.*, 1952, **74**, 3999.

[5] E. R. H. Jones and J. T. McCombie, *J.*, 1942, 733.

[6] K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J.*, 1946, 39.

(b. p. 60—80°) to give white needles, m. p. 53—54°, which were identified as 4-chromone (Found: C, 74·0; H, 4·4. Calc. for $C_9H_6O_2$: C, 74·0; H, 4·1%).

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