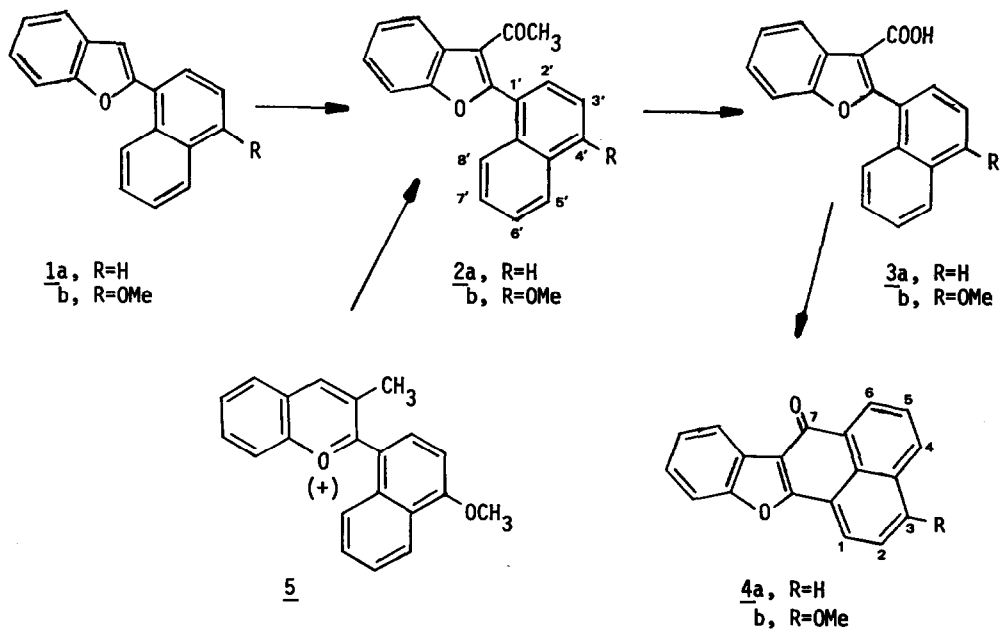


THE SYNTHESIS OF SUBSTITUTED BENZOPHENALENOFURANS
A NOVEL PENTACYCLIC RING SYSTEM

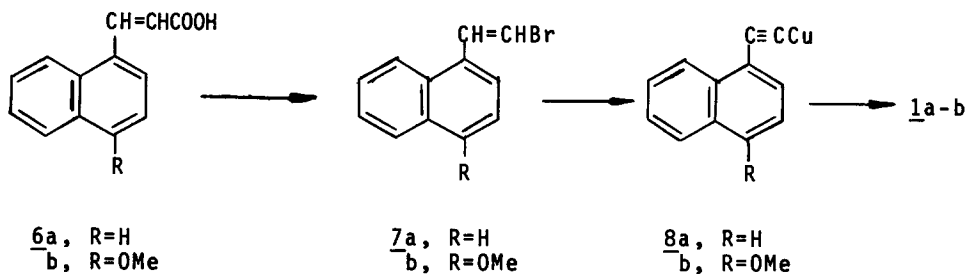
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Since Schönberg and Mamluk first prepared 7-oxo-7H-benzo[b]phenaleno-[2,1-d]furan¹ (4a) in 1972, no additional reports have appeared on this new ring system. Although Schönberg obtained 4a in high yield, we felt that this procedure would be impractical for the synthesis of substituted analogs. In this communication we describe the preparation of the 3-methoxy derivative 4b. The two methods used to obtain the key intermediate 2b can readily be extended to permit introduction of a wide variety of substituents on both the benzofuranyl and naphthyl portions of the molecule.



Bromination² of the readily available 6a-b³ followed by dehydrobromination-decarboxylation gave 7a (95%) and 7b (95%), resp. Dehydrobromination with PhLi⁴ gave the corresponding acetylenes which were converted without further purification to their cuprous salts 8a (52%) and 8b (63%) by the procedure of Castro, et.al.⁵ Condensation with o-iodophenol gave 1a-b (52%). When the pure acetylenes were first isolated by distillation (ca. 35%), higher yields (ca. 80%) of 1a-b were obtained. However, the formation of the cuprous acetylides, the initial step in the Castro method, provided a rapid, convenient purification procedure prior to condensation.



The preparation of 1b was also accomplished by acylating 1-methoxynaphthalene with phenoxyacetylchloride and AlCl₃ in dichloroethane.⁶ The product obtained, 2-phenoxy-4'-methoxy-1'-acetonaphthone⁷ (56%), mp 105-107°, was cyclodehydrated with PPA at 170° for 1 hr to give 1b.⁸

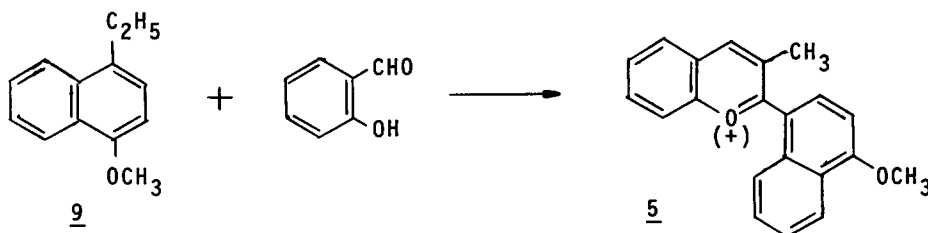
To a cold solution of acetyl chloride and AlCl₃ in nitrobenzene was added 1b and the mixture stirred for 1 hr and then poured into water. The nitrobenzene was removed by steam distillation and the residue dissolved in ether extracted with 5% NaOH, water, dried (MgSO₄) and evaporated. The residue was chromatographed on silica gel and eluted with CH₂Cl₂-hexane (1:1). Crystallization from cyclohexane gave 2b (52%), mp 136-137.5°. Nmr (CDCl₃) δ 1.98 (s, CH₃CO), 4.00 (s, OCH₃), 6.80 (d, J=8Hz, H_{3'}), 7.50 (d, J=8Hz, H_{2'}), 7.2-7.65 (m, 6H), 8.2-8.4 (m, H_{5'} and H_{8'}); Ir (KBr) ν cm⁻¹ 1652 (c=O); m/e 316.

