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Communications

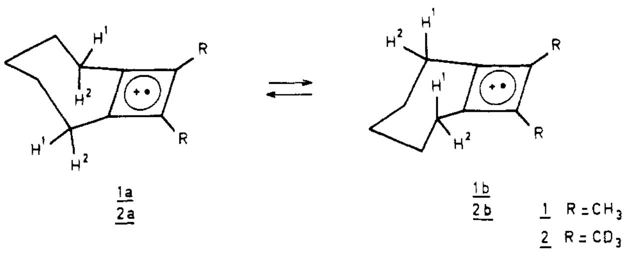
Dynamic ESR Spectroscopy of Cyclobutadiene Radical Cations Bearing One or Two Pentamethylene Chains

Summary: The process of ring inversion of the seven-membered rings in the cyclobutadiene radical cations **1**, **2**, and **3** has been studied by dynamic ESR spectroscopy. Comparison of the experimental and computer-simulated spectra (for **1** and **2**) at some temperatures has yielded the rate constants and free enthalpies of activation for this process.

Sir: Recently, we have published that tetraalkyl-substituted cyclobutadiene radical cations can be generated photochemically from the aluminum halide σ-complexes of the corresponding cyclobutadienes.[1,2] These radicals are definitely π-radicals, and thus the cyclobutadiene ring itself must be planar (or nearly so) in these species.[2] It occurred to us that cyclobutadiene radical cations might be used as a probe to study the dynamics of inversion processes of rings being annelated to the cyclobutadiene moiety. Such radical cations can indeed be generated by irradiation of 0.5 M solutions of the previously described aluminum halide σ-complexes[3] in CH_2Cl_2 or $Cl_2HCCHCl_2$. As an example we have chosen to study the cycloheptene ring inversion.[4] The free enthalpies of activation ($\Delta G^{\ddagger}$) for the ring inversion in some neutral, substituted cycloheptenes have been determined by dynamic NMR spectroscopy:[5] $\Delta G^{\ddagger} = 5.0$ kcal mol^{-1} for 4,4,5,6,6-pentadeuteriocycloheptene and $\Delta G^{\ddagger} = 7.4$ kcal mol^{-1} for 5,5-difluorocycloheptene, both values at −165 °C.[5a]

The ESR spectra of **1**, **2**, and **3** prove to be temperature dependent and show line-width alternation.[6] This can be interpreted in terms of the anticipated ring-inversion process, which is depicted in Scheme I for radical cations **1** and **2** and in Scheme II for radical cation **3**.

Scheme I



Scheme II

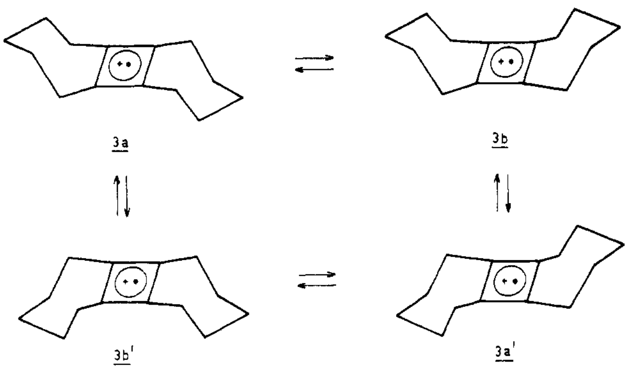


Table I. ESR Parameters of the Cyclobutadiene Radical Cations **1**, **2**, and **3**[a]

	1	2	3
$a_\beta{}^H$(ax)[b]	16.63 G	16.74 G	16.2 G
$a_\beta{}^H$(eq)[b]	4.98 G	5.01 G	5.4 G
$a_\gamma{}^H$ [c]	0.31 G	0.30 G	~0.35 G
$a_\beta{}^H$(methyl)	8.62 G	1.32 G[d]	
g (± 0.0002)[e]	2.0030	2.0030	2.0030

[a] Equipment used as described earlier.[1] [b] The β-CH bond roughly perpendicular to the cyclobutadiene moiety is called axial, and the other β-CH bond equatorial.[14] [c] Time-averaged γ-hfs. [d] Deuterium hfs. [e] Determined with DPPH as reference.

