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A NEW INTRAMOLECULAR ANNULATION APPROACH LEADING TO 1-OXO-PHENANTHRENEQUINONE DERIVATIVES

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Summary. Aromatic compounds bearing epoxide and phenylsulfonyl groups at two vicinal benzylic positions and a malonate group in the epoxidized side chain undergo chemoselectively anionic annulations leading to tricyclic angular systems.

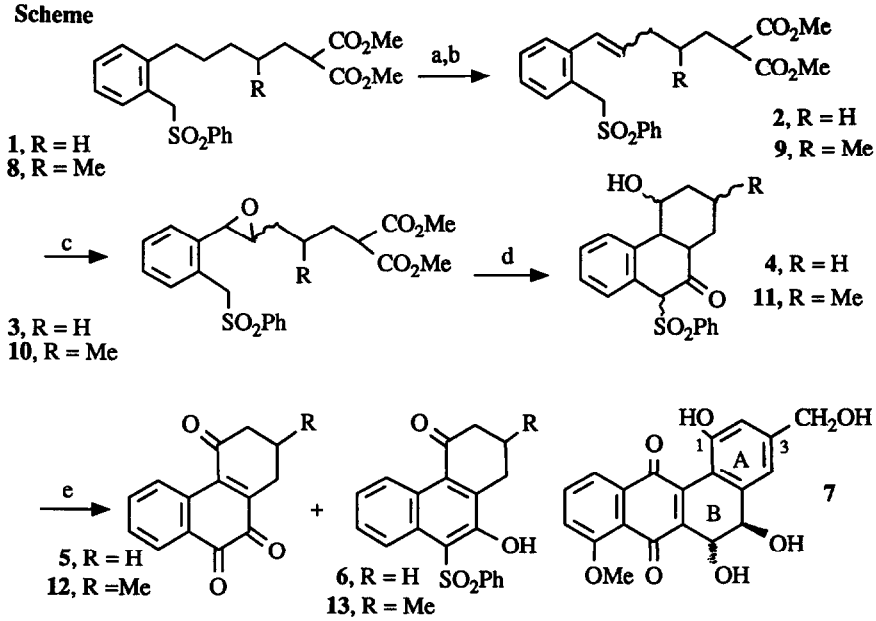
As a part of our continuing interest for one-stage anionic tandem cyclizations[3] we wish to report on a new intramolecular double annulation process in which the participation of an epoxide group ensures the formation of C-1-oxygenated phenanthrene derivatives. These efforts were motivated by our interest in developing a new synthetic route to antibiotics of benz[a]anthraquinone structure, characterized by the presence of oxygen at C-1.[4]

The required intermediate for cyclization **3** was prepared from diester **1**[5] which was converted to olefins **2** (90%, E and Z stereoisomers), and then to epoxides **3** (79%) as shown in Scheme.[6] The cyclization conditions were as follows: a solution of **3** (100 mg) in THF (2 ml) was added dropwise via syringe to a stirred solution of *t*-BuOK (prepared from 80 mg K and 4 ml *t*-BuOH followed by dilution with 24 ml THF)[7] at ambient temperature and the reaction was continued for 5 h (TLC), then quenched (aqueous NH_4Cl), extracted (ether and 20% CH_2Cl_2) and chromatographically purified to afford 41 mg (52%) of cyclized product **4**, consisting of two stereoisomers characterized by ^1H NMR signals at δ 4.91 and 5.05 (2s, 1H).[6] Hence decarboxylation occurred as well under the above cyclization conditions. Our next effort was directed to convert **4** into a desulfonylated stereohomogeneous product, oxygenated at C-9 and C-10 positions, in a manner which could eventually serve as a model for the synthesis of the antibiotic PD 116740 (**7**).[8] Utilization of CrO_3-dimethylpyrazole complex[9], under conditions used previously for allylic oxidations,[10] resulted in a one-stage oxidative desulfonylation,[11] partial dehydrogenation and C-1 oxidation to give the red quinone **5** (51%), mp 104-105°C,[12] along with a small amount of hydroxysulfone **6** (7%) separable by chromatography.

The presence of a C-3 methyl group (or hydroxymethyl, like in **7**) in ring A of benz[a]anthraquinone antibiotics[4] prompted us to perform next the cyclization on the intermediate **10**, obtained from diester **8**[5], via olefins **9** (92%) which were epoxidized in 87% yield. Cyclization as before gave three stereoisomers **11** (53%)[6] which were characterized by $C\underline{H}SO_2Ph$ signals in the NMR spectrum at δ 5.25, 4.92 and 4.77 (3s, 1H). Oxidation proceeded analogously, to give the red quinone **12**(57%)[13] mp 126-127°C and **13** (8%).

The synthetic usefulness of this new tandem cyclization process is under further investigation.

Scheme



[a] NBS, CCl_4, Δ. [b] $LiCO_3$, LiI, DMF, 80°C, 3h; [c] m-CPBA, CH_2Cl_2, rt, 6h; [d] *t*-BuOK, THF, *t*-BuOH, rt, 5h; [e] CrO_3-DMP, CH_2Cl_2, -20°C, 0°C.

References and Notes.

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4. See e.g. Thomson, R.H., "Naturally Occurring Quinones", Academic Press, New York, **1971**, p. 648 ff.; Imamura, N.; Kakinuma, K.; Ikekawa, N.; Tanaka, H.; Omura, S., *J. Antib.*, **1982**, *35*, 602.
5. The preparation of diesters **1** and **8**, by previously developed methodology,[3] will be reported elsewhere.
6. All new compounds gave satisfactory spectral data, including ^1H NMR and MS.
7. Air- and moisture-free conditions were used.
8. Wilton, J.H.; Cheney, D.C.; Hokanson, G.C.; French, J.C.; Cun-Leng, H.; Clardy, J., *J. Org. Chem.*, **1985**, *50*, 3936.
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10. Salmond, W.G.; Barta, M.A.; Havens, J.L., *J. Org. Chem.*, **1978**, *43*, 2057; the compound was added at -20°C to an excess (x 20) of reagent and after 30 min the temperature was raised to 0°C (1.5 h).
11. This unusual reaction is probably due to the oxidative liability of the C-9 position.
12. ^1H NMR: ($CDCl_3$) of **5**: δ 2.05-2.29(m, 2H), 2.70-2.81(m, 4H), 7.47(dt, J=1, 8 Hz), 7.65 (dt, J=2, 8 Hz, 1H), 8.12 (dd, J=2, 8 Hz, 1H), 8.40 (dd, J=1, 8 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 200.4, 183.9, 178.3, 144.6, 138.5, 135.6, 132.4, 130.7 (2C), 129.9 (2C), 40.2, 23.3, 21.1; MS m/e: 226 (M), 170, 142, 114.
13. ^1H NMR ($CDCl_3$) of **12**: δ 1.18 (d, J=7 Hz, 3H), 2.21-2.48 (m, 3H), 2.75-2.83 (m, 1H), 2.97-3.10 (m, 1H), 7.46 (dt, J=1, 8 Hz, 1H), 7.64 (dt, J=2, 8 Hz, 1H), 8.11 (dd, J=2, 8 Hz, 1H), 8.42 (dd, J=1, 8 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 200.7, 184, 178.3, 144.4, 138.1, 135.6, 132.3, 130.7 (2C), 129.8 (2C), 48.3, 31.4, 28.9, 21; MS m/e: 240 (M), 212, 197, 170, 142, 114.

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