Medium-sized cyclophanes. Part 46.[1] The preparation and novel [3.3]- and [1.5]-sigmatropic rearrangements of [*n*.2]cyclophanes having a spiro skeleton†

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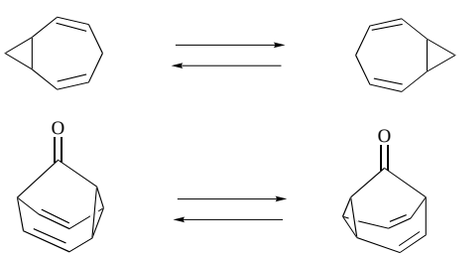
Oxidation of dihydroxy[*n*.2]metacyclophanes 4 with $K_3[Fe(CN)_6]$ affords in good yield the intramolecular O–C coupling products 5 having a spiro skeleton. Variable temperature ^{1}H NMR measurements indicate that compounds 5 are interconvertible by thermal [3.3]sigmatropic rearrangement. The free energies for the [3.3]sigmatropic rearrangement increase with increasing length of the methylene bridge in compounds 5. The substituent effect on the [1.5]sigmatropic rearrangement of [2.2]cyclophanes 3 having a spiro skeleton is also discussed.

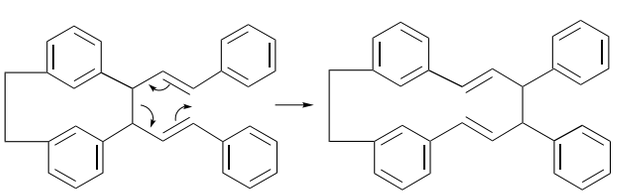
Introduction

In the case of small-ring compounds, Cope rearrangement can be facilitated considerably by Baeyer ring strain.[2] The activation parameter for the Cope rearrangement is strongly affected by the substituents and by small rings condensed to the biallyl skeleton, *e.g.* 3,4-homotropilidene,[3] bullvalene,[4] or barbaralene.[5]



Scheme 1

Some time ago, Vögtle *et al.* reported[6] the influence of the strain on the Cope rearrangement by formal replacement of small rings in the Cope system by larger, *e.g.* medium-sized or multi-membered, cyclophane rings. However, construction of a degenerated rearrangement of Cope systems induced by the strained hydrocarbons encountered difficulties.



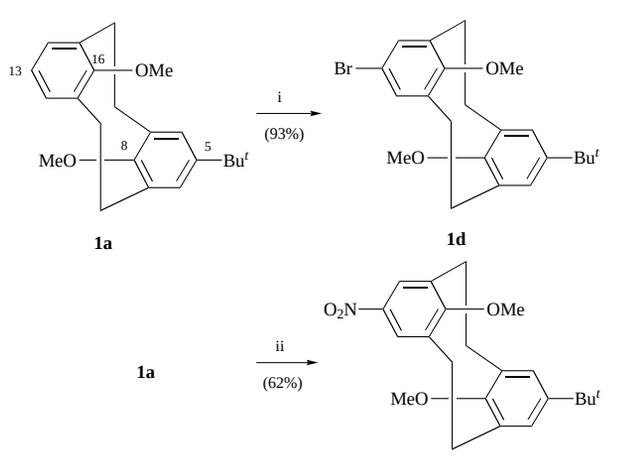
Scheme 2

Concurrently, we reported[7] that oxidation of 5,13-di-*tert*-butyl-8,16-dihydroxy[2.2]MCP (MCP = metacyclophane) **2c** with Ag_2O or $K_3[Fe(CN)_6]$ afforded the intramolecular O–C coupling product, 5,6′-di-*tert*-butyl-2-oxo-3,8′-ethanospiro-[cyclohexa-3,5-diene-1,2′-chromane] **3c**. At 25 °C (room temp.) the ^{1}H NMR proton signals of this compound were observed as broad signals but at −50 °C sharp signals were observed except for those of the bridged methylene protons. These results might suggest that both thermal [1.5]- and [3.3]-sigmatropic rearrangement occurred at room temperature. However, an estimation of the activation energy for these interconversions has not been established because the ^{1}H NMR proton signals overlap above −50 °C. Thus, there is substantial interest in investigating the effects of substituents on the benzene and cyclohexadienone rings, and the length of methylene bridges on the thermal rearrangement of the intramolecular O–C coupling products of dihydroxy[*n*.2]MCPs. We report here on the oxidation of the dihydroxy[*n*.2]MCPs **2** and **4** and the thermal rearrangement of the oxidation products **3** and **5**.

Results and discussion

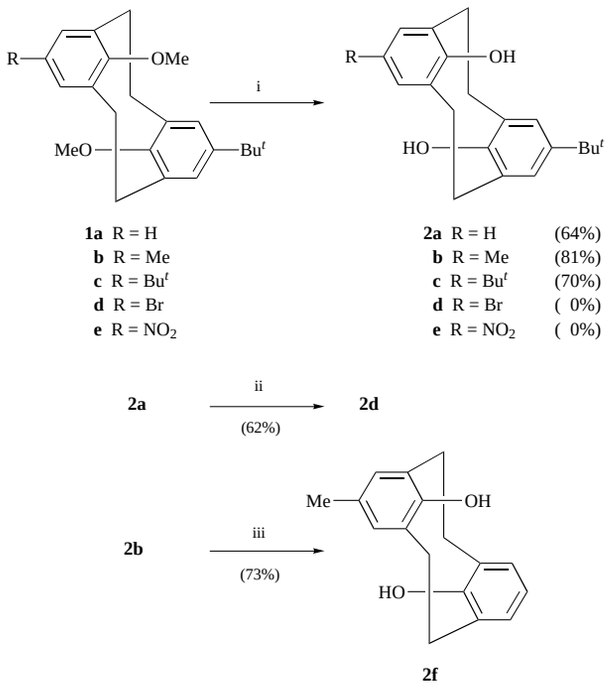
In order to introduce substituents on the aromatic ring of [2.2]MCPs having a spiro skeleton by intramolecular O–C coupling under the oxidation conditions, the starting material, 5-*tert*-butyl-8,16-dimethoxy[2.2]MCP **1a**[8], is designed so that electrophilic substitution occurs at the 13-position, thus leading to the unsymmetrically substituted 8,16-dimethoxy[2.2]MCPs.

