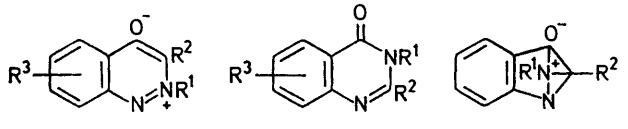
Cinnolines. Part XVI.[1] Photochemical Rearrangement of 2-Alkylcinnolinium-4-olates to 3-Alkyl-4(3*H*)-quinazolones

By **Donald E. Ames,* Sosale Chandrasekhar,** and (in part) **Roy Simpson,** Chemistry Department, Chelsea College, Manresa Road, London SW3 6LX

This rearrangement occurs in good yield on irradiation of ethanolic solutions, but 2-methylcinnolinium-4-thiolate, 1-methyl-4(1*H*)-cinnolone, and 2-methyl-3(2*H*)-cinnolone do not react.

It has recently been shown [2] that pyridazinium-3-olates rearrange in a photochemical reaction to give 4-pyrimidones. The analogous anhydro-bases of the cinnoline series have now been found to rearrange similarly; thus 2-methylcinnolinium-4-olate (Ia) gave 3-methyl-4(3*H*)-quinazolone (IIa) in a good yield as the only identifiable product. Substituted anhydro-bases (I), including 3-alkyl derivatives, reacted similarly (see Table). In each case, the change from dipolar structure (I) to the formally covalent product (II) resulted in a marked shift of the N·CH_3 or N·CH_2 resonance upfield by 0.4—0.8 p.p.m.

2,3-Dihydro-1*H*-pyrrolo[1,2-*b*]cinnolinium-10-olate (Ig) was prepared by condensation of *o*-nitrobenzoyl chloride with the sodio-derivative of di-t-butyl 3-methoxypropylmalonate, followed by acidolysis and decarboxylation [3] to give 4-methoxybutyl *o*-nitrophenyl ketone. Reduction to the amino-ketone and diazotisation [4] yielded 3-(3-methoxypropyl)-4(1*H*)-cinnolone; this was converted into the 3-bromopropyl compound, which cyclised to form the anhydro-base (Ig). Irradiation of this tricyclic compound effected rearrangement to the corresponding quinazolone (IIg), the N·CH_2 triplet in the n.m.r. spectrum shifting 0.55 p.p.m. upfield as in the previous examples.



(I) (II) (III)

The following related compounds were unchanged when irradiated under similar conditions: 2-methylcinnolinium-4-thiolate, 4(1*H*)-cinnolone, 1-methyl-4(1*H*)-cinnolone, 2-methyl-3(2*H*)-cinnolone, and 4-methoxycinnoline. Since dipolar structures can be formulated for the first four of these compounds, the rearrangement is apparently characteristic of anhydro-bases of type (I), and may therefore be of value as an alternative method for distinguishing 2-alkylcinnolinium-4-olates from the isomeric 1-alkyl-4(1*H*)-cinnolones in alkylation reactions. The photolysis of 4-methylcinnoline 1- and 2-oxides by prolonged irradiation has been reported [5] and the isolation of 4-methylcinnoline as a major product from both *N*-oxides shows the stability of the cinnoline ring system to irradiation. In contrast, the photochemical rearrangement of hexafluorocinnoline into hexafluoroquinazoline has been effected [6] in low yield. The present reaction presumably proceeds *via* a diazabenzvalene intermediate such as (III) (*cf.* refs. 2 and 6).

^{1}H N.m.r. spectra (δ values) of 2-alkylcinnolinium-4-olates and 3-alkyl-4(3*H*)-quinazolones.[a]

			(I)		(II)	
R^1	R^2	R^3	NMe	Other	NMe	Other
a; Me	H	H	4.32		3.59	
b; Me	H	8-Cl	4.39		3.59	
c; Me	H	6,7-$(OMe)_2$	4.30	3.94 and 4.03 (2-OMe)	3.58	4.00 (2-OMe)
d; Me	Bu^n	H	4.33	3.13 (t) (α-CH_2) 0.8—2.0 (m) (Pr^n)	3.62	2.85 (t) (α-CH_2) 0.8—2.1 (m) (Pr^n)
e; CH_2Ph	H	H	5.53 [b]		5.18 [b]	
f; Me	CH_2Ph	H	4.18	4.51 (CH_2Ph)	3.46	4.23 (CH_2)
g;	$[CH_2]_3$	H	4.75(t) [b]	3.43 (t) (N·CH_2·CH_2·CH_2) 2.3 [c] (N·CH_2·CH_2·CH_2)	4.20(t) [b]	3.15 (t) (N·CH_2·CH_2·CH_2) 2.25 [c] (N·CH_2·CH_2·CH_2)

[a] Solvent $CDCl_3$; Me_4Si internal reference. [b] N·CH_2. [c] Quintet.