We have recorded the ESR spectra of **1** at −114 °C, −76 °C, and at +25 °C. The process of ring inversion is not yet completely frozen out at −114 °C, but it is possible to deduce the three different β-hyperfine splittings (β-hfs's): 8.62 G (methyl protons), 16.63 G, and 4.98 G (ring protons H^1 and H^2 in Scheme I). The exchange broadening (the so-called intermediate exchange) is at its maximum at −76 °C. The ESR spectrum of **1** at high temperature (~+25 °C) proves to be very complicated. This is probably due to the fact that the hfs's of the two different sets of β-protons at this temperature, the methyl protons and the time-avaraged ring protons (H^1, H^2), are of the same magnitude, thus causing a considerable overlap of the expected signals. Therefore, it is impossible to deduce the time-averaged hfs of the β-ring protons $((a(H^1) + a(H^2))/2)$ from the spectrum. To circumvent this problem, we have replaced the CH_3 groups in **1** by CD_3 groups (**2**).

The ESR spectra of radical cation **2** have been recorded at −109 °C, −77 °C, and +43 °C. The process of ring inversion is not yet completely frozen out at −109 °C; unfortunately, however, the solution solidifies upon further cooling. As in the case of **1**, the two different hfs's for the β-ring protons can be deduced from the spectrum, the values being 16.74 and 5.01 G (H^1 and H^2 in Scheme I). The spectrum at −77 °C represents the intermediate exchange. From this spectrum it can be concluded that the hfs's of the two different sets of β-protons (H^1 and H^2 in Scheme I) have the same relative sign. This follows from the observation that the unbroadened multiplets are separated by a distance $|a(H^1) + a(H^2)|$ (see Figure 1b, 21.75 G) and not $|a(H^1) - a(H^2)|$. The same holds for **1** and **3**. The process of ring inversion is not yet entirely fast on the ESR time scale at +43 °C. But, at still higher temperatures, **2** is not stable enough to give a reasonable ESR spectrum. The ESR parameters for **1** and **2** are summa-

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(4) Part of this work has been presented orally at a meeting of the Netherlands Foundation for Chemical Research (SON) at Lunteren, Nov 9–10, 1981.

(5) Examples are found in: (a) St. Jacques, M.; Vaziri, C. *Can. J. Chem.* **1971**, *49*, 1256. (b) Knorr, R.; Ganter, C.; Roberts, J. D. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 556.

(6) Scheffler, K.; Stegman, H. B. "Elektronenspinresonanz"; Springer-Verlag: West Berlin, 1970; Chapter 5.

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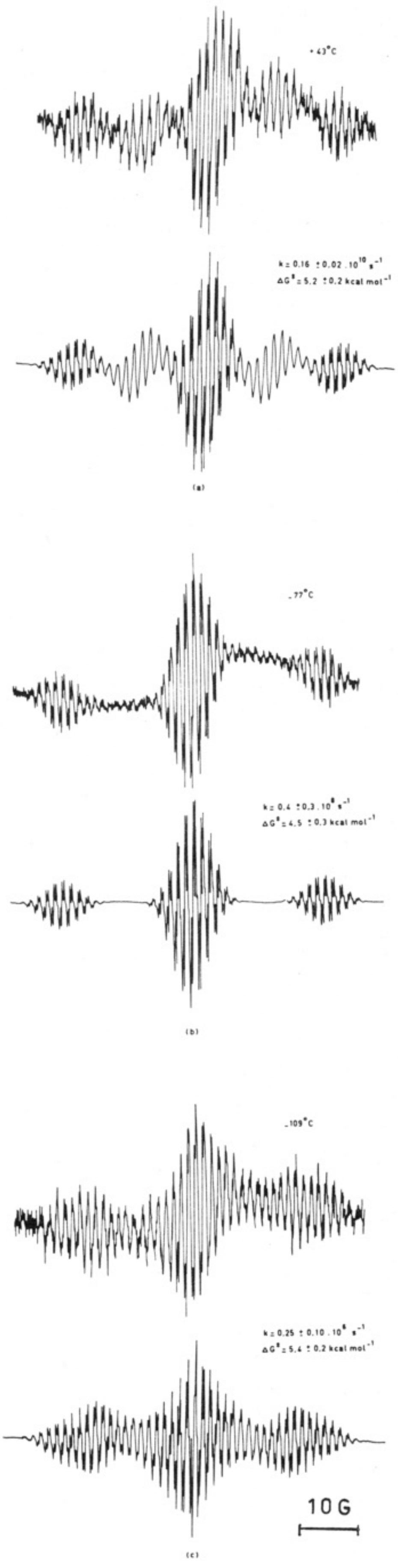