In fact, bromination of **1a** with bromine (1.2 equiv.) in the presence of iron powder afforded the desired 13-bromo-[2.2]MCP **1d** (93%). Similarly, nitration of **1a** with copper(II) nitrate in acetic anhydride gave the 13-nitro derivative (62%).



Scheme 3 *Reagents and conditions*: i, Br_2–CCl_4, Fe powder, 5 °C, 0.5 h; ii, $Cu(NO_3)_2$–Ac_2O, room temperature, 12 h

† A part of the present paper has been published as preliminary communications: T. Yamato, J. Matsumoto, K. Tokuhisa, K. Suehiro and M. Tashiro, *J. Chem. Soc., Chem. Commun.*, 1992, 865.



Scheme 4 *Reagents and conditions*: i, BBr_3–CH_2Cl_2, room temperature, 2 h; ii, BTMA Br_3, MeOH–CH_2Cl_2, room temperature, 5 min; iii, $AlCl_3$–$MeNO_2$, benzene, room temperature, 24 h

Demethylation of **1a**–**c** with BBr_3 in methylene dichloride afforded good yields of the desired dihydroxy derivatives **2a**–**c**, respectively. However, similar reaction of **1d** and **1e** gave only intractable mixtures of products. Therefore, compound **2d** was prepared by bromination of **2a** with an equimolar amount of benzyl(trimethyl)ammonium tribromide (BTMA·Br_3)[9] (62%). $AlCl_3$–$MeNO_2$ catalysed transalkylation of **2b** gave 8,16-dihydroxy-5-methyl[2.2]MCP **2f** (73%).

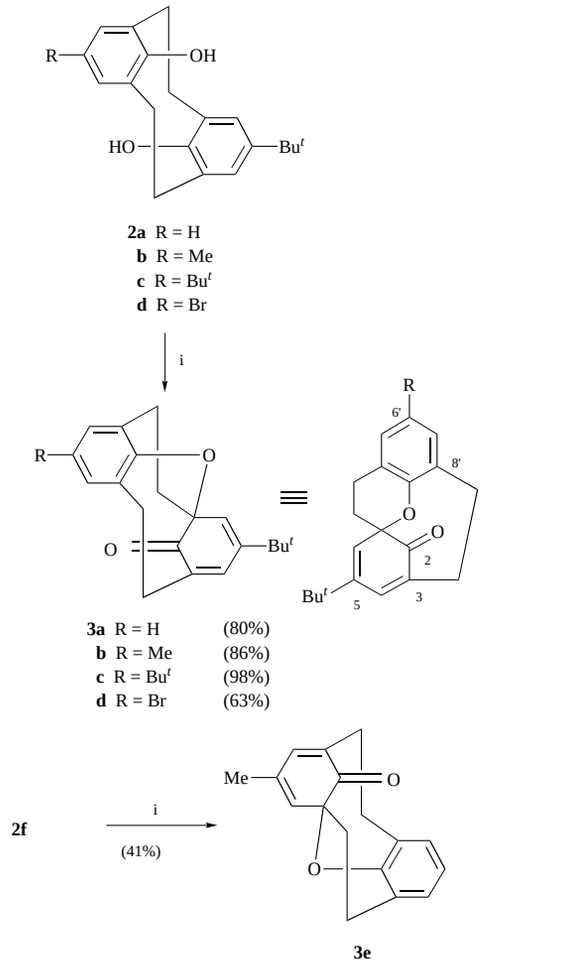
Attempted oxidation of 8,16-dihydroxy[2.2]MCPs **2a**–**d** with $K_3[Fe(CN)_6]$[10] carried out in a mixture of aq. KOH and benzene at room temperature for 1 h induced intramolecular O–C coupling to afford 5,6′-disubstituted 2-oxo-3,8′-ethanonospiro[cyclohexa-3,5-diene-1,2′-chromanes] **3a**–**d** in good yields. This reaction was also applied to the oxidation of the hydroxy[2.2]MCP **2f** to afford the spiro compound **3e** (41%).

The structures of the products obtained in the present work were determined from their elemental analyses and spectral data. However, there are two possible structures **A** or **B** as shown below; since O–C coupling occurred at both ethano bridges on the two benzene rings to give **A** and **B**.

For compounds **3a**–**e** the proton signals were broad at room temperature, 25 °C, but were sharp at −50 °C except for those of the bridged methylene protons. These results might suggest that the thermal sigmatropic rearrangement occurred at room temperature.

The ^{1}H NMR spectrum of **3a** in $CDCl_3$ at −50 °C showed a pair of singlets at δ 5.76 and 6.28 for olefinic protons and a multiplet at δ 7.02–7.09 for aromatic protons, respectively. The chemical shifts for olefinic protons are closely identical with those of the symmetrically substituted compound **3c**. No signals attributable to structure **B** were observed at this temperature. These results strongly suggest that structure **A** is much more favoured for **3a** at −50 °C. The structures of the other compounds **3b**–**e** were similarly assigned and the results are compiled in Table 1.

Interestingly, the ^{1}H NMR spectrum of compound **3b** in $CDCl_3$ below −50 °C shows the methyl protons at δ 1.91 and 2.26, the olefinic protons at δ 5.75, 6.28 and 5.76, 6.00, and the aromatic protons at δ 6.81, 6.89 and 6.98, 7.07, respectively (Fig. 1). On the basis of these results it may be inferred that



Scheme 5 *Reagents and conditions:* i, $K_3[Fe(CN)_6]$, benzene, room temperature, 1 h

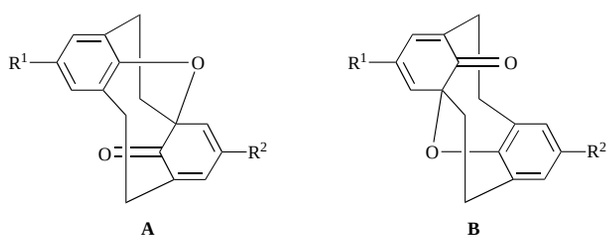


Table 1 ^{1}H NMR data for 2-oxo-3,8′-ethanospiro[cyclohexa-3,5-diene-1,2′-chromane][a]

