Scheme I

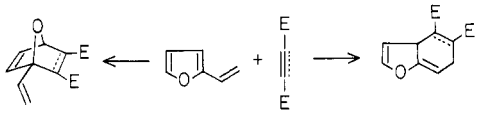


Table I. Diels–Alder Reactions of Vinylfurans (CH_2Cl_2, 15 kbar, 30 °C)[a]

vinylfuran	dienophile	time, h	products (% yield)[b]
1a	2	6[c]	4 (33)
1b	2	6[c]	5 (28)
1c	2	6	6 (20), 7 (25)
1c	2[d]	6	6 (16), 7 (36)
1a	3	24	8[e] (5), 9 (3)
1b	3	8	10 (48)[f]
1c	3	16	12[e] + 13[e] (50)[g]

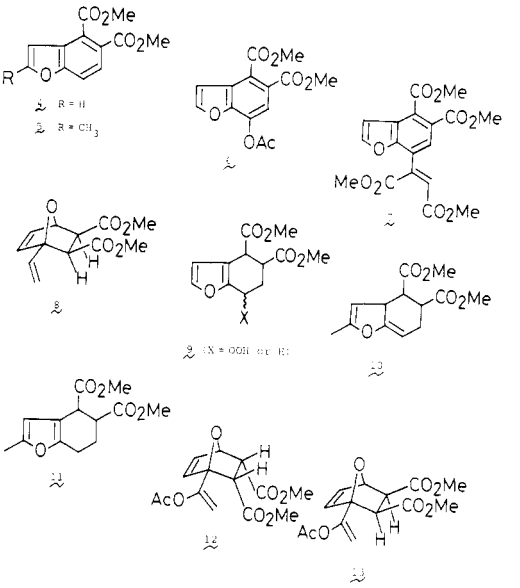
[a] All the reactions were performed at a concentration of 3 M for the reactants. The structures of all adducts were confirmed by elemental analysis and NMR, IR, and UV spectra. [b] Isolated yields after short column chromatography on neutral alumina or rapid preparative TLC on silica gel unless otherwise noted. [c] The yields could not be improved even after reaction for 24 h. [d] The molar ratio of 1c to 2 is 1:2. [e] These adducts were highly unstable at room temperature, so the elemental analyses were performed after hydrogenation with 10% Pd/C in AcOEt. [f] The yield estimated by ^{1}H NMR was 77%; see text. [g] The yield by ^{1}H NMR.

atives derived from the reaction of the furan ring diene with the dienophile.[8] The reaction of **1c** with **2** gave the 1:2 adduct **7** in addition. The formation of a similar product has been reported in the reaction of **1a** with **2** at an elevated temperature[3] and is explained by "ene" addition of a second molecule of **2** to the adduct and subsequent elimination of acetic acid. As expected, the yield of **7** was raised when the molar ratio of **2** to **1c** was increased.

In the case of the reactions with **3**, the adducts were first formed at high pressure.[9] And a remarkable difference of the reactivity between each vinylfuran was recognized. **1a** afforded the adducts **8** and **9** in comparable amounts, which represented two alternative modes of the reaction. The stereochemistry of **8** was determined as having an exo configuration from the ^{1}H NMR analysis.[7] **9** (X = OOH) is probably formed by "ene" addition with atmospheric oxygen to the initially formed adduct. Anal. Calcd for $C_{12}H_{14}O_7$: C, 53.33; H, 5.22. Found: C, 53.47; H, 5.26. **1b** gave almost a single product as revealed by the ^{1}H NMR spectrum of the crude reaction mixture and from which **10** could be successfully crystallized in 48% yield as an ether-insoluble substance.[10] Expectedly, **10** was extremely unstable and spontaneously isomerized to **11** on standing at room temperature. **1c** afforded cleanly the endo and exo adducts **12** and **13** in an approximate ratio of 2:1. No adducts derived from the reaction of the conjugated diene system containing the exocyclic double bond were obtained. Thus, the experiments demonstrated that the diene system involving the exocyclic double bond in **1b** was highly reactive, in contrast to **1c**. These differences may be attributed to the inductive and resonance effects of the substituents; i.e., the methyl group is electron donating ($\mathcal{F}$ = –0.052 and $\mathcal{R}$ = –0.141) and the acetoxy group is electron withdrawing ($\mathcal{F}$ = 0.679 and $\mathcal{R}$ = –0.071).[11]

(8) Unidentified complex byproducts were also formed.
(9) No detectable amounts of the adduct were obtained in the reaction between **1a** and **3** at reflux in toluene for 20 h.
(10) Purification by chromatography resulted in a complete decomposition.