EXPERIMENTAL

Evaporations were carried out under reduced pressure; petrol refers to light petroleum (b.p. 60—80°). ^{1}H N.m.r. spectra were recorded on a Perkin-Elmer R32 spectrometer at 90 MHz.

Rearrangement of 2-Methylcinnolinium-4-olate (Ia).—The anhydro-base (0.2 g) in ethanol (15 ml) was irradiated with a high pressure mercury vapour lamp (125 W) so that the solution boiled under reflux for 5 h. T.l.c. then indicated that a single product had been formed. The solution was evaporated and the residue dissolved in benzene; treatment with charcoal and filtration through alumina (2 × 2 cm) removed a little resinous material. The alumina was then washed thoroughly with ethyl acetate (100 ml); evaporation and crystallisation from water gave 3-methyl-4(3*H*)-quinazolone (0.16 g, 80%), m.p. and mixed m.p. 104—105° (lit.,[7] 105°).

[1] Part XV, D. E. Ames, H. R. Ansari, A. D. G. France, A. C. Lovesey, B. Novitt, and R. Simpson, *J. Chem. Soc.* (*C*), 1971, 3088.

[2] Y. Maki, M. Suzuki, T. Furuta, T. Hiramitsu, and M. Kuzuya, *Tetrahedron Letters*, 1974, 4107.

[3] G. S. Fonken and W. S. Johnson, *J. Amer. Chem. Soc.*, 1952, **74**, 831.

[4] *Cf.* J. R. Keneford and J. C. E. Simpson, *J. Chem. Soc.*, 1947. 917.

[5] W. M. Horspool, J. R. Kershaw, and A. W. Murray, *J.C.S. Chem. Comm.*, 1973, 345.

[6] R. D. Chambers, J. A. H. MacBride, and W. K. R. Musgrave, *Chem. Comm.*, 1970, 739.

[7] M. T. Bogert and G. A. Geiger, *J. Amer. Chem. Soc.*, 1912, **34**, 524.

The following compounds were prepared similarly: 8-chloro-3-methyl-4(3*H*)-quinazolone (95%), m.p. 158—159° (from petrol) (lit.,[8] 159—160°); 6,7-dimethoxy-3-methyl-4(3*H*)-quinazolone, m.p. 214—215° (from petrol) (lit.,[9] 207—209°) (Found: C, 59.8; H, 5.5; N, 12.8. Calc. for $C_{11}H_{12}N_2O_3$: C, 60.0; H, 5.5; N, 12.7%); 2-*butyl*-3-*methyl*-4(3H)-*quinazolone* (70%), m.p. 55—56° (from petrol) (Found: C, 72.7; H, 7.4; N, 12.9. $C_{13}H_{16}N_2O$ requires C, 72.2; H, 7.5; N, 13.0%); 3-benzyl-4(3*H*)-quinazolone, m.p. 117—118° (from petrol) (lit.,[10] 117—118°); 2-benzyl-3-methyl-4(3*H*)-quinazolone, m.p. 88—89° (from petrol) (lit.,[11] 86.5—88°); and 2,3-*dihydro*-1H-*pyrrolo*[2,1-b]*quinazolin*-5-*one* (IIg) (90%), m.p. 110—111° (from petrol) (Found: C, 70.8; H, 5.4; N, 15.0. $C_{11}H_{10}N_2O$ requires C, 71.0; H, 5.4; N, 15.1%), $\lambda_{max.}$ 225, 266, 304, and 316 nm (ε 26 400, 7 100, 3 500, and 3 000).

