Novel Cyclization of Bis-(bromoacetyl)heteroaromatic Compounds. Synthesis of Heterocyclic Quinones

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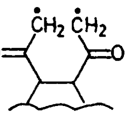
Summary A novel zinc-induced intramolecular cyclization of bis-(bromoacetyl) derivatives, leading to iso-heterocyclic quinones (IVa—c) *via* the primarily formed bicyclic diketones (IIIa—c), is described.

A great variety of intramolecular ring closure reactions is known but none seems to lead directly to saturated six-membered 1,4-cyclic diketones. The vicinal bis-α-oxomethylene biradical system (A) could, however, couple intramolecularly to the desired product.

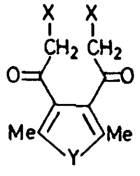
Table

Quinone	M.p./°C	δ (CDCl$_3$)
(IVa)	162	2·76 (6H), 6·74 (2H)
(IVb)	176	2·60 (6H), 6·75 (2H)
(IVc)	235	2·57 (6H), 3·48 (3H), 6·60 (2H)

We report now the use of a novel method for the generation of biradicals, which has led to the ready formation of new heteroannelated cyclic 1,4-diketones. Treatment of the 2,5-dimethyl-3,4-bis(bromoacetyl) heteroaromatic compounds (IIa—c) (1 equiv.) with Zn–Cu[1] (10 equiv.) in Me_2SO [10 ml for each mmol of (II); $NaHCO_3$ (2 equiv.) and NaI (1 equiv.) were also added] at 50° under inert atmosphere for 30 min gave the diketones (IIIa), m.p. 122°, (IIIb), m.p. 151°, and (IIIc), m.p. 219°, in 50—60% yield.[†]

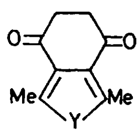


(A)

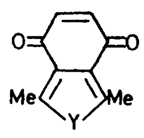


(I) X = H

(II) X = Br

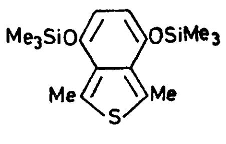


(III)



(IV)

a, Y = S; b, Y = O; c, Y = NMe



(V)

[†] The products were readily isolated by filtration on a silica G column. Analytical and spectral data (i.r., u.v., and n.m.r.) were in agreement with the assigned structures.

The intermediacy of a biradical in the ring closure step is assumed in accordance with the formerly reported evidence for zinc-induced homolytic cleavage of aromatic α-bromoketones.[2]

Cyclization under similar conditions but in ethereal hydrogen-donor solvents (tetrahydrofuran or 1,4-dioxan) gives (I) as the main product. The reductive dehalogenation probably occurs by an ionic pathway: use of [$^2H_8$]-1,4-dioxan did not result in deuterium transfer into (I).

The diketones (I), prepared by known methods,[3] were brominated using bromine in dioxan–ether [(Ia) and (Ib)] or phenyltrimethylammonium perbromide[4] in tetrahydrofuran [for (Ic)]. Overbromination may occur to some extent. Surprisingly, the overbrominated material (tri- and tetrabromodiketones) was also found to afford compounds (III) in similar yields. The coupling mechanism is believed to be different in this case, on the basis of experiments to be reported elsewhere, and may involve an intramolecular C–H insertion of a ketocarbenoid species.[5]

The availability of the diketones (III) provides an entry into the unknown isobenzothiophenquinones and isoindolequinones and the little investigated[6] isobenzofuranquinones: reflux of (III) with excess of dichlorodicyanobenzoquinone in dioxan [8 h, for (IIIa) and (IIIb)] or with chloranil in t-pentyl alcohol [6 h, for (IIIc)] afforded the respective quinones (IV) (see Table) in 70—80% yield.

The diketones (III) do not seem to enolize readily; (no change in u.v. spectra upon addition of acid or base). The dienolate (V) could, however, be prepared easily,[7] m.p. 54° (70%), δ ($CDCl_3$) 0·27 (18H), 2·78 (6H), and 5·94 (2H), thus providing an entry into the benzo[*c*]thiophen series.

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[1] Prepared according to J. B. Lambert, F. R. Koeng, and J. W. Hamersma, *J. Org. Chem.*, 1971, **36**, 2946; 1% $CuSO_4$ solution was used.

[2] E. Ghera, D. H. Perry, and S. Shoua, *J.C.S. Chem. Comm.*, 1973, 858.

[3] For Y=S, Y. Goldfarb and U. P. Litwinov, *J. Gen. Chem.* (*U.S.S.R.*), 1960, **30**, 2719; For Y=O, M. S. Newmann and J. A. Cella, *J. Org. Chem.*, 1973, **38**, 3482; For Y=NMe, D. B. Bright, *J. Amer. Chem. Soc.*, 1957, **79**, 3200.

[4] See L. F. Fieser and M. Fieser, 'Reagents for Organic Synthesis,' Vol. I, Wiley, New York, 1967.

[5] L. T. Scott and W. D. Cotton, *J. Amer. Chem. Soc.*, 1973, **95**, 2708, 5416.

[6] Two specific iso-benzofuranquinones have been previously prepared: R. Pummerer and G. Marondel, *Chem. Ber.*, 1956, **89**, 1454; G. Weisgerber and C. H. Eugster, *Helv. Chim. Acta*, 1966, **49**, 1806.

[7] See H. O. House, L. J. Czuba, M. Gall, and H. D. Olmstead, *J. Org. Chem.*, 1969, **43**, 2324.