Stereoselective Electrochemical Reduction of Geminal Dihalocyclopropanes

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Received September 19, 1967

A recent study[1] of the stereochemistry of electrochemical reduction of optically active 1-bromo-2,2-diphenylcyclopropylcarboxylic acid and derivatives of the acid demonstrated a stereochemical spectrum ranging from 56% inversion to 38% retention of configuration. The data were interpreted in terms of a competition between protonation of a carbanion-electrode complex from the rear and protonation of the carbanion in solution. The present report demonstrates both stereochemical discrimination by the electrode between two possible sites for electroreduction and a solvent effect upon stereoselectivity of the reduction; the data are summarized in Table I.

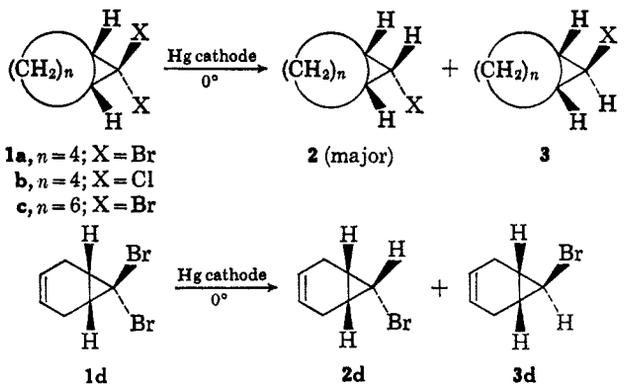
TABLE I
STEREOCHEMISTRY IN CONTROLLED POTENTIAL ELECTROLYSIS OF DIHALOCYCLOPROPANES

Expt	Substrate	Solvent	Relative % of products[c] 2	3
1	1a	100% DMF[a]	61	39
2	1a	96% DMF–4% H_2O	75	25
3	1a	100% CH_3OH	66	34
4	1a	95% CH_3OH–5% H_2O	73	27
5	1a	95% CH_3OH–5% HCl[b]	78	22
6	1a	90% CH_3OH–10% H_2O	84	16
7	1a	100% HOAc	80	20
8	1b	100% DMF	81	19
9	1b	96% DMF–4% H_2O	84	16
10	1b	100% CH_3OH	95	5
11	1b	95% CH_3OH–5% HCl	100	0
12	1b	33% HMPA[d]–67% EtOH	100	0
13	1c	100% CH_3OH	100	0
14	1c	95% CH_3OH–5% HCl	100	0
15	1d	100% CH_3OH	73	27
16	1d	90% CH_3OH–10% H_2O	91	9

[a] DMF = dimethylformamide. [b] 95% methanol–5% concentrated aqueous hydrochloric acid. [c] Precision of results ±3% after a minimum of five integrations per sample. [d] HMPA = hexamethyl phosphoramide.

The major product in all electrochemical reductions of geminal dihalocyclopropanes **1a–d** is the *cis* isomer **2**, and in solvents of higher water content the proportion of **2** is increased (*e.g.*, expt 1 and 2 or 3 and 4). Because of limited solubility of the geminal dihalides in more highly aqueous solvents, a wide range of solvent compositions was not investigated. In view of this and the fact that the solvents differ in a number of properties, including proton-donating ability and dielectric constant, detailed discussion of trends would be speculative. The synthetic advantage in increasing the stereoselectivity by use of a more highly aqueous solvent is apparent, however (*cf.* expt 15 and 16).

(1) R. Annino, R. E. Erickson, K. Michalovic, and B. McKay, *J. Amer. Chem. Soc.*, **88**, 4424 (1966).



1a, $n=4$; X = Br
b, $n=4$; X = Cl
c, $n=6$; X = Br

2 (major) **3**

1d **2d** **3d**

In terms of a mechanistic scheme previously advanced by Annino, *et al.*,[1] for electrochemical reductions of monohalocyclopropanes, there are two alternate explanations for the stereoselective formation of the *less stable* isomers **2a–d**. Either the "outside" halogen (*cis* to the two hydrogens at the ring junction) is reduced with retention of configuration, or the "inside" halogen is reduced, with inversion of configuration. We prefer the first course, for the following reasons. Assuming a substrate-electrode geometry in which the carbon–halogen bond is either parallel to the electrode surface or in which the bromine is nearest the electrode,[1,2] steric repulsions are far greater in the transition state for reduction of the "inside" halogen. If, then, reduction of the "outside" halogen is involved, it is necessary to postulate that the initially formed halocyclopropyl carbanion must diffuse into solution and be protonated before it can lose much, or any, of its configuration. Experiment 12 is consistent with this interpretation. Sternberg, *et al.*,[3] have demonstrated that the solvent system 33 mol % hexamethylphosphoramide (HMPA)–67% EtOH provides an effectively *aprotic* region at the electrode surface, presumably because of preferential adsorption of the highly polar HMPA. Even though the carbanion in expt 12 must move away from the electrode, therefore, to seek a proton, the stereochemistry of reduction is the same as in the other runs. Reduction of the "inner" halogen would require subsesequent isomerization to a less stable anion before protonation.