Figure 1. Experimental (top) and simulated (bottom) ESR spectra of **2**: (a) +43 °C (solvent $Cl_2HCCHCl_2$); (b) −77 °C (solvent CH_2Cl_2);[11] (c) −109 °C (solvent CH_2Cl_2).[12]

rized in Table I. $a_\beta^D(CD_3)/a_\beta^H(CH_3)$ is calculated to be 0.1531 in agreement with the theoretical value ($\mu_D I_H/\mu_H I_D$ = 0.1535). The data in the table also show that the ratio a_β^H(axial)/a_β^H(equatorial) has the same value for **1** and **2**: 3.34. Because the β-proton hfs's, and thus the ratio a_β^H(ax)/a_β^H(eq), depend largely on the dihedral angle between the orbital containing the unpaired electron and the β-CH bond,[7] this equality shows that the conformation of the seven-membered ring is the same in **1** and in **2**.

Furthermore, the ESR spectra of **1** and **2** have been computer simulated,[8] and the rate constants (k) and the free enthalpies of activation ($\Delta G^\ddagger$) have been obtained from a comparison of the experimental and computer-simulated spectra. For **2**: $k = 0.16 \pm 0.02 \times 10^{10}$ s^{-1} at +43 °C ($\Delta G^\ddagger$ = 5.2 ± 0.2 kcal mol^{-1}); $k = 0.4 \pm 0.3 \times 10^8$ s^{-1} at −77 °C ($\Delta G^\ddagger$ = 4.5 ± 0.3 kcal mol^{-1}); $k = 0.25 \pm 0.10 \times 10^6$ s^{-1} at −109 °C ($\Delta G^\ddagger$ = 5.4 ± 0.2 kcal mol^{-1}).[9] For **1**: $k = 0.7 \pm 0.4 \times 10^8$ s^{-1} at −76 °C ($\Delta G^\ddagger$ = 4.3 ± 0.3 kcal mol^{-1}); $k = 2.2 \pm 0.5$ 10^6 s^{-1} at −114 °C ($\Delta G^\ddagger$ = 4.5 ± 0.2 kcal mol^{-1}). Extrapolation of the values found for **1** (at −76 and −114 °C) and **2** (at −77 and −109 °C)[9] to −165 °C leads to $\Delta G^\ddagger$ = 4.8 ± 0.9 kcal mol^{-1} for **1** and $\Delta G^\ddagger$ = 7.0 ± 1.2 kcal mol^{-1} for **2**. The average value for $\Delta G^\ddagger$ at −165 °C (for **1** and **2**) of ~6 kcal mol^{-1} is almost the same as that for 4,4,5,6,6-pentadeuteriocycloheptene[5a] (5.0 ± 0.3 kcal mol^{-1} at −165 °C).