2,3-*Dihydro*-1H-*pyrrolo*[1,2-b]*cinnolium*-10-*olate* (Ig).—Sodium hydride (9.9 g; 50%) in t-butyl alcohol (250 ml) was treated successively with di-t-butyl malonate (129 g), sodium iodide (7.65 g), and 3-chloropropyl methyl ether (22.5 g) in t-butyl alcohol (80 ml). The mixture was stirred and heated at 65 °C for 4 h; it was then cooled and poured into water. Isolation with ether and fractional distillation gave *di-t-butyl* 3-*methoxypropylmalonate* (44.6 g), b.p. 89—91° at 0.2 mmHg (Found: C, 62.5; H, 9.9. $C_{15}H_{28}O_5$ requires C, 62.5; H, 9.8%). This (31.7 g) in benzene (220 ml) was added gradually to a stirred suspension of sodium hydride (2.88 g; 50%) in benzene (110 ml). The mixture was stirred and heated at 100 °C under reflux for 6 h and then cooled. *o*-Nitrobenzoyl chloride (20.4 g) in benzene (110 ml) was added slowly (internal temp. 50 °C). After the mixture had been stirred at 45 °C for 1 h, it was treated gradually with acetic acid (110 ml) containing concentrated sulphuric acid (5 ml). The mixture was heated under reflux (bath at 110 °C) for 7.5 h and poured into water. Isolation with benzene and distillation gave 4-*methoxybutyl* o-*nitrophenyl ketone* (13.4 g) as a yellow oil, b.p. 149—150° at 0.3 mmHg (Found: C, 60.9; H, 6.3; N, 6.0. $C_{12}H_{15}NO_4$ requires C, 60.8; H, 6.4; N, 5.9%). The nitro-ketone (16.3 g) in acetic acid (300 ml) and water (70 ml) was stirred and heated under reflux while iron powder (29.6 g) was added over 30 min and then for a further 4 h.[4] The cooled mixture was filtered through kieselguhr which was washed with hot ethyl acetate. Evaporation of the filtrates, addition of water, and isolation with ethyl acetate gave o-*aminophenyl* 4-*methoxybutyl ketone* (10.5 g), b.p. 126—128° at 0.4 mmHg (Found: C, 69.4; H, 8.2; N, 6.4. $C_{12}H_{17}NO_2$ requires C, 69.6; H, 8.3; N, 6.7%).

The base (20.4 g) in concentrated hydrochloric acid (700 ml) and water (70 ml) was cooled at 0—5 °C while sodium nitrite (8.25 g) was added in small portions during 40 min. The solution was left at room temperature for 3 days and then concentrated to 200 ml by distillation at 50 °C under reduced pressure. Neutralisation with solid sodium carbonate and isolation with chloroform yielded 3-(3-*methoxypropyl*)-4(1H)-*cinnolone* (9.9 g), m.p. 148—149° (from ethyl acetate–petrol) (Found: C, 65.9; H, 6.6; N, 12.8. $C_{12}H_{14}N_2O_2$ requires C, 66.0; H, 6.5; N, 12.8%); $\nu_{max.}$ 1 580 cm^{-1} (C:O); $\lambda_{max.}$ 237, 251, 281, 292, 340, and 356 nm (ε 14 500, 7 900, 4 800, 4 800, 12 600, and 12 600). The cinnolone (10.5 g) and hydrobromic acid (150 ml; 48%) were heated under reflux (bath at 160 °C) for 1.5 h. After the solution had been evaporated (<70 °C), the residue was brought to pH 9 by addition of 2N-sodium carbonate and the solution was left at room temperature for 3 h. Isolation with chloroform and crystallisation from acetone–ether gave the *pyrrolocinnoline* (Ig) (7.1 g, 79%), m.p. 167—168° (Found: C, 70.9; H, 5.4; N, 15.3%; M^+, 186. $C_{11}H_{10}N_2O$ requires C, 71.0; H, 5.4; N, 15.1%; *M*, 186); $\nu_{max.}$ 1 580 cm^{-1} (C:O); $\lambda_{max.}$ 254, 357, and 370 nm (ε 12 100, 15 300, and 17 500).

We thank the Governors of this college for a grant (to S. C.)

[5/390 *Received*, 25*th February*, 1975

[8] Neth. P. 6,403,115/1965 (*Chem. Abs.*, 1966, **64**, 5114).

[9] J. Maillard, M. Benard, M. Vincent, Vo-Van-Tri, R. Jolly, R. Morin, M. Benharkate, and C. Menillet, *Chim. ther.*, 1967, **2**, 231.

[10] P. A. Petyunin and Y. V. Kozhevnikov, *Zhur. obshchei Khim.*, 1960, **30**, 2352.

[11] B. C. Lawes and H. C. Scarborough, U.S.P., 3,127,401, 1964.