Simple One-step Route to Substituted Anthraquinones

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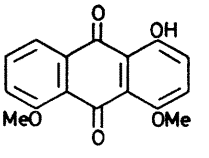
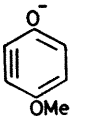
Summary A new synthetic method for the preparation of functionalized anthraquinones is described.

ALTHOUGH we have previously described the use of phthalide anions under aprotic conditions for the preparation of substituted naphthols,[1] recent communications on closely related topics[2–4] have prompted us to report our preliminary results on a simple one-step procedure for the preparation of substituted anthraquinones.

Recent methods available for the preparation of synthetic precursors of these systems include the conjugate addition of acyl anions to $\alpha\beta$-unsaturated esters[5] and a recently described eight-stage method[4] which gave (**1**) in an overall yield of 18·3% from *N*-phenyl-*m*-anisamide. We

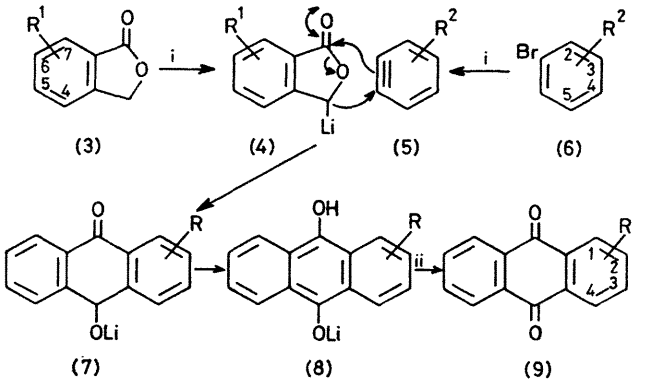


(1)



(2)

describe herein a shorter method for the preparation of substituted anthraquinones (**9**), that involves the nucleophilic addition of lithium phthalides (**4**) to benzynes (**5**); the overall reaction sequence is indicated in the Scheme.



SCHEME. i, lithium di-isopropylamide; ii, H_3O^+, air. For compound (**9**):

a; R = H	**e**; R = 1,4-$(MeO)_2$
b; R = 1-MeO	**f**; R = 2-Me
c; R = 2-MeO	**g**; R = 1,2-benzo
d; R = 2,3-$(MeO)_2$	**h**; R = 1-HO, 4-MeO

Addition of the lithium phthalide (**4**) to the benzyne (**5**), generated *in situ* by reaction of the substituted bromobenzene with lithium di-isopropylamide, would be expected to give the 10-hydroxyanthrone derivative (**7**). Formation of (**7**) is presumed to occur *via* nucleophilic addition of the phthalide anion to the benzyne followed by intramolecular cyclization with concomitant opening of the lactone ring. It is known that 10-hydroxyanthrones (**7**) are converted into the enol form (**8**) under basic conditions;[6] acidification of the reaction medium followed by air oxidation of the unstable anthrahydroquinone (**8**) would thus give the anthraquinone (**9**). The experimental procedure is exemplified by the preparation of anthraquinone (**9a**). Treatment of phthalide (1 equiv.) with lithium di-isopropylamide (2·2 equiv.) in tetrahydrofuran at −60 °C gave the orange carbanion. At −45 °C the solution of the carbanion was treated with bromobenzene (1 equiv.) in tetrahydrofuran. After warming to room temperature the reaction mixture was stirred in contact with air. Acid work-up and chloroform extraction gave a mixture from which was readily separated anthraquinone (**9a**), m.p. 269—271 °C (sublimation) (mixed m.p. 273—275 °C), in 28·5% yield. When the lithium phthalide was treated with 2 equiv. of benzyne the yield of isolated anthraquinone increased to 74·5%. The use of substituted phthalides and substituted benzyne precursors permits the preparation of a wide range of substituted anthraquinones; examples include the following reactions (see also Table). Treatment of 5,6-di-

TABLE. Preparation of the anthraquinones (**9**)

(**3**) R^1	(**6**) R^2	Product	% Yield[a]
H	H	(**9a**)	28·5 (74·5[b])
4-MeO	H	(**9b**)	51·4[b]
H	4-MeO	(**9c**)	44·7
5,6-$(MeO)_2$	H	(**9d**)	32·3
H	2,5-$(MeO)_2$	(**9e**)	46·3
H	4-Me	(**9f**)	40·0
H	2,3-benzo	(**9g**)	61·7
H	2-HO, 5-MeO	(**9h**)	25·8

[a] All with 1 equiv. of benzyne precursor except where stated. [b] 2 equiv. of benzyne precursor used.

methoxyphthalide (1 equiv.) with lithium di-isopropylamide gave the corresponding lemon-green carbanion which reacted with the benzyne precursor (1 equiv.) to give 2,3-dimethoxyanthraquinone (**9d**), m.p. 248—250 °C (lit.,[8] 237 °C), in 32·3% yield. Similarly the reaction of lithium phthalide with 1,4-dimethoxybenzyne gave 1,4-dimethoxyanthracene (**9e**), m.p. 175—177 °C (lit.,[9] 170—171 °C), in 46% yield. The aryne generated from 1-bromonaphthalene also reacted with lithium phthalide to give 1,2-benzanthraquinone (**9g**), m.p. 166—167 °C (lit.,[10] 168 °C). Interestingly, lithium phthalide (**4**) reacted with the anionic benzyne (**2**), generated from 2-bromo-4-methoxyphenol, to give the hydroxyanthraquinone (**9h**), m.p. 170—171 °C (lit.,[11] 167—168 °C).

In all cases the anthraquinones were readily identified and separated either by direct crystallisation from the reaction mixture or by chromatography; yields have not been optimised. The preparation of anthraquinones from phthalides and related species would seem to offer a general reaction of wide scope. Since the addition of carbanions to arynes occurs regioselectively, further control on the eventual substitution pattern of the anthraquinone is also possible with this method.

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[1] N. J. P. Broom and P. G. Sammes, *J.C.S. Chem. Comm.*, 1978, 162.
[2] G. A. Kraus and H. Sugimoto, *Tetrahedron Letters*, 1978, 2263.
[3] F. M. Hauser and R. P. Rhee, *J. Org. Chem.*, 1978, **43**, 178.
[4] J. E. Baldwin and K. W. Bair, *Tetrahedron Letters*, 1978, 2559.
[5] K. A. Parker and J. L. Kallmerter, *Tetrahedron Letters*, 1977, 4557.
[6] K. H. Meyer, *Annalen*, 1911, **379**, 37.
[7] H. W. Underwood and W. L. Walsh, *Org. Synth.*, 1936, **16**, 74.
[8] C. Liebermann and W. Hohenemser, *Ber.*, 1902, **35**, 1778.
[9] Höchster Farbwerk, Gr. Offen. 242, 379; Beilstein, 8(I), 715.
[10] (a) K. Elbs, *Ber.*, 1886, **19**, 2209; (b) P. H. Groggins and H. P. Newton, *Ind. Eng. Chem.*, 1930, **22**, 157.
[11] K. Waldeman, *J. prakt. Chem.*, 1931, **130**, 92.