Chart I



All attempted reactions between vinylfurans (**1**) and other dienophiles such as methyl acrylate and α-chloroacrylonitrile under same conditions were unsuccessful due to considerable polymerization. We are continuing our investigation to elucidate the scope of these reactions.

Acknowledgment. We thank Professor T. Tokoroyama, Osaka City University, for his helpful discussion and continuous encouragement.

Registry No. **1a**, 1487-18-9; **1b**, 10504-13-9; **1c**, 41019-60-7; **2**, 762-42-5; **3**, 624-48-6; **4**, 19665-37-3; **5**, 79816-77-6; **6**, 79816-78-7; **7**, 79816-79-8; **8**, 79816-80-1; **8** (tetrahydro), 79816-81-2; **9**, 79816-82-3; **10**, 79816-83-4; **11**, 79816-84-5; **12**, 79816-85-6; **13**, 79816-86-7.

(11) Swain, C. G.; Lupton, E. C., Jr. *J. Am. Chem. Soc.* **1968**, *90*, 4328.

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Electrochemical Reductive Cyclizations to the β-Position of Cyclic α,β-Unsaturated Ketones. Formation of Fused Ring Systems[1]

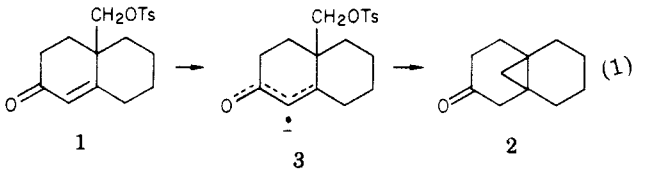
Summary: The electrochemical reductive cyclization of certain conjugated cyclohexenone sulfonate esters has been shown to be a synthetically useful method for the preparation of bicyclo[4.3.0]nonan-3-ones and bicyclo[4.1.0]-heptan-3-ones.

Sir: The recent report of a mechanistic study of the electrochemical reduction of **1**[2] has prompted us to report our synthetically useful findings on the alkylation of the β-position of α,β-unsaturated ketones by electrochemical methods. In 1965, Stork and co-workers demonstrated[3]

(1) Taken in part from: Rasmy, O. M.S. Thesis, University of Minnesota, 1978.
(2) Smith, R. A. J.; Hannah, D. J. *Tetrahedron Lett.* **1980**, *21*, 1081.

0022-3263/81/1946-5455$01.25/0

that the reduction of 1 (eq 1) with lithium in liquid ammonia gave 45% of **2**, presumably via the intramolecular displacement of the tosylate anion by the radical anion of **3**. This cyclization has been of interest to many groups[1-6] and has been accomplished with dimethyllithium cuprate[5] and electrochemically.[1,2] We now report that such reductive cyclizations are general reactions which can often be accomplished in synthetically significant yields.

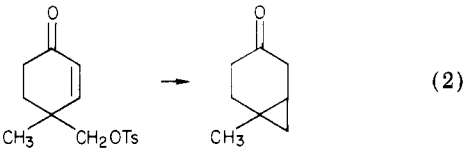


1 3 2

Preliminary studies in our laboratory[1] have shown that 1 could be readily reduced at −1.75 V (vs. SCE) in dry dimethylformamide containing either tetra-*n*-butylammonium perchlorate or tetra-*n*-butylammonium tetrafluoroborate (0.10 M) as the supporting electrolyte to give a 98% yield of a 99:1 mixture of **2** and **4**.[7,8] The current efficiency for a series of runs varied from 70% to 80% for a two-electron reduction process.[9]

In order to explore the versatility of this electrochemical reductive cyclization process, we applied the reaction conditions outlined above to two relatively simple α,β-unsaturated cyclohexenone systems. Two questions required answers: (1) was the rigidity of the decalin skeleton of **1** a requirement for efficient reductive cyclization, and (2) could rings other than cyclopropanes be efficiently formed in such intramolecular displacements by radical anions?