Compd.	R^1	R^2	Olefinic protons	Ar protons	Assignment
3a	H	Bu^t	5.76, 6.28	7.05[b]	**A**
3b	Bu^t	Me	5.75, 6.28	6.81, 6.89	**A**[c]
	Me	Bu^t	5.76, 6.00	6.98, 7.07	**B**[c]
3c	Bu^t	Bu^t	5.73, 6.25	6.95, 7.04	**AB**
3d	Br	Bu^t	5.75, 6.30	7.15, 7.19	**A**
3e	Me	H	5.78, 6.02	7.03[b]	**B**

[a] Chemical shifts are expressed in ppm (δ) against TMS as internal standard. Temperature: −50 °C; solvent: $CDCl_3$. [b] Midpoint value of multiplet. [c] The **A**:**B** ratio was 7:3.

compound **3b** at this temperature exists as a mixture of **A** and **B** in a ratio of 70:30. However, as the temperature of the solution of the respective compound in $CDCl_3$ is increased, the individual signals for the olefinic and aromatic protons begin to merge above 0 °C and 30 °C, respectively. A pair of single peaks is, then, eventually observed above 120 °C in [$^2H_6$]-DMSO. Similarly, two singlet signals for the methyl protons are also

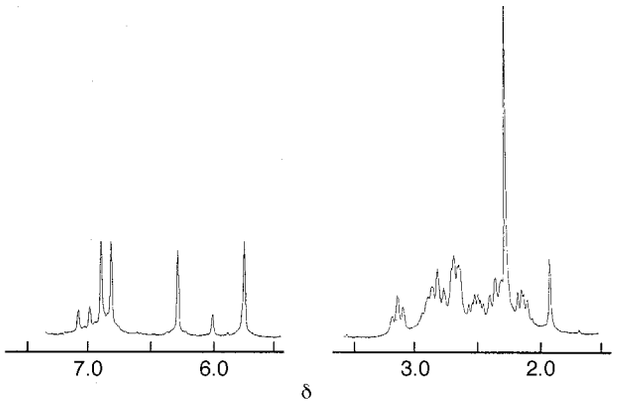


Fig. 1 ^{1}H NMR spectrum of **3b** at −50 °C ($CDCl_3$; 270 MHz)

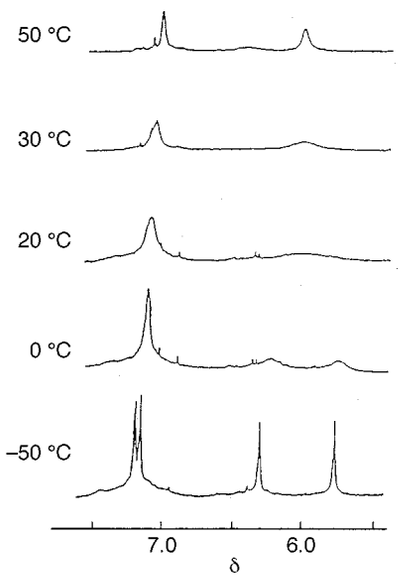
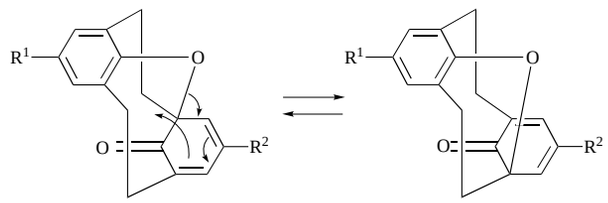


Fig. 2 Dynamic ^{1}H NMR spectra of **3d** ($CDCl_3$; 270 MHz)

observed as a singlet above 120 °C. These phenomena indicate that above 120 °C **3b** is rapidly interconvertible by thermal [1.5]- and [3.3]-sigmatropic rearrangements like **3c**.

In the case of **3d** in $CDCl_3$, however, as the temperature is raised, the individual signals for the olefinic protons (δ 5.75 and 6.30) and aromatic protons (δ 7.15 and 7.19) fuse and, finally, at 30 °C the two singlets at δ 6.05 and 7.05 broaden (Fig. 2). This observation indicates that above 30 °C the two olefinic protons and the two aromatic protons in **3d** are equivalent on the NMR time-scale because of the rapid interconvertible thermal [1.5]sigmatropic rearrangement. The other possible [3.3] sigmatropic rearrangement was not observed below 150 °C in [$^2H_6$]-DMSO.

Similar phenomena arising from [1.5]sigmatropic rearrangement were observed for the unsymmetrically substituted spiro compounds **3a** and **3e**; in these, which were different from those of compounds **3b** and **3c**, two kinds of sigmatropic rearrangements occurred simultaneously above room temperature. Thus, substituent effects were observed in the present system. As shown in Table 2, the free energies for the [1.5]sigmatropic rearrangement for **3a**, **3d** and **3e** are almost equal and estimated to be 13.8–14.1 kcal mol^{-1}. In contrast, the free energy for the other [3.3]sigmatropic rearrangements are thought to increase to >25 kcal mol^{-1} because there was no fusion below 150 °C in [$^2H_6$]-DMSO of the signals for olefinic and aromatic protons. Dependency on R^1 and R^2 with different distributions of structures **A** and **B** in unsymmetrically substituted [2.2]cyclophanes having a spiro skeleton **3** was observed. Thus, electron-releasing groups such as methyl and *tert*-butyl favoured attachment to



3

Table 2 Energy barriers of [1.5]sigmatropic rearrangement of **3**

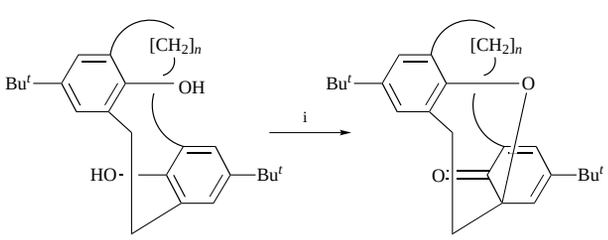
Compd.	R^1	R^2	Solvent	T_c/°C	$\Delta G_c^{\ddagger}$/kcal mol^{-1}
3e	H	Me	$CDCl_3$	30	13.8
3a	H	Bu^t	$CDCl_3$	20	14.1
3d	Br	Bu^t	$CDCl_3$	30	13.8
3d	Br	Bu^t	CD_3CN	20	13.8
3d	Br	Bu^t	[$^2H_6$]-DMSO	30	14.1

Table 3 Yield and IR data for the oxidation products **3c** and **5**

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

the cyclodienone ring, whilst an electron-withdrawing group, such as bromo favoured attachment to the aromatic ring. In the case of compound **3b** where the electronic character is almost the same in the two rings, both **A** and **B** can exist as a mixture in a ratio of 70:30 below −50 °C. These observations suggested that the [3.3]sigmatropic rearrangement might be strongly affected by the substituents R^1 and R^2. No dependency of the present thermal interconversion on the polarity of the solvent (for $CDCl_3$, CD_3CN, and [$^2H_6$]-DMSO) was observed, a finding which strongly supports a sigmatropic rearrangement in the present systems.

