HETEROCYCLES, Vol. 57, No. 10, 2002, pp. 1897 - 1900, Received, 12th June, 2002

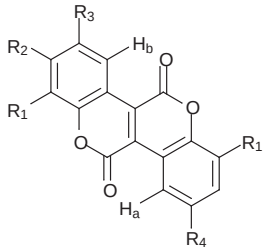
A PHOTOCHEMICAL ROUTE TO DIBENZONAPHTHYRONES

Yvette A. Jackson* **and Karla-Sue C. Marriott**

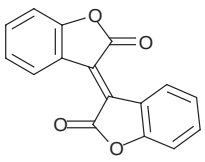
Department of Chemistry, University of the West Indies, Mona, Kingston 7, Jamaica, West Indies

Abstract–Irradiation of 2-methyl 3-phenyl 5,6-dimethoxy-1-benzofuran-2,3-dicarboxylate (**5**) gave 2,3-dimethoxybenzopyrano[4,3-*c*]benzopyran-5,11-dione (**1b**).

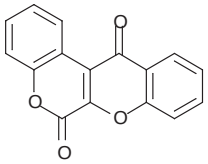
Dibenzonaphthyrones (**1a**), are isomeric with isoxindigos (**2**) and are usually obtained from this group of compounds in good yield by treatment with pyridine and refluxing methanol.[1] They have also been synthesised by treatment of 2,2-dimethoxyphenylsuccinonitrile or 2,2-dimethoxydicyanostilbene with pyridine hydrochloride.[2] Dibenzonaphthyrones are, as well, isomeric with rotenonoids (**3**), 6-oxorotenoids which have been found to co-occur with insecticidal rotenoids in plants.[3-6]



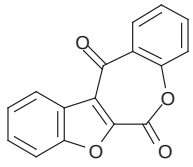
1a $R_1 = R_2 = R_3 = R_4 = H$
1b $R_1 = R_4 = H$; $R_2 = R_3 = OMe$
1c $R_1 = i$-Pr; $R_2 = H$; $R_3 = R_4 = OMe$



2

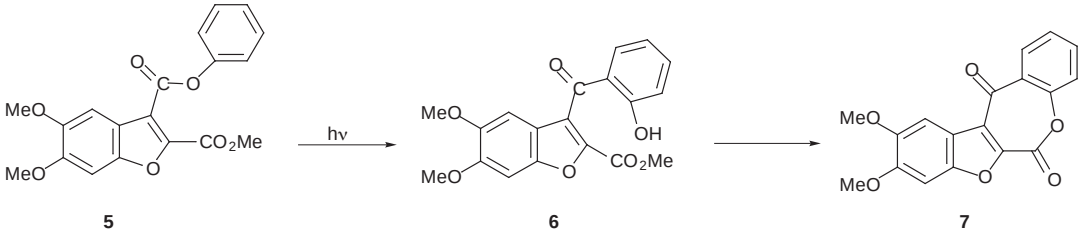


3



4

In our efforts to synthesise rotenonoids, we focused on β-rotenonoids (general structure (**4**)) as the initial target molecules since their rearrangement to rotenonoids in aqueous alkali is known,[7] and they seemed quite amenable to synthesis. Fries rearrangement of the ester (**5**) should readily give compound (**6**) which, on hydrolysis and lactonization, would provide the desired (**7**) (Scheme 1). We set out to synthesize compound (**5**) by the pathway shown in Scheme 2, and then to effect Fries rearrangement.

