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Access to the spiro hydrindandione ring system of Fredericamycin A through a Friedel-Crafts reaction.

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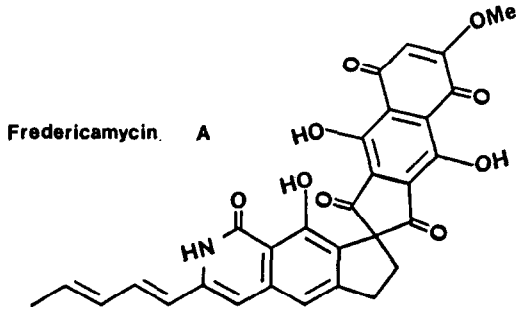
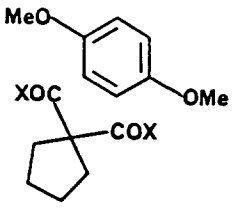
Summary : *Condensation of 1,4-dimethoxybenzene with 1,1-cyclopentane dicarboxylic acid or 1,1-indan dicarboxylic acid derivatives led to the title compounds.*

The antitumour properties and the unusual spiro structure of Fredericamycin A [1] have aroused much interest. Syntheses of a model spiro (4,4) nonane system 4a from 2-phenyl-1,1-indanedione [2] and of 2,2-dimethyl4,9-dihydroxy-1H-benz (f) indene-1,3(2H-1)dione [3] have been recently published.

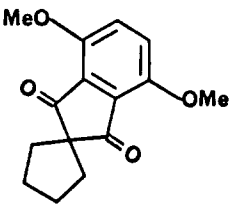


We wish to report in this and the accompanying letter syntheses of spiro compounds such as 2 and 4a. In our first approach the key step was a Friedel-Crafts reaction of a disubstituted malonyldichloride with an aromatic compound and $AlCl_3$ in CS_2 [4] or CH_2Cl_2 [5].

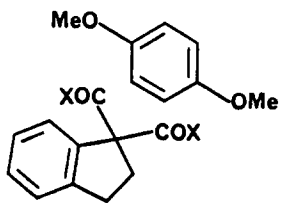
The readily available [5][6] 1,1-cyclopentane dicarbonyldichloride 1b was condensed with 1,4-dimethoxybenzene with aluminium trichloride in dichloromethane to afford the spiro-indanedione 2 in 30% yield (m.p.:131-132°C(ethanol)). The same dione could be obtained in 50% yield by heating the diacid 1a (50°, 2h) with 1,4-dimethoxybenzene with methane sulfonic acid-phosphoric anhydride reagent[7].



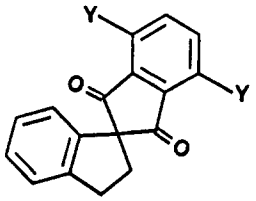
1a X = OH
1b X = Cl



2



3 X = OH



4a Y = OMe
4b Y = H

The benzologous 1,1-indanedicarboxylic acid [8] was similarly condensed in Me_2SO_3H-P_2O_5(same conditions) with 1,4-dimethoxybenzene to give the spiro indanedione 4b in 10% yield (m.p. 246°C with decomposition (methanol)).

The spiro compound 4a was identical with a sample prepared by another route (accompanying paper). The ^{13}C NMR signals for the spiro atom (60.5 ppm) and for non aromatic cyclopentane atoms (32.9 and 32.1 ppm) are in agreement with those reported for Fredericamycin A [9].

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All the compounds gave analytical results in agreement with their structure :
2 ^1H NMR : $\delta(CDCl_3)$: 1.96(s,8H) ; 4.02(s,6H) ; 7.32(s,2H).
^{13}C NMR : $\delta(CDCl_3)$: 202.5(2C) ; 150.6(2C) ; 128.8(2C) ; 119.5(2C) ; 60.5 ; 56.4(2C) ; 35.5(2C) ; 27.4(2C).
MS(EI) m/z : 219(100) ; 260(44.6) ; 163(25.8).

REFERENCES

1. R. Misra and R.C. Pandey, J. Am. Chem. Soc., 1982, 104, 4478.
2. A.V. Rama Rao, D.R. Reddy and V.H. Deshpande, J. Chem. Soc., Chem. Comm., 1984, 1119.
3. K.A. Parker, K.A. Koziski and G. Breault, Tetrahedron Lett., 1985, 26, 2181.
4. M. Freund and K. Fleischer, Ann., 1913, 399, 182.
M. Freund, K. Fleischer and E. Gofferje, Ann., 1917, 414, 26.
K. Fleischer, Ann., 1919, 422, 238.
5. E.J. Cragoe, O.W. Woltersdorf, (Merck and Co, Inc.) Ger. Offen, 2.448.438, 24 apr. 1975 ; C.A., 1975, 83, 206001y.
6. G.S. Skinner, G. Limperos and R.H. Pettebowe, J. Am. Chem. Soc., 1950, 72, 1648.
7. P.E. Eaton, G.R. Carlson and J.T. Lee, J. Org. Chem., 1973, 38, 4071.
R.O. Duthaler and R. Maienfisch, Helv. Chim. Acta, 1984, 67, 858.
8. O. Blum Bergmann, Ann., 1930, 484, 26.
9. K.M. Byrne, B.D. Hilton, R.J. White, R. Misra and R.C. Pandey, Biochemistry, 1985, 24, 478.

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