Attempted oxidation of 6,14-di-*tert*-butyl-9,17-dihydroxy-[3.2]MCP **4a**[7b,11] with $K_3[Fe(CN)_6]$ carried out in a mixture of

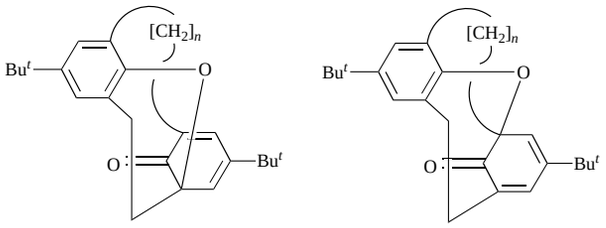


4 **5**

Scheme 6 (see Table 3). *Reagents and conditions:* i, $K_3[Fe(CN)_6]$, KOH aq. Benzene, room temperature for 1h

aqueous KOH and benzene at room temperature for 1 h as used in the oxidation of **2** led to intramolecular O–C coupling to afford 5,6′-di-*tert*-butyl-2-oxo-3,8′-propanospiro[cyclohexa-3,5-diene-1,2′-chromane] **5a** (85%). This reaction was also applied to the oxidation of the other hydroxy[*n*.2]metacyclophanes **4b–f** having longer methylene bridges; the yields of **5** are summarized in Table 3.

The structures of the products obtained in the present work were determined from their elemental analyses and spectral data. However, there are two possible structures **C** or **D** as shown below (Fig. 3); the O–C coupling reaction occurred at the ethano bridge to give **C** and at the propano bridge to give



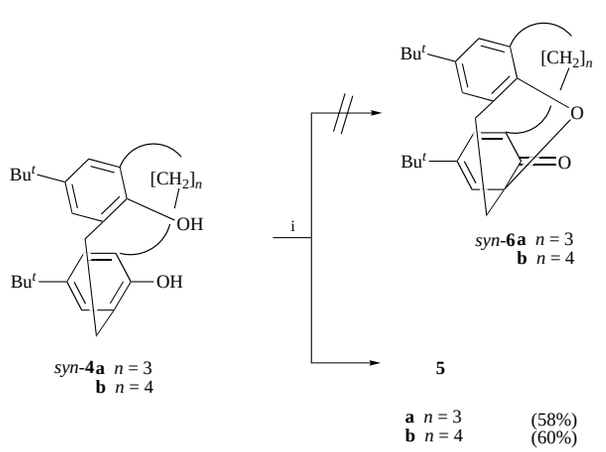
C **D**

Fig. 3 Possible structure for the intramolecular O–C coupling products **5**

D. In the IR spectra of **3c** and **5a**–**f**, the carbonyl stretching vibration shifted to lower wavenumbers with an increasing number of methylenes in the bridge (see Table 3). This finding strongly suggests that the structure of **C** is much more favourable since the carbonyl group in structure of **C** is located in a different ring system as the number of methylenes in the bridge changes, but in the latter structure **D** it is located in a similar system.

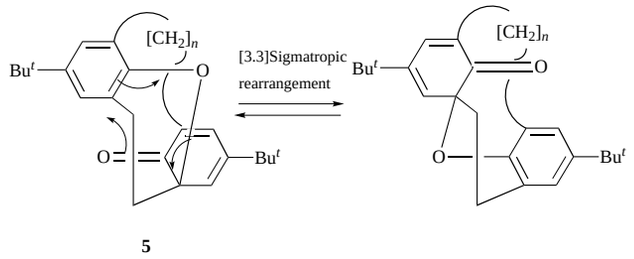
Interestingly, similar oxidation of the corresponding *syn*-[3.2]-MCP (*syn*-**4a**) and *syn*-[4.2]-MCP (*syn*-**4b**) with $K_3[Fe(CN)_6]$ under the same reaction conditions as *anti*-**4**, led to the spiro compound **5a** and **5b**, in 58 and 60% yields, respectively. No formation of the *syn*-type oxidation product **6** has been observed under the reaction conditions used. This finding strongly suggests that the ring inversion to the thermodynamically more stable *anti*-conformation is possible in the dihydroxy[3.2]- and [4.2]-MCP **4**.

On the other hand, we have reported [11] that *syn*- and *anti*-**4a**,**b** are thermally stable and are not interconverted at 150 °C in $[^2H_6]$-DMSO solution and at 400 °C in the solid state. Although a detailed mechanism for the rationalization of the observed *syn*-to-*anti*-conversion remains to be formulated, it seems likely that $K_3[Fe(CN)_6]$ generates a phenoxy radical anion intermediate, similar to that in the oxidation of phenols with $K_3[Fe(CN)_6]$, which then undergoes ring inversion to the thermodynamically more stable *anti*-conformation; subsequently, a spiro skeleton **5** is formed by intramolecular O–C coupling of the intermediate.



Scheme 7 *Reagents and conditions:* i, $K_3[Fe(CN)_6]$, aq. KOH, benzene, room temperature for 1 h

The ^{1}H NMR spectrum of **5a** in $[^2H_6]$-DMSO at room temperature showed two sets of doublets (J 1.5 Hz) at δ 5.86 and 6.40 for the olefinic 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 olefinic protons and the aromatic protons fused and, finally, at 80 °C a broadened singlet was observed around δ 6.7. This phenomenon indicates that above 80 °C all olefinic and aromatic protons in **5a** are equivalent on the NMR time-scale owing to a rapid interconvertible thermal [3.3]sigmatropic rearrangement. The free energy for the [3.3]sigmatropic rearrangement for **5a** is estimated as 17.0 kcal mol^{-1}. The same thermal rearrangement was also observed for compounds **5b**, **5c** and **5d**. However, for compounds **5e** and **5f** no such thermal behaviour was observed, even at 150 °C in $[^2H_6]$-DMSO. As shown in Table 4 the free energy for the present [3.3]sigmatropic rearrangement of compounds **5** increased as the number of methylenes in the bridge increased.