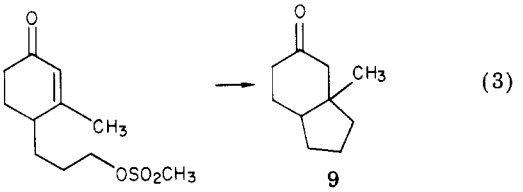
The first question was readily answered by the controlled-potential electrochemical reduction of 1-oxo-4-methyl-4-(hydroxymethyl)cyclohex-2-enyl *p*-toluenesulfonate (**5**)[10] under the conditions described above (eq 2), except for the use of a controlled potential of −2.15 V



5

(vs. SCE). The complete disappearance of **5** was accompanied by the formation of **6** as the only isolable product[11] in 80% yield. Thus, it was apparent that the rigidity of the decalin system was not a requirement for efficient cyclization.

In order to determine whether five-membered rings could be formed by our electrochemical reductive cyclizations, we reduced **7**[12] at −2.20 (vs. SCE) to obtain an 82% yield of 1-methyl-*cis*-bicyclo[4.3.0]nonan-3-one (**9**, eq 3).



7 9

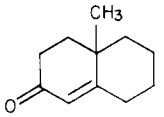
While the reduction of **7** was relatively clean, it did produce 5% of 3-methyl-4-*n*-propylcyclohex-2-en-1-one as a side product. The relatively clean formation of **9** indicates that the electrochemical reductive cyclization process described above may have a broad range of applications. Particular attention should be focused on the very acceptable yield of **9**. This can be contrasted with the less than 2% yield for five-membered ring formation observed by Scheffold and co-workers for a mechanistically different reductive cyclization process.

We are continuing to study the scope of this and other electrochemical reductive cyclization processes.

Acknowledgment. We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the Dow Chemical Co. Foundation for grants which supported this investigation.

Registry No. 1, 741-43-5; 2, 5689-11-2; 4, 826-56-2; 5, 24730-91-4; 6, 79839-54-6; 7, 79839-55-7; 8, 79839-56-8; 8 methanesulfonate,

(3) Stork, G.; Rosen, R.; Goldman, N.; Coombs, R. V.; Tsuji, J. *J. Am. Chem. Soc.* **1965**, *87*, 275.
(4) House, H. O.; Kinloch, E. F. *J. Org. Chem.* **1974**, *39*, 1173.
(5) Smith, R. A. J.; Hannah, D. J. *Tetrahedron* **1979**, *35*, 1183.
(6) A related electrochemical reductive cyclization, which requires catalysis by vitamin B_{12} or vitamin B_{12} model compounds, has been reported. It is believed that these cyclizations, which work well for the formation of six- and seven-membered rings but poorly for five-membered systems, involve the initial formation of an organometallic cobalt–carbon species, followed by Michael addition of this organometallic to the enone. A potential of −1.4 to −1.9 V (Ag/Ag^+) was required, and for some systems, reduction of the alkylating agent was the major reaction path. Scheffold, R.; Dike, M.; Dike, S.; Herold, T.; Walder, L. *J. Am. Chem. Soc.* **1980**, *102*, 3642.
(7) The formation of trace amounts of **4** is believed to result from the acid-catalyzed opening of **2** under the reaction conditions. Control experiments demonstrated that **2** was stable to potassium *tert*-butoxide in refluxing *tert*-butyl alcohol but that **2** was converted into **4** at room temperature in dimethylformamide in the presence of catalytic amounts of *p*-toluenesulfonic acid.[3]



