ORGANIC LETTERS

2007
Vol. 9, No. 9
1671−1674

Experimental/Computational Study of the Electrochemical Oxidation of Cyclooctatetraene in Protic Media. Solvent Effects

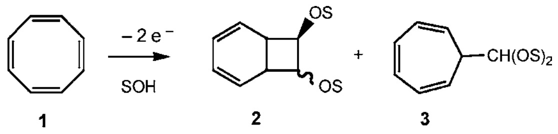
Grayson Connors, Xin Wu, and Albert J. Fry*

Chemistry Department, Wesleyan University, Middletown, Connecticut 06459

afry@wesleyan.edu

Received February 9, 2007

ABSTRACT

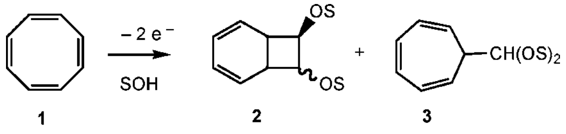


2:**3** = 70:30 in HOAc; **2**:**3** = 0:100 in MeOH

Electrochemical oxidation of cyclooctatetraene (COT) in methanol affords a ring-contracted acetal in high yield. Ring contraction is only a minor process in acetic acid. Ab initio computational methods were applied to understand and explain the effect of solvent. The computations show considerable differences between the thermodynamic and kinetic preferences for ring contraction vs bicyclo[4.2.0] product formation.

Recently there has been a resurgence of activity in the chemistry of cyclooctatetraene (COT) and its derivatives[1] and in annulenes generally.[1,2] One area which has attracted interest for many years is the electrochemical behavior of COT and its derivatives.[1c,d,3] The reductive electrochemical behavior of cyclooctatetraene (COT) (**1**) in particular has been the subject of many studies, and the general outlines of its cathodic behavior are well established.[4] The first electron-transfer step exhibits a rather low heterogeneous electron-transfer rate, associated with a change in molecular geometry from the tub-shaped COT to a planar anion radical. This step is followed by a fast second electron-transfer step at more negative potential to afford the planar COT dianion. In the course of a recent study of ion pairing effects on the electrochemical reduction of COT in tetrahydrofuran in the presence of a lithium ion,[5] our attention was drawn to the fact that the electrochemical oxidation of COT has received surprisingly little attention (Scheme 1). In fact, the only literature reference to anodic oxidation of COT is a 1967 study by Eberson et al., in which the preparative-scale

Scheme 1. Electrochemical Oxidation of Cyclooctatetraene in Protic Media



a, OS = OAc ; **b**, OS = OMe

---

[1] (a) Spitler, E. L.; Johnson, C. A., II; Haley, M. M. *Chem. Rev.* **2006**, *106*, 5344. (b) Kiesewetter, M. K.; Reiter, R. C.; Stevenson, C. D. *J. Am. Chem. Soc.* **2005**, *127*, 1118. (c) Shaw, M. J.; Hyde, J.; White, C.; Geiger, W. E. *Organometallics* **2004**, *23*, 2205. (d) Geiger, W. E. *J. Am. Chem. Soc.* **1993**, *115*, 2314. (e) Paquette, L. A. *Acc. Chem. Res.* **1993**, *26*, 57.

[2] (a) Moll, J. F.; Pemberton, R. P.; Gutierrez, M. G.; Castro, C.; Karney, W. L. *J. Am. Chem. Soc.* **2007**, *129*, 274. (b) Caramori, G. F.; de Oliveira, K. T.; Galembeck, S. E.; Bultinck, P.; Constantino, M. G. *J. Org. Chem.* **2007**, *72*, 76. (c) Pemberton, R. P.; McShane, C. M.; Castro, C.; Karney, W. L. *J. Am. Chem. Soc.* **2006**, *128*, 16692. (d) Ajami, D.; Hess, K.; Koehler, F.; Naether, C.; Oeckler, O.; Simon, A.; Yamamoto, C.; Okamoto, Y.; Herges, R. *Chem.−Eur. J.* **2006**, *12*, 5434. (e) Rzepa, H. S. *Chem. Rev.* **2005**, *105*, 3697.