5

Table 4 Energy barriers for the [3.3]sigmatropic rearrangement of [2.*n*]cyclophanes having a spiro skeleton **5a**–**f**

Compd.	n	T_c/°C	$\Delta G_c^{\ddagger}$/kcal mol^{-1}
5a	3	80	17.0
5b	4	80	17.1
5c	5	110	18.6
5d	6	140	21.0
5e	8	>150	>25.0
5f	10	>150	>25.0

It is well known that thermal [3.3]sigmatropic rearrangements generally proceed *via* a chair or boat form transition state at high temperature (>250 °C).[12,13] A study of molecular models suggests that the chair conformation is preferred in the ground and transition states for the spiro compounds **5**, but decreasingly so as the number of methylenes in the bridge increases.

Conclusions

Oxidation of dihydroxy[2.2]MCPs **2** with $K_3[Fe(CN)_6]$ afforded in good yield the intramolecular O–C coupling product **3** having a spiro skeleton. A similar spiro compound **5** was formed by oxidation of the *syn*- and *anti*-di-*tert*-butyldihydroxy[*n*.2]MCPs **4** with $K_3[Fe(CN)_6]$. These findings suggest that the above novel oxidation of hydroxy groups in *anti*-intraannular positions is attributed to not only the strain of a medium ring which can be released by conversion into a less strained spiro skeleton, but also the conformational fixation of the reaction site by means of an ethylene bridge.

The variable-temperature ^{1}H NMR measurements indicated that compounds **5** are interconvertible by a thermal [3.3]sigmatropic rearrangement. The free energies for the [3.3]sigmatropic rearrangement were increased with increasing length of the methylene bridge in compounds **5**. Substituent effects on the sigmatropic rearrangement of [2.2]cyclophanes having a spiro skeleton **3** have been observed.

In conclusion, we have 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 a [3.3]sigmatropic rearrangement by means of the bridge. The possibility of fixing conformations in the ground and transition state thus opens up new mechanistic horizons for sigmatropic reactions.

Further studies on the present [1.5]- and [3.3]-sigmatropic rearrangement of **3** and **5** are now in progress.

Experimental

All mps (Yanagimoto MP-S1) and bps are uncorrected. NMR

spectra were determined at 270 MHz with a Nippon Denshi JEOL FT-270 NMR spectrometer with $SiMe_4$ as an internal reference: *J* values are given in Hz. IR spectra were measured for samples as KBr pellets or a liquid film on NaCl plates in a Nippon Denshi JIR-AQ2OM spectrophotometer. Mass spectra were obtained on a Nippon Denshi JMS-01SA-2 spectrometer at 75 eV using a direct-inlet system through GLC.

Materials

The 5-*tert*-butyl-8,16-dimethoxy[2.2]metacyclophane **1a** and di-*tert*-butyldihydroxy[*n*.2]metacyclophanes **4** were prepared as previously described.[8,11*b*,*c*]

Bromination of 5-*tert*-butyl-8,16-dimethoxy[2.2]metacyclophane 1a

To a mixture of **1a** (400 mg, 1.2 mmol) and a small amount of iron powder in CCl_4 (4 cm^3) was added a solution of Br_2 (200 mg, 1.33 mmol) in CCl_4 (2 cm^3) at 5 °C. After the reaction mixture had been stirred for 30 min at 5 °C, it was poured into water (20 cm^3) and extracted with CH_2Cl_2 (20 cm^3 × 2). The extract was washed with 10% aqueous sodium thiosulfate (10 cm^3) and water (10 cm^3), dried (Na_2SO_4) and concentrated. The residue was recrystallized from methanol gave 5-*bromo*-13-tert-*butyl*-8,16-*dimethoxy*[2.2]*metacyclophane* **1d** (450 mg, 93%) as *prisms*, mp 142–144 °C; ν_{max}(KBr)/cm^{-1} 2950, 1570, 1480, 1450, 1420, 1360, 1300, 1260, 1250, 1170, 1110, 1020, 870, 850, 830, 770, 710, 690 and 650; δ_H($CDCl_3$) 1.30 (9 H, s), 2.47–2.78 (8 H, m), 2.88 (3 H, s), 2.99 (3 H, s), 7.03 (2 H, s) and 7.14 (2 H, s); *m*/*z* 402 and 404 (M^+) (Found: C, 65.3; H, 6.69. $C_{22}H_{27}O_2Br$ requires C, 65.51; H, 6.74%).

Nitration of 5-*tert*-butyl-8,16-dimethoxy[2.2]metacyclophane 1a with $Cu(NO_3)_2$ in acetic anhydride

To a solution of **1a** (450 mg, 1.39 mmol) in acetic anhydride (200 cm^3) was added $Cu(NO_3)_2 \cdot 3H_2O$ (610 mg, 0.492 mmol) at 0 °C. After the mixture had been stirred at room temperature for 12 h, it was poured into ice–water and extracted with CH_2Cl_2 (20 cm^3 × 2). The combined extracts were washed with water and 10% aqueous sodium hydrogen carbonate, dried (Na_2SO_4) and concentrated. The residue was subjected to silica gel (Wako, C-300; 100 g) column chromatography using hexane–benzene (1 : 1) as an eluent to afford a colourless solid. Recrystallization of this from methanol gave 5-tert-*butyl*-8,16-*dimethoxy*-13-*nitro*[2.2]*metacyclophane* **1e** (318 mg, 62%) as *prisms*, mp 159–161 °C; ν_{max}(KBr)/cm^{-1} 2931, 2872, 2819, 1582, 1508, 1480, 1474, 1464, 1428, 1419, 1362, 1357, 1341, 1305, 1289, 1263, 1241, 1222, 1205, 1175, 1167, 1104, 1087, 1026, 1008, 894, 867, 769 and 745; δ_H($CDCl_3$) 1.32 (9 H, s), 2.62–2.84 (8 H, m), 2.93 (3 H, s), 3.02 (3 H, s), 7.06 (2 H, s) and 7.96 (2 H, s); *m*/*z* 392 and 369 (M^+) (Found: C, 71.25; H, 7.62; N, 3.84. $C_{22}H_{27}O_4N$ requires C, 71.52; H, 7.37; N, 3.79%).