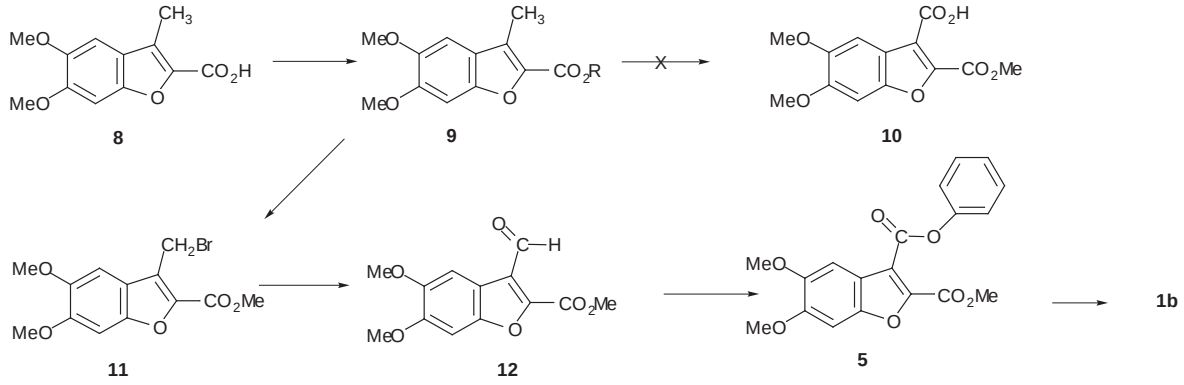


5 **6** **7**

Scheme 1

5,6-Dimethoxy-3-methyl-1-benzofuran-2-carboxylic acid (**8**)[8] was methylated (MeI/K_2CO_3) to produce ester (**9**) in 88% yield. Since direct oxidation of **9** with aqueous $KMnO_4$ led only to starting acid, we

proceeded *via* allyl bromide (**11**), formed in 51% yield from (**9**) by *N*-bromosuccinimide (NBS) bromination. Treatment of compound (**11**) with trimethylamine-*N*-oxide (TMANO) in DMF at room temperature, yielded a bright yellow solid in 50% yield. The singlet at 10.8 ppm in the ^{1}H-NMR spectrum of this compound was clear evidence that aldehyde (**12**) had been obtained.



Reagents: i) MeI, K_2CO_3, acetone ii) NBS, CCl_4 iii) TMANO, DMF iv) NBS, CCl_4 then phenol, py.

Scheme 2

Oxidation of **12** to the corresponding carboxylic acid (**10**) was attempted using Jones reagent but the ester group was cleaved under these conditions. Diester (**5**) was thus prepared from **12** in 31% yield by treatment with NBS (which yielded the acid bromide), and subsequent reaction *in situ* with phenol. IR spectral absorptions at 1735 and 1715 cm^{-1}, and two downfield peaks at 158 and 161 ppm in the ^{13}C-NMR spectrum of the product indicated the presence of two ester groups. The Fries rearrangement was then pursued under photochemical conditions since, in our experience,[9,10] these reactions were relatively clean.

A 0.2% solution of diester (**5**) in benzene/ethanol (1:1) was irradiated by sunlight, in an atmosphere of nitrogen. The reaction progressed very slowly with only a trace of side products. ^{13}C-NMR spectral data of the resultant bright orange-coloured product showed absence of the methoxy group of the methoxycarbonyl, (expected to appear at 52 ppm). IR spectral data showed no absorption corresponding to hydroxyl or keto groups. There were however peaks at 1744 and 1727 cm^{-1}, and from ^{13}C-NMR spectral data, the farthest downfield signals were two peaks at 158.2 and 158.3 ppm, indicating ester carbonyls. DEPT 90 experimental data showed that six C-H bonds were present in the reaction product and MS showed a molecular ion peak at 324 [HRMS calcd for $C_{18}H_{12}O_6$: 324.0634. Found: 324.0643].

The reaction product was novel 2,3-dimethoxybenzopyrano[4,3-*c*]benzopyran-5,11-dione (**1b**) which had been formed in 24% yield. Further confirmation of structure was obtained by the reactivity of the compound and comparison with spectral properties of analogues.

Treatment with KOH/EtOH at reflux resulted in hydrolysis to a polar compound which, on acidification with 0.5 M HCl resulted in reformation of the starting material. ^{1}H-NMR data comparison showed that for unsubstituted dibenzonaphthyrone (**1a**), H_a resonated at 9.26 ppm. When this proton was adjacent to the electron-releasing methoxyl group as in compound (**1c**), there was a significant upfield shift of the corresponding signal to 8.76 ppm.[1] Compound (**1b**) has H_b adjacent to a methoxyl group and H_a on an unsubstituted benzene ring, and, in accordance with the observation for compounds (**1c**) and (**1a**), these

protons give rise to peaks at 8.79 and 9.20 ppm respectively. Compound (**1a**) exhibits IR spectral absorptions at 1725, 1605 and 1590 cm^{-1}.[3] Correspondingly, compound (**1b**) showed IR spectral absorptions at 1744, 1727, 1612 and 1578 cm^{-1}. We have not yet confirmed the mechanism of this rearrangement, but we continue our investigation into the photochemistry of compounds of type **5**.