The two cycloheptene rings in **3** move independently of each other. This can be concluded from the ESR spectrum of **3** at −50 °C, at which temperature the process is in the intermediate exchange. The five unbroadened signals that remain visible in the intermediate exchange are those for which the total z component of the nuclear spin angular momenta of the methylene protons equal −4, −2, 0, +2, and +4. It is known[10] that the expected intensity distribution for these unbroadened signals is different for a synchronized ring inversion (**3a** ⇄ **3a′** and **3b** ⇄ **3b′**) and a nonsynchronized ring inversion (Scheme II). The expected intensity distribution is 1:16:36:16:1 for a synchronized and 1:8:18:8:1 for a nonsynchronized ring movement.[10] The experimentally observed intensity distribution is 1:7:17:7:1, which proves the nonsynchronized nature of the ring inversions in **3**. The process is at −110 °C not yet completely frozen out, and the ESR signals are therefore not completely sharp. Because of this fact, and considering that

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[7] This dependency is expressed in the well-known Heller–McConnell equation: $a_\beta^H = B_0 + B_1 \langle \cos^2 \theta \rangle$. Heller, C.; McConnell, H. J. *Chem. Phys.* **1960**, *32*, 1535.

[8] Heinzer, J. *QCPE* **1973**, *No. 209.*

[9] For the measurement at +43 °C, $Cl_2HCCHCl_2$ has been used as solvent. All other ESR spectra of **1**, **2**, and **3** have been recorded in CH_2Cl_2. $\Delta G^\ddagger$ and k can be strongly solvent dependent,[13] and thus values determined in different solvents cannot be used for a plot of $\Delta G^\ddagger$ vs. T.

[10] Pijpers, F. W.; Arick, M. R.; Hendriks, B. M. P.; de Boer, E. *Mol. Phys.* **1971**, *22*, 781.

[11] The broad ESR signal underneath the sharp signals is caused by the corresponding dimeric radical cation (analogous to the case of the cyclobutadiene radical cation **3**[15]).

[12] The simulated spectrum at −109 °C shows more fine structure than the corresponding experimental spectrum. This is caused by the fact that in the simulation the γ-protons are not allowed to become exchange-broadened. All γ-protons are taken equivalent, on account of the fact that the limiting values for the two types of γ-protons are unknown. In principle these values can be obtained from the spectrum provided that the ring inversion is completely frozen out, which is not yet the case at −109 °C. The approach of taking all γ-protons equivalent breaks down at low temperatures, as has been noticed before.[10]

[13] For a striking example of the influence of the solvent on the rate of a conformational change, see: Jonkman, L.; Kommandeur, J. *Chem. Phys. Lett.* **1970**, *5*, 579.

[14] The axial β-protons have the larger hfs because the $\langle \cos^2 \theta \rangle$ term in the Heller–McConnell equation[7] is larger for the axial than for the equatorial orientation. Therefore, H^2 in **1a** (**2a**) and H^1 in **1b** (**2b**) have the larger β-hfs and H^1 in **1a** (**2a**) and H^2 in **1b** (**2b**) the smaller β-hfs.

[15] Kok, D. M. Ph.D. Thesis, University of Groningen, 1981; Chapter 4.

the difference in hfs's between **3a** and **3b** is unknown, it is not possible to conclude whether at low temperature only **3a**, **3b**, or a mixture of both is present.

It seems possible that cyclobutadiene radical cations substituted with oligomethylene chains of a different length or with additional substituents on the pentamethylene chain(s) can be studied in a similar way.

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Anodic α-Methoxylation of N-Carbomethoxylated or N-Acylated α-Amino Acid Esters and α-Amino β-Lactams[1]

Summary: A new practical method of introducing a methoxyl group to the α-position of α-amino acid derivatives and α-amino β-lactams has been exploited by utilizing indirect electrochemical oxidation as a key reaction.

Sir: Since the discovery of 7α-methoxycephalosporins, potent antibiotics against Gram-negative bacteria,[2] much effort has been devoted to the development of new methods for introducing a methoxyl group to the 6-position of penicillins[3] or the 7-position of cephalosporins[4] and 1-oxacephems.[5] In general, the α-methoxylation of these β-lactams is the same type of reaction as the α-methoxylation[6] of α-amino acid esters. The α-methoxylated α-amino acids are also versatile reagents for amidoalkylation[6a–e] and useful intermediates leading to α,β-unsaturated α-amino acids.[6e–g]

