The Preparation and Novel [3.3] Sigmatropic Rearrangement of Cyclophanes having a Spiro Skeleton†

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Oxidation of dihydroxy[*n*.2]metacyclophanes **1** with $K_3[Fe(CN)_6]$ afforded the intramolecular O–C coupling product **2**, which has a spiro skeleton in good yield; variable temperature ^1H NMR measurements indicated that compounds **2** are interconvertible by a thermal [3.3] sigmatropic rearrangement, and the activation free energies for the [3.3] sigmatropic rearrangement increased with increasing length of the methylene bridge in compounds **2**.

The activation parameters of the Cope rearrangement are strongly affected by the substituents and by small rings condensed with the biallyl skeleton.[1,2] Recently, Vögtle *et al.* reported the influence of strain on the Cope rearrangement by formal replacement of small rings in the Cope system (*cf.* 3,4-homotropylidene,[2] bullvalene[3] or barbaralene[4]) by larger, *e.g.* medium-sized or multi-membered rings.[5–7]

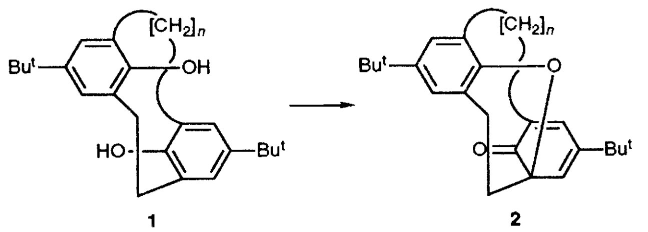
Recently, we reported[8,9] that the oxidation of 5,13-di-*tert*-butyl-8,16-dihydroxy[2.2]metacyclophane **1a** with Ag_2O or $K_3[Fe(CN)_6]$ afforded the intramolecular O–C coupling product **2a**. The ^1H NMR signals of this compound were broad at room temperature, but at −50 °C they were sharp, except for the bridging methylene protons. These results suggested that both [1.5] and [3.3] thermal sigmatropic rearrangements possibly occurred at room temperature.

Thus there is substantial interest in investigating the effects of the length of methylene bridges of the intramolecular O–C coupling products of dihydroxy[*n*.2]metacyclophanes on the thermal rearrangement. We report here on the oxidation of dihydroxy[*n*.2]metacyclophanes **1** and the thermal rearrangement of the oxidation products **2**.

Attempted oxidation of the [3.2]metacyclophane **1b** with $K_3[Fe(CN)_6]$ carried out in a mixture of aq. KOH and benzene at room temperature for 1 h as used in the oxidation of **1a** led to the intramolecular O–C coupling reaction to afford compound **2b** in 85% yield. This reaction was also applied to the oxidation of the other hydroxy[*n*.2]metacyclophanes **1c–g** having longer methylene bridges and the yields of **2**‡ are summarized in Table 1.

Table 1 Yields and IR data of oxidation products **2**

n	Yield (%)	IR: $\nu_{C=O}/cm^{-1}$
2	**2a** (98)	1725
3	**2b** (85)	1692
4	**2c** (90)	1684
5	**2d** (83)	1682
6	**2e** (63)	1680
8	**2f** (80)	1666
10	**2g** (60)	1650

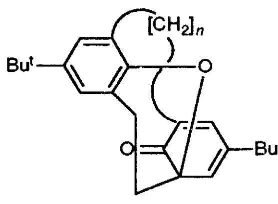


1 **2**

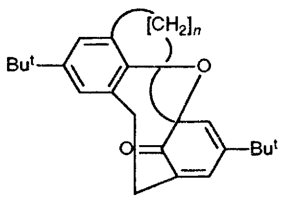
Scheme 1 *Reagents and conditions*: $K_3[Fe(CN)_6]$, aq. KOH–C_6H_6, room temp., 1 h

The structures of the products were determined from their elemental analyses and spectral data. However, there are two possible structures **A** or **B**, with O–C coupling occurring at the ethano-bridge to give **A** or at the propano-bridge to give **B**. In the IR spectra of the series **2**, the carbonyl stretching vibration shifted to lower wavenumbers as the number of methylene groups in the bridge increased, as shown in Table 1. This result strongly suggests that structure **A** is more likely since the carbonyl group in structure **A** is located in a different ring from that in which the number of methylene groups in the bridge changes, but in structure **B** it is located in the same ring.