Demethylation of 1 with BBr_3

Typical procedure. To a solution of **1a** (324 mg, 1 mmol) in CH_2Cl_2 (10 cm^3) was added a solution of BBr_3 (0.4 cm^3) in CH_2Cl_2 (2 cm^3) at 0 °C. After the reaction mixture had been stirred at room temperature for 2 h, it was poured into ice–water (10 cm^3) and extracted with CH_2Cl_2 (20 cm^3 × 2). The combined extracts were washed with water (10 cm^3 × 2), dried (Na_2SO_4) and concentrated. The residue was subjected to silica gel (Wako, C-300; 100 g) column chromatography using hexane–benzene (1 : 1) as an eluent to afford a colourless solid. Recrystallization of this from hexane gave 5-tert-*butyl*-8,16-*dihydroxy*[2.2]*metacyclophane* **2a** (180 mg, 64%) as *prisms*, mp 140–143 °C; ν_{max}(KBr)/cm^{-1} 3450 (ν_{OH}), 2900, 1640, 1580, 1470, 1430, 1360, 1280, 1250, 1180, 1070, 900, 860, 810 and 770; δ_H($CDCl_3$) 1.31 (9 H, s), 2.34 (1 H, s, replaced by D_2O), 2.37 (1 H, s, replaced by D_2O), 2.69–2.85 (8 H, m), 6.84–6.95 (1 H, m) and 7.10–7.10 (4 H, m); *m*/*z* 296 (M^+) (Found: C, 80.89; H, 8.25. $C_{20}H_{24}O_2$ requires C, 81.04; H, 8.16%).

Similarly, compounds **2b** and **2c** were prepared in the same manner as described above in 81 and 70% yields, respectively. However, attempted demethylation of **1d** and **1e** failed, only intractable mixtures being obtained.

5-*tert*-Butyl-8,16-dihydroxy-13-methyl[2.2]metacyclophane 2b. This compound was obtained as *prisms* (from methanol), mp 122–125 °C; ν_{max}(KBr)/cm^{-1} 3450 (ν_{OH}), 2950, 1480, 1430, 1360, 1340, 1280, 1190, 1150, 1000, 940, 890, 865, 850, 810 and 760; δ_H($CDCl_3$) 1.31 (9 H, s), 2.08 (1 H, s, replaced by D_2O), 2.27 (3 H, s), 2.34 (1 H, s, replaced by D_2O), 2.70–2.90 (8 H, m), 6.93 (2 H, s) and 7.13 (2 H, m); *m*/*z* 310 (M^+) (Found: C, 81.15; H, 8.30. $C_{21}H_{26}O_2$ requires C, 81.25; H, 8.44%).

5,13-Di-*tert*-butyl-8,16-dihydroxy[2.2]metacyclophane 2c. This compound was obtained as prisms (from methanol), mp 267–268 °C (lit.,[14] 267–268 °C).

trans-*tert*-Butylation of 2b

To a solution of **2b** (40 mg, 0.129 mmol) in benzene (1 cm^3) was added a solution of $AlCl_3$ (88 mg, 0.66 mmol) in nitromethane (0.2 cm^3) at room temperature. After being stirred at room temperature for 24 h, the reaction mixture was poured into ice–water (10 cm^3) and extracted with benzene (10 cm^3 × 2). The combined extracts were washed with water (10 cm^3 × 2), dried (Na_2SO_4), and concentrated. The residue was subjected to silica gel (Wako, C-300; 100 g) column chromatography using as an eluent hexane–benzene (1 : 1) to afford a colourless solid. Recrystallization of this from hexane–benzene (1 : 1) gave 8,16-*dihydroxy*-5-*methyl*[2.2]*metacyclophane* **2f** (24 mg, 73%) as *prisms*, mp 206–209 °C; ν_{max}(KBr)/cm^{-1} 3534 (ν_{OH}), 2927, 1471, 1457, 1448, 1436, 1253, 1197, 1174, 1157, 904, 860 and 784; δ_H($CDCl_3$) 2.27 (3 H, s), 2.30 (1 H, s, replaced by D_2O), 2.53 (1 H, s, replaced by D_2O), 2.69–2.87 (8 H, m), 6.93 (3 H, br s) and 7.13 (2 H, d, *J* 7.3); *m*/*z* 254 (M^+) (Found: C, 79.98; H, 7.10. $C_{17}H_{18}O_2$ requires C, 80.29; H, 7.13%).

Bromination of 5-*tert*-butyl-8,16-dihydroxy[2.2]metacyclophane 2a

To a solution of **2a** (100 mg, 0.36 mmol) in a mixture of CH_2Cl_2 (5 cm^3) and methanol (1.6 cm^3) was added benzyl(trimethyl)-ammonium tribromide (169 mg, 0.43 mmol) at room temperature. After the reaction mixture had been stirred for 5 min at room temperature, it was poured into water (10 cm^3). The organic layer was extracted with CH_2Cl_2 (10 cm^3 × 2). The combined extracts were washed with 10% aqueous sodium thiosulfate (5 cm^3) and water (10 cm^3), dried (Na_2SO_4), and concentrated. The residue was recrystallized from hexane to give 5-*bromo*-13-tert-*butyl*-8,16-*dihydroxy*[2.2]*metacyclophane* **2d** (80 mg, 62%) as *prisms*, mp 172 °C; ν_{max}(KBr)/cm^{-1} 3425 (ν_{OH}), 2963, 2950, 2933, 2859, 1481, 1476, 1458, 1442, 1434, 1360, 1336, 1291, 1284, 1257, 1240, 1192, 1165, 881, 869, 855, 846, 839 and 748; δ_H($CDCl_3$) 1.30 (9 H, s), 2.23 (1 H, s, replaced by D_2O), 2.70–2.88 (8 H, m), 3.01 (1 H, s, replaced by D_2O), 7.12 (2 H, s) and 7.20 (2 H, s); *m*/*z* 374 and 376 (M^+) (Found: C, 64.32; H, 6.43. $C_{20}H_{23}O_2Br$ requires C, 64.01; H, 6.18%).