EXPERIMENTAL

General

All mp are uncorrected. IR spectra were obtained on a Perkin Elmer 1600 FT-IR spectrophotometer and are for KBr discs. NMR spectra (Bruker 200 MHz spectrometer) were determined in $CDCl_3$ solution and the resonances are in δ units downfield from TMS; *J* values are given in Hz. Elemental analyses were carried out by MEDAC Ltd., Egham, Surrey, UK.

Methyl 5,6-dimethoxy-3-methyl-1-benzofuran-2-carboxylate (9)

To a solution of compound (**8**)[8] (0.26 g, 1.14 mmol) in dry acetone (12 mL) was added K_2CO_3 (0.75 g, 5.41 mmol) with stirring, followed by iodomethane (0.39 mL, 6.26 mmol). This mixture was heated at reflux for 6 h, then filtered and the filter cake was washed with hot acetone. The filtrate was concentrated *in vacuo* and the crude product was recrystallised from MeOH to yield **9** as light brown fluffy crystals (0.24 g, 88%): mp 133-135^{0}C; ν_{max}/cm^{-1} 1703, 1624, 1585; ^{1}H NMR δ 2.55 (1H, s, -CH_3), 3.93 and 3.94 (each 3H, s, -O-CH_3), 3.95 (3H, s, CO_2CH_3), 6.95 (1H, s, 7-H), 7.03 (1H, s, 4-H); ^{13}C NMR δ 9.4, 51.7, 56.2, 56.2, 94.9, 100.9, 120.7, 126.5, 139.9, 147.1, 149.6, 151.1, 160.7. Anal. Calcd for $C_{13}H_{14}O_5$: C, 62.38; H, 5.64. Found: C, 61.96; H, 5.61.

Methyl 3-bromomethyl-5,6-dimethoxy-1-benzofuran-2-carboxylate (11)

To compound (**9**) (2.0 g, 8.0 mmol) in carbon tetrachloride (41 mL) was added NBS (1.54 g, 8.70 mmol) with stirring. The reaction vessel was enclosed in a box and illuminated with a 100 W bulb for 20 h. The mixture was filtered and the filtrate was concentrated *in vacuo*. Recrystallisation of the crude product from $CHCl_3$/MeOH yielded **11**, as straw-colored needles (1.6 g, 61%): mp 162^{0}C; ν_{max}/cm^{-1} 1732, 1684, 1670, 1621; ^{1}H NMR δ 3.90, 3.91 and 3.95 (each 3H, s, -OCH_3), 4.99 (2H, s, -CH_2-Br), 7.05 (1H, s, 7-H), 7.10 (1H, s, 4-H). Since allyl bromides are known to be relatively unstable, this was used immediately.

Methyl 3-formyl-5,6-dimethoxy-1-benzofuran-2-carboxylate (12)

Compound (**11**) (1.56 g, 4.73 mmol) was added to a mixture of anhydrous TMANO (1.45 g, 19.3 mmol) in DMF (31 mL) with stirring. This mixture was stirred at rt for 2 h, then poured into a 10 % saline solution, and the yellow precipitate formed was collected by filtration. This was recrystallised from $CHCl_3$/MeOH to yield **12** as bright yellow crystals (0.63 g, 50%): mp 175-177^{0}C; ν_{max}/cm^{-1} 1720, 1679, 1621, 1566; ^{1}H NMR δ 3.90 and 3.95 (each 3H, s, -O-CH_3), 4.09 (3H, s, -CO_2CH_3), 7.10 (1H, s, 7-H),

7.70 (1H, s, 4-H), 10.8 (1H, s, -CHO); ^{13}C NMR δ 52.9, 56.2, 56.3, 94.5, 103.0, 116.0, 125.1, 147.8, 149.0, 151.6, 158.9, 188.4. Anal. Calcd for $C_{13}H_{12}O_6$: C, 59.08; H, 4.58. Found: C, 58.74; H, 4.54.