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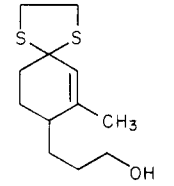
(8) It should be noted that the direct electrochemical reduction of *p*-toluenesulfonate esters has been extensively studied. These investigations have shown that reductive cleavage of the O–S bonds occurs to regenerate the starting alcohol. This rules out any mechanism for our transformations which would involve reduction of the *p*-toluenesulfonate ester to an alkyl anion followed by Michael addition to the α,β-unsaturated ketone.[6] For examples of the electrochemical reduction of sulfonate esters see: Horner, L.; Singer, R. *Chem. Ber.* **1968**, *101*, 3329. Yousefzadeh, P.; Mann, C. K. *J. Org. Chem.* **1968**, *33*, 2716.
(9) The anode was a platinum gauze which was separated from the cathode compartment by means of a medium-porosity sintered-glass frit. The saturated calomel electrode (SCE) was separated from the electrolysis solution with a fine-porosity sintered-glass frit and an agar–potassium chloride plug. The cathode was a magnetically stirred mercury pool. The current was measured with an in-series coulometer. The controlled potential power was supplied from a Model ASA 50-2 Tacussal potentiostat.
(10) Mukharji, P. C.; Sen Gupta, P. K.; Sambamurti, G. S. *Tetrahedron* **1969**, *25*, 5287.
(11) Satisfactory elemental analysis and/or exact mass molecular weights were obtained on all new compounds. In all cases spectral data were consistent with the assigned structure.
(12) The details of the synthesis of **7** will be provided in a full paper on electrochemical reductive cyclizations. The known alcohol **8**[13] was converted to the methanesulfonate, and the ketal protecting group was removed with mercuric-ion catalysis to give **7**.



8

(13) Johnson, W. S.; McCarry, B. E.; Markezich, R. L.; Boots, S. G. *J. Am. Chem. Soc.* **1980**, *102*, 352.

79839-57-9; 9, 19297-11-1; 3-methyl-4-propylcyclohex-2-en-1-one, 79839-58-0.

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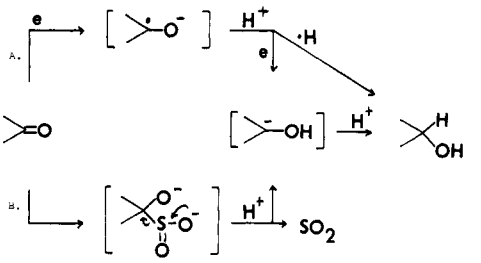
Mechanism of Sodium Dithionite Reduction of Aldehydes and Ketones

Summary: A reduction mechanism involving an α-hydroxy sulfinate intermediate has been suggested for the title reaction, on the basis of a radical ring-opening probe and the source of the hydrogen.

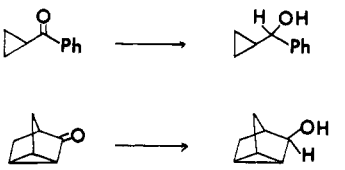
Sir: Sodium dithionite is a readily available, inexpensive reducing agent which is capable of reducing a variety of functional groups, e.g., nitro,[1] nitroso,[1] diazonium salts,[2] various pyridinium salts,[3] imines,[4] oximes,[4] aldehydes and ketones,[5] and α-halo ketones.[6] The reducing power of $Na_2S_2O_4$ is known to be generally enhanced in basic pH.[5,6] Sodium dithionite is a unique reducing agent in that it reduces a variety of pyridinium salts exclusively to the 1,4-dihydropyridine.[3,7] This reactivity has been explained in terms of the 1,4-addition of the SO_2 dianion equivalent to form a sulfinate intermediate, followed by the loss of SO_2.[8] More recently, however, Krapcho and Seidman studied the stereochemistry of the $Na_2S_2O_4$ reduction of cyclic ketones and found that cyclohexanones yielded mainly equatorial alcohols while bicyclic ketones gave primarily endo alcohols. On the basis of this stereochemical result, they suggested that reduction of the carbonyl group by $Na_2S_2O_4$ proceeded by an electron-transfer mechanism in a manner similar to that of Li–liquid NH_3–alcohol reduction of the ketones.[9]