Oxidation of 2 with $K_3[Fe(CN)_6]$

Typical procedure. To a solution of **2a** (300 mg, 1.10 mmol) in benzene (6 cm^3) was gradually added at room temperature a solution of $K_3[Fe(CN)_6]$ (1.44 g, 4.37 mmol) and KOH (1.04 g, 18.6 mmol) in water (30 cm^3) over a period of 10 min. After the reaction mixture had been stirred at room temperature for 1 h, the organic layer was separated, washed with water, dried (Na_2SO_4), and evaporated *in vacuo* to leave a residue. This was chromatographed over silica gel (Wako, C-300; 100 g) with hexane–benzene (1 : 1) as eluent to give a pale yellow solid recrystallization of which from hexane afforded 5-tert-*butyl*-2-*oxo*-3,8′-*ethanospiro*[*cyclohexa*-3,5-*diene*-1,2′-*chromane*] **3a** (259 mg, 80%) as *pale yellow prisms*, mp 142–145 °C; ν_{max}(KBr)/cm^{-1} 2950, 1700 (C=O), 1460, 1360, 1250, 1200, 1150, 1060, 940, 860, 800 and 680; δ_H($CDCl_3$) at 20 °C, 1.14 (9 H, s), 2.45–

2.97 (8 H, br m), 6.10 (2 H, br s) and 6.96 (3 H, br s); at −50 °C, 1.12 (9 H, s), 2.10–3.19 (8 H, br m), 5.76 (1 H, s), 6.28 (1 H, s) and 7.01–7.09 (3 H, m); *m*/*z* 294 (M^+) (Found: C, 81.72; H, 7.51. $C_{20}H_{22}O_2$ requires C, 81.60; H, 7.53%).

Similarly, compounds **3b**–**e** were prepared in the same manner as described above. Yields are compiled in Scheme 5.

5-*tert*-Butyl-6′-methyl-2-oxo-3,8′-ethanospiro[cyclohexa-3,5-diene-1,2′-chromane] 3b. This compound was obtained as *pale yellow prisms* (from hexane), mp 142–145 °C; ν_{max}(KBr)/cm^{-1} 2950, 1720 (C=O), 1470, 1430, 1365, 1205, 1130, 870 and 805; δ_H($CDCl_3$) at 20 °C, 1.16 (9 H, s), 2.14 (3 H, br s), 2.22–3.00 (8 H, br m) and 6.10 (4 H, br s); at −50 °C (structure **A**): 1.12 (9 H, s), 2.09–3.20 (8 H, br m), 2.26 (3 H, s), 5.75 (1 H, s), 6.28 (1 H, s), 6.81 (1 H, s) and 6.89 (1 H, s); (structure **B**): 1.29 (9 H, s), 1.91 (3 H, s), 2.09–3.20 (8 H, br m), 5.76 (1 H, s), 6.00 (1 H, s), 6.98 (1 H, s) and 7.07 (1 H, s); *m*/*z* 308 (M^+) (Found: C, 81.59; H, 7.84. $C_{21}H_{24}O_2$ requires C, 81.78; H, 7.84%).

5,6′-Di-*tert*-butyl-2-oxo-3,8′-ethanospiro[cyclohexa-3,5-diene-1,2′-chromane] 3c. This compound was obtained as *pale yellow prisms* (from hexane), mp >280 °C (lit.,[11a] mp >280 °C); ν_{max}(KBr)/cm^{-1} 3050, 2960, 1725 (C=O), 1475, 1430, 1360, 1200, 1160, 1000, 870, 820 and 745; δ_H($CDCl_3$) at 20 °C, 1.20 (18 H, br s), 2.56 (8 H, br s) and 6.40 (4 H, br s); at −50 °C, 1.26 (9 H, s), 1.28 (9 H, s), 2.02–3.20 (8 H, m), 5.73 (1 H, s), 6.25 (1 H, s), 6.95 (1 H, s) and 7.04 (1 H, s).

5-*tert*-Butyl-6′-bromo-2-oxo-3,8′-ethanospiro[cyclohexa-3,5-diene-1,2′-chromane] 3d. This compound was obtained as *pale yellow prisms* (from hexane), mp 230 °C (decomp.); ν_{max}(KBr)/cm^{-1} 2964, 2952, 2867, 1725 (C=O), 1634, 1378, 1468, 1431, 1362, 1215, 1199, 1174, 1159, 1147, 1002, 998, 875, 781 and 744; δ_H($CDCl_3$) at 20 °C, 1.13 (9 H, s), 2.46–2.94 (8 H, br m), 6.05 (2 H, br s) and 7.05 (2 H, br s); at −50 °C, 1.13 (9 H, s), 2.10–3.15 (8 H, br m), 5.75 (1 H, s), 6.30 (1 H, s), 7.15 (1 H, s) and 7.19 (1 H, s); *m*/*z* 372 and 374 (M^+) (Found: C, 64.77; H, 6.01. $C_{20}H_{21}O_2Br$ requires C, 64.35; H, 5.67%).

6′-Methyl-2-oxo-3,8′-ethanospiro[cyclohexa-3,5-diene-1,2′-chromane] 3e. This compound was obtained as *pale yellow prisms* (from hexane), mp 154–156 °C (decomp.); ν_{max}(KBr)/cm^{-1} 1718 (C=O); δ_H($CDCl_3$) at 20 °C, 1.93 (3 H, s), 2.44 (4 H, br s), 2.71 (2 H, br s), 2.95 (2 H, br s), 5.96 (2 H, br s) and 6.92 (3 H, br s); at −50 °C, 1.92 (3 H, s), 2.06–3.12 (8 H, m), 5.78 (1 H, s), 6.02 (1 H, s) and 7.02–7.05 (3 H, m); *m*/*z* 252 (M^+) (Found: C, 80.61; H, 6.55. $C_{17}H_{16}O_2$ requires C, 80.93; H, 6.39%).

