Tandem Cope–cheletropic reaction: a new molecular rearrangement

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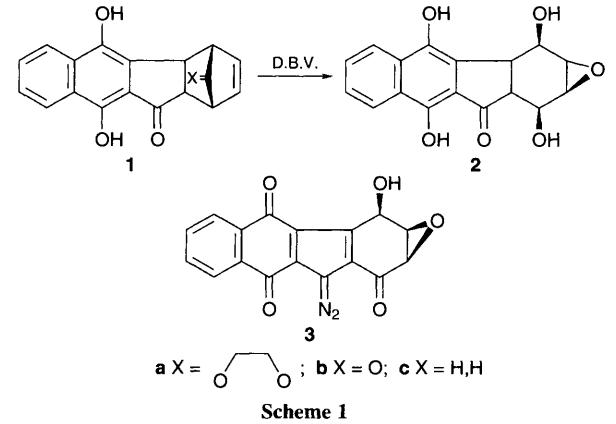
The pentacyclic naphthoquinones 8 undergo unprecedented thermal rearrangement to cyclopent[*a*]anthraquinones 7 or 9 *via* a tandem Cope–cheletropic reaction path.

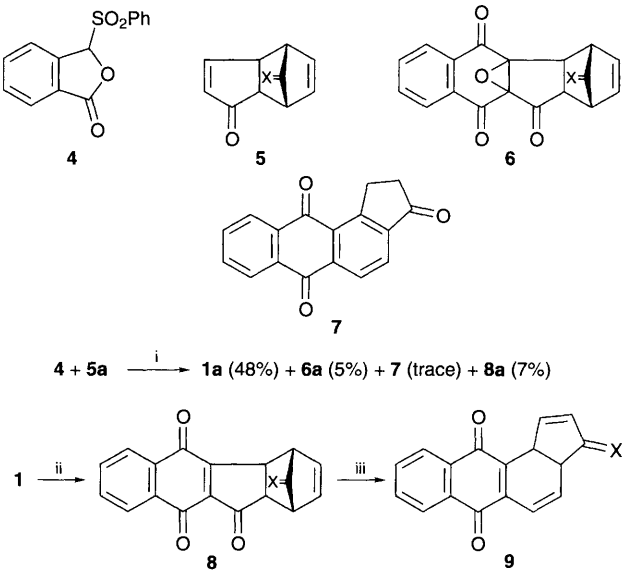
The combination of two or more reactions in tandem is a powerful technique in organic chemistry. Not only does it bring about a multistep synthesis in fewer steps but also leads to interesting and novel molecules. Tandem reactions,[1] reminiscent of Robinson annulation, have made enormous impact in organic synthesis and are well documented. Reported here is a new tandem reaction, based upon the two thermally allowed reactions, Cope and cheletropic reactions. On thermolysis, pentacyclic quinones **8** unprecedentedly rearranged to hitherto unreported angularly fused cyclopentanthraquinones **7** or **9** in good yields (≥80%).

As a part of our programme[2] on the synthesis of kinamycins, a structurally unique group of antiobiotics, we were interested in constructing the basic skeleton **3** of ketoanhydrokinamycin[3] starting from pentacyclic quinol **1** (Scheme 1). In particular, we were intrigued by the possibility of effecting Bailey's double Baeyer–Villiger (D.B.V.) reaction[4] on **1b**, which has been totally unexploited.