[3] Fry, A. J. In *Topics in Organic Electrochemistry*; Fry, A. J., Britton, W. E., Eds.; Plenum Press: New York, 1986; pp 1−34.

[4] (a) Fry, A. J.; Hutchins, C. S.; Chung, L. L. *J. Am. Chem. Soc.* **1975**, *97*, 591. (b) Allendoerfer, R. D.; Rieger, P. H. *J. Am. Chem. Soc.* **1965**, *87*, 2336. (c) Huebert, B. J.; Smith, D. E. *J. Electroanal. Chem.* **1971**, *31*, 333.

[5] Fry, A. J. *Electroanalysis* **2006**, *18*, 391.

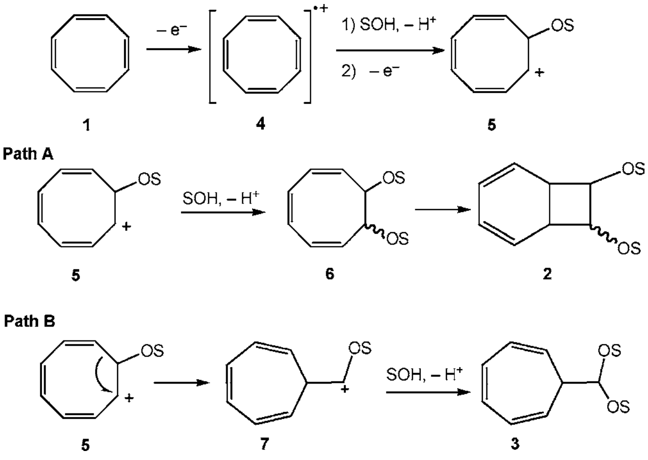
10.1021/ol070349s CCC: $37.00

oxidation of COT was carried out in acetic acid.[6] The products at a carbon anode were found to be a 70:30 mixture of 5,6-diacetoxybicyclo[4.2.0]octadiene (**2a**, as a mixture of diastereomers) and cycloheptatrienyl acylal (**3a**). The anodic processes leading to **2a** and **3a** are clearly complex. We felt therefore that a reexamination of the anodic behavior of **1** was in order. We chose methanol as a neutral solvent for this purpose. Because methanol is less acidic than acetic acid, the occurrence of acid-promoted side reactions was considered less likely.

The anodic oxidation of COT was carried out at constant current at a graphite carbon cloth anode in methanol containing lithium tetrafluoroborate as the supporting electrolyte.[7] The cathode was a platinum mesh electrode. The electrolysis afforded a single major product in 95% yield. ^{1}H and COSY NMR spectra (see Supporting Information), together with the mass spectral fragmentation pattern, clearly established the product as the known dimethyl acetal of 7-formylcycloheptatriene (**3b**).[8] A few other substances were formed in 1% yield or less in the reaction, but none exhibited a mass spectrum suggestive of **2b**. (One was phenylacetaldehyde, presumably produced by the presence of a small amount of adventitious water in the electrolysis medium).[8]

The probable pathways for production of **2** and **3** are shown in Scheme 2. The first intermediate is undoubtedly **4**, the cation radical of **1**. Attack by solvent SOH upon **4**, followed by loss of a second electron, should afford the key intermediate, cation **5**. There is a great deal of literature precedent on the anodic oxidation of alkenes for this conversion of **1** to **5**.[9,10] Attack of solvent on **5** to afford the cyclooctatriene **6** and subsequent orbital symmetry allowed disrotatory electrocyclization would lead to the bicyclic product **2** (path A). On the other hand, a 1,2 shift in **5** would afford first the rearranged cation **7**, followed by attack by solvent to afford **3** (path B).