The ^1H NMR spectrum of **2b** in $(CD_3)_2SO$ at room temperature shows two sets of doublets (*J* 1.5 Hz) at δ 5.86 and 6.40 for the diene protons and a broad singlet at δ 6.93 for the aromatic protons. This result indicates that the desired [3.3] sigmatropic rearrangement does not occur at this temperature. However, on raising the temperature, the signals for the diene and aromatic protons fused, and finally at 80 °C a broad singlet was observed. This phenomenon indicates that above 80 °C **2b** undergoes rapid interconversion by the thermal [3.3] sigmatropic rearrangement. The free energy for the [3.3] sigmatropic rearrangement of **2b** is estimated to be 71.1 kJ mol^{-1}. The same thermal rearrangement was also observed for compounds **2c**, **2d** and **2e**. However, for compounds **2f** and **2g** this thermal behaviour was



A



B

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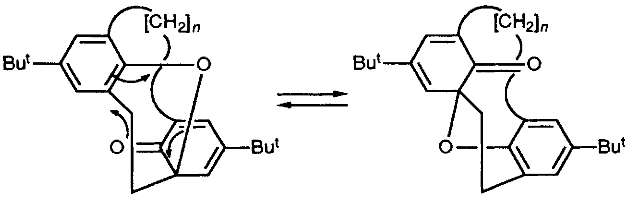
† For Part 21 of the series Medium-Sized Cyclophanes, see: T. Yamato, J. Matsumoto, M. Kajihara, K. Tokuhisa, K. Suehiro and M. Tashiro, *J. Org. Chem.*, accepted for publication.

‡ Compounds **2** were obtained as pale yellow prisms and gave satisfactory elemental analyses: **2b**: m.p. 168–172 °C; ^1H NMR ($CDCl_3$) δ 1.14 (9H, s), 1.25 (9H, s), 1.50–1.70 (1H, m), 2.05–2.80 (8H, m), 3.25–3.40 (1H, m), 5.86 (1H, d, *J* 1.5 Hz), 6.40 (1H, d, *J* 1.5 Hz) and 6.93 (2H, s); *m/z* 364 (M^+). **2c**: m.p. 162 °C; ^1H NMR ($CDCl_3$) δ 1.14 (9H, s), 1.24 (9H, s), 1.79–3.41 (12H, m), 5.90 (1H, d, *J* 1.5 Hz), 6.49 (1H, d, *J* 1.5 Hz) and 6.93 (2H, s); *m/z* 378 (M^+). **2d**: m.p. 64–67 °C; ^1H NMR ($CDCl_3$) δ 0.85–0.92 (2H, m), 1.16 (9H, s), 1.24 (9H, s), 1.77–3.24 (12H, m), 5.77 (1H, d, *J* 2.4 Hz), 6.43 (1H, d, *J* 2.4 Hz) and 6.88 (2H, s); *m/z* 392 (M^+). **2e**: m.p. 67–71 °C; ^1H NMR ($CDCl_3$) δ 1.10 (9H, s), 1.26 (9H, s), 1.46–2.91 (16H, m), 5.88 (1H, d, *J* 2.2 Hz), 6.56 (1H, d, *J* 1.5 Hz) and 6.93 (2H, s); *m/z* 406 (M^+). **2f**: m.p. 147–150 °C; ^1H NMR ($CDCl_3$) δ 0.83–0.92 (1H, m), 1.14 (9H, s), 1.28 (9H, s), 1.30–1.43 (6H, m), 1.65–1.82 (4H, m), 1.91–2.07 (1H, m), 2.24–2.50 (4H, m), 2.82–2.97 (4H, m), 3.25–3.40 (1H, m), 6.06 (1H, d, *J* 1.5 Hz), 6.88 (1H, d, *J* 1.5 Hz) and 6.93 (2H, s); *m/z* 434 (M^+). **2g**: m.p. 81–83 °C; ^1H NMR ($CDCl_3$) δ 1.12 (9H, s), 1.24 (9H, s), 0.88–3.56 (24H, m), 6.06 (1H, d, *J* 2.4 Hz), 6.90 (1H, d, *J* 2.0 Hz), 6.92 (1H, d, *J* 2.0 Hz) and 7.08 (1H, d, *J* 2.4 Hz); *m/z* 462 (M^+).

Table 2 Energy barriers of [3.3] sigmatropic rearrangement of the [*n*.2]cyclophanes **2** having spiro skeletons

	n	T_c/°C	$\Delta G^{\ddagger}$/kJ mol^{-1}
2b	3	80	71.1
2c	4	80	71.5
2d	5	110	77.8
2e	6	140	87.9
2f	8	>150	>105
2g	10	>150	>105



2

[3.3] Sigmatropic rearrangement

not observed even on heating to 150 °C in $(CD_3)_2SO$. As shown in Table 2 the free energy for the present [3.3] sigmatropic rearrangement increases with increasing number of methylene groups in the bridge.

It is well known that thermal [3.3] sigmatropic rearrangements generally proceed *via* the chair or boat form as the transition state at high temperatures (>250 °C).[10,11] Molecular model considerations suggest that conformational fixation in the chair form in the ground and transition state is possible in the spiro compounds **2**, the extent of which decreases as the number of methylene groups in the bridge increases.

In conclusion, we systematically demonstrated for the first time that the strain of a medium ring should lower not only the rearrangement barriers but also the conformational fixation of the [3.3] sigmatropic rearrangement system by means of the bridge. The possibility of fixing conformations in the ground and transition state thus opens up new mechanistic aspects for sigmatropic reactions.

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