A solution of 2b and NaOBr in aq dioxane was mechanically shaken (16 hr). The excess NaOBr was destroyed with NaHSO₃ and the solution shaken twice with ether. The aqueous portion was acidified and the precipitate digested for 30 min on a steam bath, cooled and filtered. Recrystallization from EtOH gave 3b (78%), mp 255-257° (dec).¹⁰ Nmr (CDCl₃-DMSO-d₆) δ 4.03 (s, OCH₃), 6.88 (d, J=8Hz, H_{3'}), 7.66 (d, J=8Hz, H_{2'}), 7.2-7.75 (m, 6H), 8.1-8.4 (m, H_{5'} and H_{8'}); Ir (KBr) ν cm⁻¹ 1675 (c=O), m/e 318.

Conversion of 3b to its acid chloride gave an oil which was dissolved in CH₂Cl₂. AlCl₃ was added and after stirring 90 min at 0° and 30 min at ambient temperature, the mixture was poured into water. The resulting yellow precipitate was redissolved in additional CH₂Cl₂ and the organic portion washed (5% Na₂CO₃), dried (MgSO₄) and evaporated. Recrystallization of the orange

solid from toluene gave 4b (80%), mp 235-238^o.^{11,12} Nmr (CDCl₃) δ 4.02 (s, OCH₃), 6.84(d, J=8Hz, H₂), 8.18(d, J=8Hz, H₁), 8.1-9.0(m, 7H); Ir (KBr) ν cm⁻¹ 1635 (c=o); m/e 300; UV (95% EtOH) nm (ε) 244(22,200), 266(19,900), 285(22,500), 331(6520), 360(5170). Demethylation of 4b with pyridine.HCl gave 4 (R=OH) as a brick-red, highly insoluble solid (80%), mp 374^o (by DTA): Ir (KBr) ν cm⁻¹ 1350-1380 (OH), 1639-1629(sh) (c=o); m/e 286.

A rapid method giving 2b in high yield resulted from the oxidation of the flavylum salt 5.¹³ A solution of salicylaldehyde and 4'-methoxy-1'-pro-pionaphthone¹⁴ (9) in EtOAc-EtOH was saturated with dry HCl. After standing 16 hr, 5 precipitated as a deep red solid (95%). A methanolic solution of



30% H₂O₂ was added to a methanolic solution of 5 and after 1 hr the mixture was poured into water and extracted with CH₂Cl₂. The dark oil obtained after evaporation was chromatographed on Florisil to give 2b (62%), identical in all respects with 2b prepared by the Castro procedure. The mechanism of flavylum salt oxidations has been previously discussed.¹⁵

It would appear that the flavylum salt oxidation procedure affords a very versatile method for the synthesis of a wide variety of substituted benzofurans of type 2 which in turn can readily be converted to the novel penta-cyclic ring system 4.

References and Notes

1. A. Schönberg and M. Mamluk, Chem. Ber., 105, 1562 (1972).
2. G. Manecke and D. Zerpner, Chem. Ber., 105, 1943 (1972).
3. Adapted from J. Koo, M.S. Fish, G.N. Walker and J. Black, Org. Syntheses, Coll. Vol. 4, 327, (1963).
4. G. Wittig and H. Witt, Chem. Ber., 74, 1474 (1941). When BuLi was used (as in ref. 2), the major product was the naphthylethylene.
5. C.E. Castro, E.J. Gaughan and D.C. Owsley, J. Org. Chem., 31, 4071 (1966).
6. The order of addition of reagents was important; see R. Stoermer and P. Atenstadt, Chem. Ber., 35, 3560 (1902).
7. All new compounds gave satisfactory elemental analyses and spectral data.

8. 1b made by this procedure was identical in all respects to 1b made by the unambiguous method of Castro (see ref.5). The nmr spectra showed superimposable singlets at 6.95 δ , characteristic of the proton at position three. The rearrangement of 3-to 2-substitued benzofurans is well known; see P. Cagniant and D. Cagniant, "Advance in Heterocyclic Chemistry" Academic Press, New York, Vol. 18, 1975, pp 367-369 and A. Mustafa, "Benzofurans," J. Wiley, New York, 1974, pp 13-17.
9. 1a was acetylated with SnCl₄ in CH₂Cl₂ to give 2a (45%), mp 105-107⁰ (MeOH).
10. 3a, mp 200-201⁰ (73%).
11. 4a, mp 199-201⁰ (80%), lit., mp 196-197⁰ (ref.1); spectral data in agreement.
12. 4b was also formed in small amount by just refluxing with SOCl₂.
13. L. Jurd, J. Org. Chem., 29, 2602 (1964); we found that buffer was not necessary.
14. E. Chapiro, Compt. rend., 234, 2080 (1952).
15. A. Mustafa, "Benzofurans," J. Wiley, New York, 1974, p.86.