Scheme 2. Mechanism of Electrochemical Oxidation of Cyclooctatetraene in Protic Media



The failure to produce **2b** in methanol presents an interesting mechanistic problem. This might be accounted for by a greater driving force for rearrangement of cation **5b** to **7b** compared to the **5a** to **7a** conversion because of the greater electronegativity of the acetoxy group in **7a** compared to methoxy and/or the higher polarity of methanol, allowing **5b** a longer lifetime in which to rearrange. On the other hand, the greater nucleophilicity of methanol ought to favor formation of **6b**. We have examined this question computationally.

Computational Results. The most likely geometry for each structure was first established by a global minimum energy conformational search using the GMMX subroutine in PCMODEL 9.0.[11] The energies of the neutral species **2a**,**b**, **3a**,**b**, and **6a**,**b** and cations **5a**,**b** and **7a**,**b** were then computed at the Hartree−Fock 6-31G* level,[12] both for the unsolvated species and with solvation included, using the PCM (polarized continuum method) of Tomasi.[13] The computations (Table 1) indicate that rearrangement of the eight-membered ring cation **5b** to the corresponding seven-membered ring species **7b** is exothermic by 1.8 kcal/mol in the absence of solvent and by 0.9 kcal/mol in methanol. The transition-state energy for the rearrangement of **5b** to **7b**, respectively, was computed by the synchronous transit-guided quasi-Newton method of Schlegel,[14] as implemented (QST2) in the Gaussian 03 suite of programs.[12] The activation energy for rearrangement of **5b** is computed to be 7.0 kcal/mol in methanol. The low value of the activation energy is unsurprising because the structures of the two ions are very similar: like its chloro analogue,[15] **5b** is a nonplanar 8-homotropylium ion, and therefore the ends of its heptatrienylic system are held closely together (Figure 1). Conversion of **5b** to **7b** requires a simple shift of an electron pair with relatively little motion of the other atoms. Conversion of the neutral dimethoxycyclooctatriene **6b** to acetal **3b** is computed to be exothermic by 14.2 kcal/mol. Electrocyclization of **6b** to **2b** is exothermic by 5.4 kcal/mol. Acetal **3b** is the most stable of the three neutral dimethoxy substances in this system, and the kinetic barrier to rearrangement of **5b** to **7b** is quite low. Formation of acetal **3b** is therefore favored both kinetically and thermodynamically in methanol.

In dramatic contrast, the conversion of **5a** to **7a** is computed to be *endothermic* by 15.0 kcal in acetic acid, with an activation energy of 15.3 kcal/mol in that solvent. Acylal **3a** is however similar to **3b** in that it is the most stable of the three neutral diacetoxy species; it is more stable than

---

(6) Eberson, L.; Nyberg, K.; Finkelstein, M.; Peterson, R. C.; Ross, S. D. *J. Org. Chem.* **1967**, *32*, 16.

(7) COT was found to exhibit a single irreversible voltammetric wave at +1.50 V vs SCE.

(8) Cope, A. C.; Nelson, N. A.; Smith, D. S. *J. Am. Chem. Soc.* **1954**, *76*, 1100.

(9) Halas, S.; Okyne, K.; Fry, A. J. *Electrochim. Acta* **2003**, *48*, 1837.

(10) Steckhan, E.; Schafer, H. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 472.

(11) Serena Software, Bloominton, IN.

(12) Frisch, M. J. et al. *Gaussian 03*, revision B. 04; Gaussian, Inc.: Pittsburgh, PA, 2003. Full references for Gaussian programs are provided in the Supporting Information.

(13) (a) Tomasi, J.; Persico, M. *Chem. Rev.* **1994**, *94*, 2027. (b) Tomasi, J.; Mennucci, B.; Cammi, R. *Chem. Rev.* **2005**, *105*, 716.

(14) Peng, C.; Schlegel, H. B. *Isr. J. Chem.* **1994**, *33*, 449.