Table I. Anodic α-Methoxylation[a] of **1b–e**

run	**1**	supporting electrolyte MX (equiv)[b]	electricity passed, F/mol	yield of **2** (%)[c]
1	**1b**	NaCl (0.1)	10	**2b** (89)[d]
2	**1b**	NaCl (0.25)	10	**2b** (80)[e]
3	**1b**	NaCl (0.5)	10	**2b** (83)
4	**1b**	NaCl (1.0)	10	**2b** (70)[f]
5	**1b**	LiCl (0.5)	10	**2b** (76)
6	**1b**	KCl (0.5)	10	**2b** (78)
7	**1b**	Et_4NCl (0.5)	10	**2b** (90)
8	**1b**	NaBr (0.5)	10	**2b** (47)
9	**1b**	KI (0.5)	10	**2b** (0)[g]
10	**1b**	Et_4NOTs (0.1)	10	**2b** (6)[g]
11	**1b**	NaOAc (0.5)	10	**2b** (0)[g]
12	**1c**	NaCl (0.5)	10	**2c** (90)
13	**1d**	NaCl (0.5)	10	**2d** (91)
14	**1e**	NaCl (0.5)	31	**2e** (62)

[a] Platinum plates were used as electrodes. [b] The ratio of MX to 1. [c] Constant current; 0.3 A. [d] Constant current; 0.1 A. [e] Constant current; 0.2 A. [f] Constant current; 0.5 A. [g] Most of starting compound was recovered.

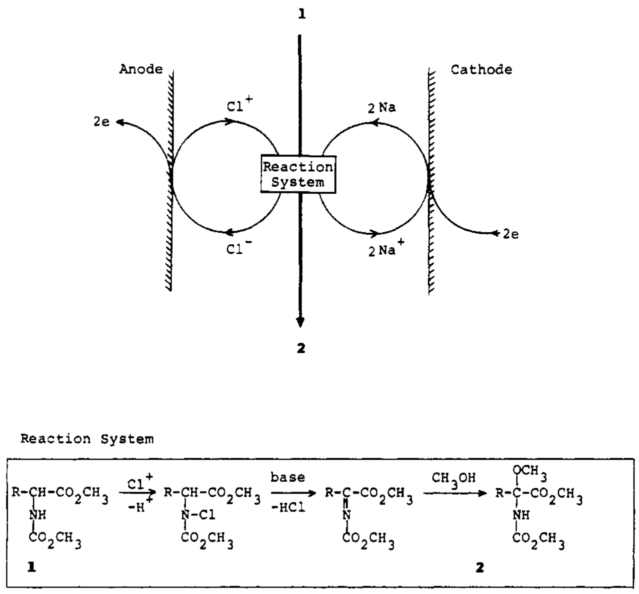
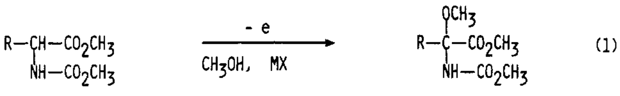


Figure 1. Schematic representation of the indirect α-methoxylation.

Thus, we have studied a new useful anodic α-methoxylation of α-amino acid derivatives **1** (eq 1), which is



$$R\text{—}\underset{\displaystyle NH\text{—}CO_2CH_3}{CH}\text{—}CO_2CH_3 \xrightarrow[CH_3OH,\ MX]{-\,e} R\text{—}\underset{\displaystyle NH\text{—}CO_2CH_3}{\overset{\displaystyle OCH_3}{C}}\text{—}CO_2CH_3 \qquad (1)$$

1 a-e
a : R = H
b : R = CH_3
c : R = CH_2Ph
d : R = i-Pr
e : R = Ph

MX : alkali metal halide

2 a-e

applicable to the methoxylation of β-lactams. The yields of **2b** obtained under several conditions are summarized as runs 1–11 of Table I,[7] which also shows the results of the α-methoxylation of **1c–e** (runs 12–14). Also, it was found that this anodic α-methoxylation successfully worked in the α-methoxylation of lactams **3a,b** without cleavage of the β-lactam ring (eq 2).[7]

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