Oxidation of *anti*-4 with $K_3[Fe(CN)_6]$

Typical procedure. To a solution of 6,14-di-*tert*-butyl-9,17-dihydroxy[3.2]metacyclophane **4a** (100 mg, 0.27 mmol) in benzene (2 cm^3) was gradually added over a period of 10 min at room temperature a solution of $K_3[Fe(CN)_6]$ (508 mg, 1.54 mmol) and KOH (369 mg, 6.58 mmol) in water (10 cm^3). After the reaction mixture had been stirred at room temperature for 1 h, the organic layer was separated, washed with water, dried (Na_2SO_4), and evaporated *in vacuo* to leave a residue. This was chromatographed over silica gel (Wako, C-300; 100 g) with hexane–benzene (1:1) as eluent to give a pale yellow solid. Recrystallization of this from hexane afforded 5,6′-*di*-tert-*butyl*-2-*oxo*-3,8′-*propanospiro*[*cyclohexa*-3,5-*diene*-1,2′-*chromane*] **5a** (84.7 mg, 85%) as *pale yellow prisms*, mp 168–172 °C; ν_{max}(KBr)/cm^{-1} 1705 (C=O); δ_H($CDCl_3$) 1.14 (9 H, s), 1.25 (9 H, s), 1.50–1.70 (1 H, m), 2.05–2.80 (8 H, m), 3.25–3.40 (1 H, m), 5.86 (1 H, *J* 1.5), 6.40 (1 H, d, *J* 1.5) and 6.93 (2 H, s); *m*/*z* 364 (M^+) (Found: C, 82.26; H, 8.86. $C_{25}H_{32}O_2$ requires C, 82.37; H, 8.85%).

Oxidation of di-*tert*-butyldihydroxy[*n*.2]metacyclophanes **4b**–**f** was carried out as a same procedure as described above. The yields are compiled in Table 3.

5,6′-Di-*tert*-butyl-2-oxo-3,8′-butanospiro[cyclohexa-3,5-diene-1,2′-chromane] 5b. This compound was obtained as *pale yellow prisms*, mp 162 °C; ν_{max}(KBr)/cm^{-1} 1700 (C=O); δ_H($CDCl_3$) 1.14 (9 H, s), 1.24 (9 H, s), 1.79–3.41 (12 H, m), 5.90 (1 H, *J* 1.5), 6.49 (1 H, d, *J* 1.5) and 6.93 (2 H, s); *m*/*z* 378 (M^+) (Found: C, 82.44; H, 9.00. $C_{26}H_{34}O_2$ requires C, 82.49; H, 9.05%).

5,6′-Di-*tert*-butyl-2-oxo-3,8′-pentanospiro[cyclohexa-3,5-diene-1,2′-chromane] 5c. This compound was prepared as *pale yellow prisms* (from hexane), mp 64–67 °C; ν_{max}(KBr)/cm^{-1} 1682 (C=O); δ_H($CDCl_3$) 0.85–0.92 (2 H, m), 1.16 (9 H, s), 1.24 (9 H, s), 1.77–3.24 (12 H, m), 5.77 (1 H, d, *J* 2.4), 6.43 (1 H, d, *J* 2.4) and 6.88 (2 H, s); *m*/*z* 392 (M^+) (Found: C, 82.52; H, 9.85. $C_{27}H_{36}O_2$ requires C, 82.62; H, 9.24%).

5,6′-Di-*tert*-butyl-2-oxo-3,8′-hexanospiro[cyclohexa-3,5-diene-1,2′-chromane] 5d. This compound was prepared as *pale yellow prisms* (from hexane), mp 67–71 °C; ν_{max}(KBr)/cm^{-1} 1680 (C=O); δ_H($CDCl_3$) 1.10 (9 H, s), 1.26 (9 H, s), 1.46–2.91 (16 H, m), 5.88 (1 H, d, *J* 2.4), 6.56 (1 H, d, *J* 2.4) and 6.93 (2 H, s); *m*/*z* 406 (M^+) (Found: C, 82.52; H, 9.80. $C_{28}H_{38}O_2$ requires C, 82.71; H, 9.42%).

5,6′-Di-*tert*-butyl-2-oxo-3,8′-octanospiro[cyclohexa-3,5-diene-1,2′-chromane] 5e. This compound was prepared as *pale yellow prisms* (from hexane), mp 147–150 °C; ν_{max}(KBr)/cm^{-1} 1666 (C=O); δ_H($CDCl_3$) 1.14 (9 H, s), 1.28 (9 H, s), 1.30–1.43 (6 H, m), 1.65–1.82 (4 H, m), 1.91–2.07 (1 H, m), 2.42–2.50 (4 H, m), 2.82–2.97 (4 H, m), 3.25–3.40 (1 H, m), 6.06 (1 H, d, *J* 1.5), 6.88 (1 H, d, *J* 1.5) and 6.93 (2 H, s); *m*/*z* 434 (M^+) (Found: C, 82.52; H, 9.80. $C_{30}H_{42}O_2$ requires C, 82.71; H, 9.42%).

5,6′-Di-*tert*-butyl-2-oxo-3,8′-decanospiro[cyclohexa-3,5-diene-1,2′-chromane] 2f. This compound was prepared as *pale yellow prisms* (from hexane), mp 81–83 °C; ν_{max}(KBr)/cm^{-1} 1650 (C=O); δ_H($CDCl_3$) 1.24 (9 H, s), 1.29 (9 H, s), 0.88–3.56 (24 H, m), 6.06 (1 H, d, *J* 2.4), 6.90 (1 H, d, *J* 2.0), 6.92 (1 H, d, *J* 2.0) and 7.08 (1 H, d, *J* 2.4); *m*/*z* 462 (M^+) (Found: C, 83.56; H, 10.31. $C_{32}H_{46}O_2$ requires C, 83.06; H, 10.02%).

Oxidation of *syn*-4a,b with $K_3[Fe(CN)_6]$

syn-6,14-Di-*tert*-butyl-9,17-dihydroxy[3.2]metacyclophane *syn*-**4a** and *syn*-7,15-di-*tert*-butyl-10,18-dihydroxy[4.2]metacyclophane *syn*-**4b** were treated with $K_3[Fe(CN)_6]$ in a similar manner to that described above to give **5a** and **5b** in 58 and 60% yields, respectively.

Estimation of the activation energy for the sigmatropic rearrangement

The rate constant (k_c) of the observed conformational interconversion at the coalescence (T_c) can be calculated by using [Eqn. (1)].[15] The free energy of activation ($\Delta G_c^{\ddagger}$) at coalescence can be estimated by using Eyring equation [Eqn. (2)].[15]

$$k_c = \pi/2^{\frac{1}{2}}(\Delta\nu^2 + 6J^2)^{\frac{1}{2}} \quad (1)$$

$$\Delta G_c^{\ddagger} = 2.303\ RT_c(10.32 + \log T_c - \log k_c) \quad (2)$$

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