(15) (a) Huisgen, R.; Gasteiger, J. *Tetrahedron Lett.* **1972**, *13*, 3661. (b) Gasteiger, J.; Huisgen, R. *Tetrahedron Lett.* **1972**, *13*, 3665.

Table 1. Computed Energies of Reaction Intermediates in the Anodic Oxidation of Cyclooctatetraene

entry	species	energy (Hartrees)[a]	relative energy[b] (kcal/mol)
	cations (solvated)[c]		
1	**5a**	−534.5978532	0
2	**7a**	−534.5739889	+15.0
3	**5a** to **7a** transition state	−534.5734324	+15.3
4	**5a** to **7a** activation energy	–	15.3
5	**5b**	−421.8469985	+0.9
6	**7b**	−421.8484060	0
7	**5b** to **7b** transition state	−421.8358114	+7.9
8	**5b** to **7b** activation energy	–	7.0
	cations (unsolvated)[d]		
9	**5a**	−534.5325605	0
10	**7a**	−534.5145553	+11.3
11	**5a** to **7a** transition state	−534.5132481	+12.1
12	**5a** to **7a** activation energy	–	12.1
13	**5b**	−421.7661886	+1.8
14	**7b**	−421.7690091	0
15	**5b** to **7b** transition state	−421.7571821	+7.4
16	**5b** to **7b** activation energy	–	+5.65
	neutral species (solvated)[c]		
17	**2a**	−762.0197786	+ 2.5
18	**3a**	−762.0237641	0
19	**6a**	−762.0035744	+15.9
20	**2b**	−536.4773009	+ 9.0
21	**3b**	−536.4915217	0
22	**6b**	−536.4689008	+14.2
	neutral species (unsolvated)[d]		
23	**2a**	−762.0081691	+3. 0
24	**3a**	−762.0033567	0
25	**6a**	−761.9852704	+14.4
26	**2b**	−536.4684373	+ 8.5
27	**3b**	−536.4819731	0
28	**6b**	−536.4593783	+14.2

[a] 1 Hartree = 627.5 kcal/mol. [b] PCM solvation energy is included. [c] Energies of (solvated) structures relative to the lowest-energy species in each set, for cations and again for neutral species. [d] Same as previous but for unsolvated species.

the corresponding cyclooctatriene **6a** by 15.9 kcal/mol and more stable than bicyclic **2a** by 2.5 kcal/mol. Electrocyclization of initially formed cyclooctatriene **6a** to **2a** is highly exothermic (13.4 kcal/mol). We conclude that formation of **2a** as the major product, via **6a**, in acetic acid[3] is the result of kinetic control. The principal difference for the product difference between the two solvents is the much higher activation energy for rearrangement of **5a** compared to **5b**. There is a good literature precedent in a different system for the failure of an α-acetoxy carbocation to rearrange even though the corresponding α-methoxy species does rearrange: electrochemical oxidation of stilbene in acetic acid affords unrearranged 1,2-diacetate,[16] whereas oxidation in methanol affords 36% of a rearranged dimethoxy compound along with 64% of an unrearranged 1,2-dimethoxy compound.[17]

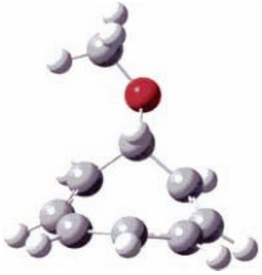


Figure 1. Computed structure of cation **5b**.