2-Methyl 3-phenyl 5,6-dimethoxy-1-benzofuran-2,3-dicarboxylate (5)

To compound (**12**) (400 mg, 1.52 mmol) in carbon tetrachloride (40 mL), was added NBS (362 mg, 2.03 mmol) with stirring. This mixture was enclosed in a box and illuminated with a 100 W bulb for 1.5 h and then cooled. A solution of phenol (1.56 g, 0.02 mol) in pyridine (3 mL) was added with stirring and the mixture was stirred at rt for 21 h, filtered, and the filtrate was concentrated *in vacuo*. The crude product was chromatographed (SiO_2, dichloromethane) to yield **5** as pale blue/green crystals (0.17 g, 31%), mp 161-163^{0}C; ν_{max}/cm^{-1} 1735, 1715, 1624, 1578; ^{1}H NMR δ 3.92 and 3.95 (each 3H, s, -O-CH_3), 4.00 (3H, s, CO_2CH_3), 7.10 (1H, s, 7-H), 7.27-7.41(4H, m, 4-H, 3'-, 4'-, 5'-H), 7.42-7.53 (2H, m, H-2', 6'-H); ^{13}C NMR δ 52.7, 56.3, 94.8, 102.1, 117.8, 117.9, 121.5, 126.2, 129.6, 144.7, 148.5, 149.5, 150.4, 151.4, 158.8, 161.2. Anal. Calcd $C_{19}H_{16}O_7$: C, 64.03; H, 4.53. Found: C, 63.87; H, 4.48.

2,3-Dimethoxybenzopyrano[4,3-*c*]benzopyran-5,11-dione (1b)

Compound (**5**) (130 mg, 0.36 mmol) was dissolved in a mixture of benzene/ethanol (1:1) (70 mL) in a 100 mL RB-flask. The reaction vessel was then flushed with nitrogen for 15 min and sealed and placed on the roof to be irradiated by sunlight for 2 weeks. The reaction mixture was then concentrated *in vacuo* and the crude product was chromatographed (SiO_2, dichloromethane-hexane (2:1)) to yield **1b** as a bright orange solid (28 mg, 24%), mp 264-266^{0}C; ν_{max}/cm^{-1} 1743, 1724, 1612, 1579; ^{1}H NMR δ 3.95 and 4.09 (each 3H, s, -O-CH_3), 6.93 (1H, s, 1-H), 7.40-7.50 (2H, m, 9-H, 10-H), 7.50-7.70 (1H, m, 8-H), 8.79 (1H, s, 4-H), 9.20-9.30 (1H, dd, *J* 1, 8, 10-H); ^{13}C NMR δ 56.4, 56.4, 99.3, 108.3, 108.4, 116.4, 123.1, 125.4, 126.6, 127.9, 131.6, 145.0, 146.9, 149.0, 152.0, 153.3, 158.5; *m/z* (relative intensity) 324 (100), 309 (13), 281 (19), 149 (93); HRMS calcd for $C_{18}H_{12}O_6$: 324.0634. Found: 324.0643.

REFERENCES

1. H-D. Becker and H. Lingnert, *J. Org. Chem.*, 1982, **47**, 1095.
2. J. N. Chatterjea and N. Prasad, *J. Ind. Chem. Soc.*, 1968, **45**, 35.
3. T. Shiengtong, T. Donavanik, V. Uaprasert, and S. Roengsumran, *Tetrahedron Lett.*, 1974, 2015.
4. M. E. Oberholzer, G. Rall, and D. G. Roux, *Phytochemistry*, 1976, **15**, 1283.
5. S. K. Sripathi, R. Gandhidasan, P. V. Raman, N. R. Krishnasamy, and S. Nanduri, *Phytochemistry*, 1994, **37**, 911.
6. Y. L. Lin and Y. H. Kuo, *Heterocycles*, 1995, **41**, 1959.
7. M. O. Takei, *Ber.*, 1932, **65**, 1041.
8. M. G. Patel and S. Sethna, *J. Indian Chem. Soc.*, 1960, **37**, 227.
9. K. C. Marriott, M. Anderson, and Y. A. Jackson, *Heterocycles*, 2001, **55**, 91.
10. V. G. S. Box and Y. A. Jackson, *Heterocycles*, 1980, **14**, 1265.