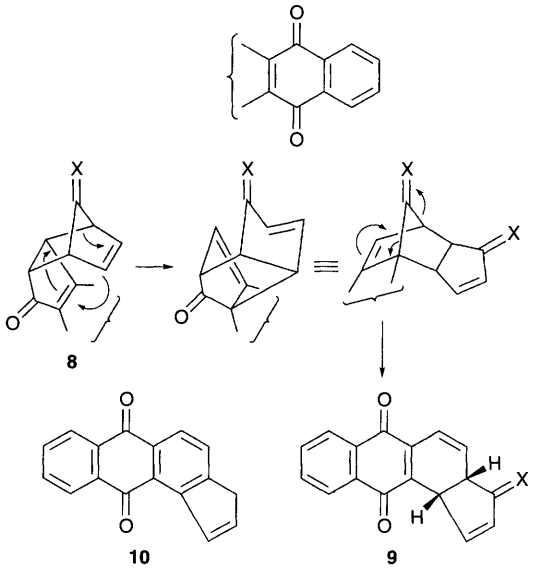
The projected quinol **1a** was prepared in 48% yield by anionic cyclocondensation[5] of phthalide sulfone **4** and enone **5a** in the presence of Bu^{t}OLi at −60 °C. Interestingly, it was accompanied by three co-products: **6a** (5%), **7** (trace) and **8a** (7%). While the formation of epoxy ketone **6a** and quinone **8a** was easily explicable in the light of aerial oxidation of **1a**, that of **7** was less obvious. Examination of the oxidation numbers[6] of all the four products revealed that anthraquinone **7** must have arisen from quinone **8a**, which was subsequently prepared by oxidation of **1a** with DDQ or ceric ammonium nitrate (CAN) (Scheme 2). Thermolysis of **8a** in refluxing *o*-dichlorobenzene for 1 h, followed by silica gel chromatography provided **7** (80%) as the sole isolable product, further arousing our interest to probe the mechanism of the transformation. As a consequence, quinone **8b**, prepared from **4** and **5b** in similar way to **8a**, was subjected to thermolysis in boiling toluene for 1 h. This reaction also gave the anthraquinone **7** (83%). At this juncture, it occurred to us that the rearrangement (**8a** → **7**) might have proceeded through a cascade of reactions, tandem Cope and cheletropic CO elimination being the key steps (Scheme 3). Although **9a** and **9b** are expected to be intermediates for **8a** and **8b** respectively, they were not isolable, possibly due to rapid enolisation–1,5-sigmatropic hydrogen shift–aromatisation.[7] To arrest the latter named reaction sequence and intercept an intermediate of the type **9**, we undertook the thermolysis of **8c**,† prepared similarly to **8a**. Expectedly, it furnished **9c** in 89% yield,† supporting the proposed mechanism. In the case of **8a**, hydrolytic cleavage of the ethylenedioxy bridge during silica



Scheme 1



Scheme 2 *Reagents and conditions*: i, Bu^{t}OLi; ii, DDQ; iii, heat



Scheme 3 Proposed mechanism for **8** → **9**

gel chromatography may be invoked to explain the formation of **7**.

Structural assignments of all the new compounds reported here are in agreement with their spectral data. Compound **9c** was aromatised to **10**†,‡ by oxidation with DDQ for further structure confirmation. The stereochemistry at the ring junction of **9c** was tentatively assigned *cis*, on the basis of outcome of incipient Cope rearrangement[8] of the bicyclo[2.2.1]heptane core of **8**.

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Footnotes

† *Selected spectroscopic data* for **8c** mp 168–70 °C; ν_{max}/cm^{-1}, 1729, 1661, 1289; δ_H: 8.16–8.06 (m, 2 H), 7.85–7.70 (m, 2 H), 6.04 (dd, 1 H, *J* 2.8, 5.2 Hz), 5.74 (dd, 1 H, *J* 3, 5.7 Hz), 3.82 (dd, 1 H, *J* 4.2, 5.6 Hz), 3.47–3.40 (m, 2 H), 3.16 (t, 1 H, *J* 5 Hz), 1.9–1.7 (m, 2 H). For **9c** mp 115–117 °C; ν_{max}/cm^{-1}, 1657, 1293; δ_H: 8.11–8.04 (m, 2 H), 7.75–7.64 (m, 2 H), 6.7 (dd, 1 H, *J* 2, 10 Hz), 6.15 (dd, 1 H, *J* 3.6, 9.8 Hz), 5.96–5.89 (m, 1 H), 5.7–5.63 (m, 1 H), 4.28–4.19 (m, 1 H), 3.5–3.37 (m, 1 H), 3.06–2.9 (m, 1 H), 2.5–2.38 (m, 1 H); δ_C: 185.21, 183.52, 140.49 (CH), 137.34, 135.76, 133.57 (CH), 133.29 (CH), 132.64, 132.19, 131.73 (CH), 130.8 (CH), 126.29 (CH), 125.96 (CH), 116.42 (CH), 41.96 (CH_2), 41.42 (CH), 36.78 (CH). For **10** mp 146–147 °C; ν_{max}/cm^{-1}, 1666, 1281; δ_H: 8.34–8.28 (m, 2 H), 8.23 (d, 1 H, *J* 7.8 Hz), 8.19–8.15 (m, 1 H), 7.83 (d, 1 H, *J* 7.8 Hz), 7.81–7.76 (m, 2 H), 7–6.95 (m, 1 H), 3.52 (brt, 2 H).

‡ This was contaminated with its double bond isomerised product (*ca.* 2%), which was not separable.

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