The activation energy for rearrangement of **5b** is computed to be 5.65 kcal/mol in the absence of solvent, whereas it is 7.0 kcal/mol in methanol. Similarly, the conversion of **5a** to **7a** is computed to be endothermic by 11.3 kcal in the absence of solvent and by 15.0 kcal in acetic acid, with an activation energy of 15.3 kcal/mol in that solvent. Our initial interpretation of the higher activation energies in the presence of solvent was that this was because the charge is more highly dispersed in the transition state, which would therefore demand less solvation than the starting and final cations. This does not seem to be the case, however. This can be seen by examining the solvation energies (in kcal/mol) of the various species, i.e., the difference in energy between the solvated and unsolvated forms (Table 2). For the conversion of **5a** to **7a**, the Hammond postulate predicts that the transition state for this endothermic process should resemble the product ion, and indeed the solvation energies of the transition state and **7a** are very similar. However, conversion of **5b** to **7b** is

Table 2. Computed Solvation Energies of Reaction Intermediates in the Anodic Oxidation of Cyclooctatetraene in Protic Solvents

entry	species	solvation energy[a] (kcal/mol)
	cations	
1	**5a**	41.0
2	**7a**	37.3
3	**5a** to **7a** transition state	37.8
4	**5b**	50.7
5	**7b**	49.8
6	**5b** to **7b** transition state	49.3
	neutrals	
7	**2a**	10.3
8	**3a**	12.8
9	**6a**	11.5
10	**2b**	5.6
11	**3b**	6.0
12	**6b**	6.0

[a] Difference in energy between solvated and unsolvated species, computed from Table 1 using the factor 1 Hartree = 627.5 kcal/mol.

---

(16) Mango, F. D.; Bonner, W. A. *J. Org. Chem.* **1964**, *29*, 1367.

(17) Halas, S. M.; Okyne, K.; Fry, A. J. *Electrochim. Acta* **2003**, *48*, 1837.

almost thermoneutral, suggesting that the transition state is roughly midway between the two structures, and in fact, the solvation energies of **5b**, **7b**, and the transition state connecting them are identical within 1 kcal/mol.

Failure to obtain substituted cyclooctatrienes **6a** or **6b** from these reactions is not surprising. Huisgen[15] and Kaupp[18] have shown that, except for the parent substance, 7,8-disubstituted cyclooctatrienes generally convert rapidly and exothermically to the corresponding bicyclo[4.2.0]octadienes.

As noted above, the first intermediate produced in the electrochemical conversion of COT must be cation radical **4**. Earlier, UMP2 (unrestricted second-order Møller−Plesset) and density functional UB3LYP/6-31G* computations[19] both showed that **4** retains the geometry of COT, but as a shallower tub (folding angle[19] $\omega = 42.3°$; for neutral COT, $\phi = 58.3°$). The computations also demonstrate that **4** retains other vestiges of the neutral COT structure: like **1**, the bond lengths in **4** alternate (between 1.44 and 1.37 Å). In contrast, the $6e^-$ Hückel dication is computed to be planar with all bond lengths equal. Each CH group of the cation radical carries a charge of $+0.125$, i.e., one-eighth of the total (and an equal share of the unpaired electron density), indicating that even though the ring is nonplanar there is sufficient overlap around the ring to permit delocalization over the whole system.[20]

Summary. Anodic oxidation of cyclooctatetraene in acetic acid affords a bicyclo[4.2.0]octadiene as the major product. Oxidation in methanol affords a cycloheptatrienyl acetal as the only product. An extended series of ab initio computations reveal the reasons for this difference. The initial intermediate in each case is an 8-substituted cyclooctatrienyl cation. Ring contraction of the 8-acetoxy ion exhibits a high activation barrier, whereas the barrier to rearrangement of the 8-methoxy ion is much lower.

Acknowledgment. Financial support was provided by the National Science Foundation (Grant #CHE-0411699) and by Wesleyan University.

Supporting Information Available: Experimental procedures, characterization data, and information on the computational procedure. This material is available free of charge via the Internet at http://pubs.acs.org.

OL070349S

---

(18) Kaupp, G.; Jostkleigrewe, E. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 779.

(19) Bally, T.; Truttmann, L.; Williams, F.; Dai, S. *J. Am. Chem. Soc.* **1995**, *117*, 7916.

(20) Havenith, R. W. A.; Fowler, P. W.; Jenneskens, L. W. *Org. Lett.* **2006**, *8*, 1255.