In connection with our interest in the mechanism of the NADH-dependent alcohol dehydrogenase reactions utilizing the coenzyme recycling method with excess $Na_2S_2O_4$,[10] we have also examined the mechanistic possibilities of $Na_2S_2O_4$ reduction of carbonyl compounds. We have considered two basically distinct mechanisms. The first mechanism involves stepwise electron transfer from the reducing agent to the carbonyl group to form a ketyl radical intermediate. The ketyl radical then can either abstract a hydrogen atom from the medium, dimerize to pinacol, or undergo further reduction (Scheme I, pathway A). The second pathway involves a nucleophilic addition of the SO_2 dianion or its equivalent to the carbonyl group to form an intermediate α-hydroxy sulfinate which then loses SO_2 to give the carbanionic species (Scheme I, pathway B).[11]

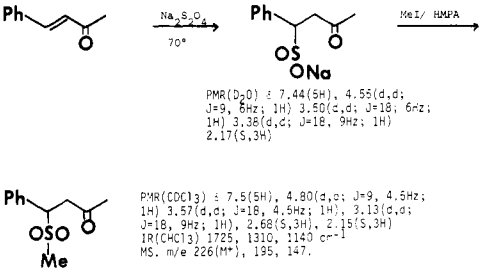
Scheme I



Scheme II



Scheme III



We have reasoned that if the ketyl radical were involved as a distinct intermediate as in dissolving-metal reductions,[13] the $Na_2S_2O_4$ reduction of cyclopropyl ketones should yield the ring-opened products. Thus, reductions of phenyl cyclopropyl ketone and nortricyclanone were carried out with $Na_2S_2O_4$ and $NaHCO_3$ in aqueous DMF solution at 120 °C under N_2.[9] The reduction products were found to be phenylcyclopropylcarbinol and *exo*-nortricyclyl alcohol, respectively, and careful product analyses by GC and NMR failed to reveal the presence of any ring-opened products (Scheme II).

Next, the source of the hydrogen in the reduced product was examined by running the $Na_2S_2O_4$ reduction of benzaldehyde in D_2O–DMF (1:1 by volume) at 105 °C in the presence of excess $NaHCO_3$. The benzyl alcohol product showed the following properties: mass spectrum, *m/e* (relative intensity) 108 (47.0), 109 (72.3), 110 (5.9), 111 (0.7); ^1H NMR ($CDCl_3$) δ 2.18 (br s, 1 H, OH), 4.60 (t, 1 H, J = 1.8 Hz, CHD), 7.31 (br s, 5 H, aromatic); ^{13}C NMR ($CDCl_3$) δ 64.91 (t, J = 22 Hz), 126.87, 127.54, 128.45, 140.68. These spectral data unambiguously indicate that the protic hydrogen of D_2O rather than the hydrogen atom of DMF was selectively incorporated into the benzylic position of the product.[14] The above results suggest that

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(4) Pojer, P. M. *Aust. J. Chem.* **1979**, *32*, 201.
(5) Minato, H.; Fujie, S.; Okuma, K.; Kobayashi, M. *Chem. Lett.* **1977**, 1091; De Vries, J. G.; van Bergen, T. J.; Kellogg, R. M. *Synthesis* **1977**, 246.
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(10) Taylor, K. E.; Jones, J. B. *J. Am. Chem. Soc.* **1976**, *98*, 5689.
(11) Although dithionite ions are known to dissociate reversibly to SO_2 anion radicals in aqueous solution,[12] the identity of the immediate reducing species is not yet clear. Electron exchange may be possible between the anion radicals to form SO_2 and the SO_2 dianion as reducing species.
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(13) Bellamy, A. J.; Campbell, E. A.; Hall, I. R. *J. Chem. Soc., Perkin Trans. 2* **1974**, 1347. Dauben, W. G.; Wolf, R. E. *J. Org. Chem.* **1970**, *35*, 374.

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