Experimental Section[4]

Dihalocyclopropanes (1a–d) were prepared according to published procedures.[5–7]

General.—Electrolyses were carried out in a divided cell of conventional design[1] equipped with platinum gauze anode and magnetically stirred mercury pool cathode and immersed in an ice bath. The reference electrode was a silver wire immersed in saturated aqueous potassium chloride in a Fisher Remote Reference Junction and positioned 1 mm from the cathode surface. Cathode potentials were controlled by a solid-state potentiostat to be described elsewhere.

(2) J. W. Sease, P. Chang, and J. L. Groth, *ibid.*, **86**, 3154 (1964).
(3) H. W. Sternberg, R. E. Markby, I. Wender, and D. M. Mohilner, *ibid.*, **89**, 186 (1967).
(4) Nmr spectra were measured on a Varian A-60A spectrometer. Solvents were reagent grade used without further purification. Vapor phase chromatography (vpc) was carried out on a Varian Aerograph Model P-3 instrument using 10% Carbowax on Fluoropak.
(5) D. Seyferth, J. M. Burlitch, and J. K. Heeren, *J. Org. Chem.*, **27**, 1491 (1962).
(6) W. von E. Doering and A. K. Hoffmann, *J. Amer. Chem. Soc.*, **76**, 6164 (1954).
(7) S. Winstein and J. Sonnenberg, *ibid.*, **83**, 3235 (1961).
(8) L. Meites in "Technique of Organic Chemistry," Vol. 1, A. Weissberger, Ed., Interscience Publishers, Inc., New York, N. Y., 1960, p 3297.

Electrolyses.—A 1 *M* solution of lithium chloride (50 ml) in the appropriate solvent was placed in the cathode compartment; the anolyte was identical, but also contained 5 ml of 95% hydrazine. The solvent was purified by pre-electrolysis in a nitrogen stream for 30 min at a cathode potential of −1.1 V *vs.* Ag–AgCl for **1a**, **c**, and **d**, and −2.0 V for **1b**. The dihalide (5–7 mmol) was added and electrolysis was allowed to proceed until current had decayed to background. The catholyte was poured into water, extracted with pentane, washed with water, and dried over magnesium sulfate. The pentane was carefully distilled; the **2**–**3** mixtures were analyzed by nmr spectroscopy by the method of Seyferth, *et al.*[9] Results generally agreed with results of independent vpc analyses. Yields of halocyclopropanes were in the range 80–90%.

Registry No.—**1a**, 15649-61-3; **1b**, 15649-62-4; **1c**, 15649-58-8; **1d**, 15834-79-4.

Acknowledgment.—Financial support by the Petroleum Research Fund is gratefully acknowledged.

(9) D. Seyferth, H. Yamazaki, and D. L. Alleston, *J. Org. Chem.*, **28**, 703 (1963).

Ethyl (Dimethylsulfuranylidene)acetate. II. Reactions with α,β-Unsaturated Esters in Ethanol Solutions

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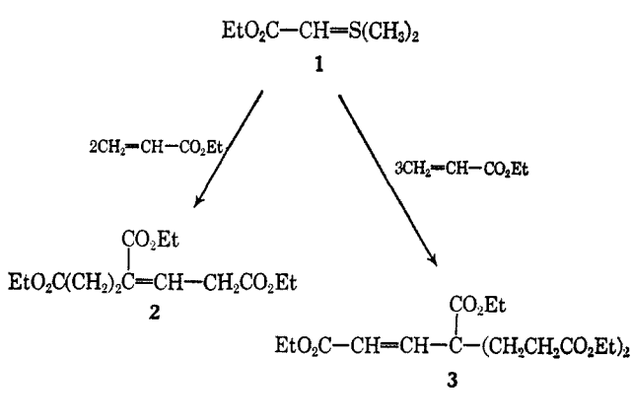
Received October 10, 1967

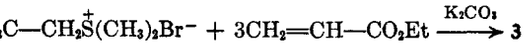
The general reaction between ethyl (dimethylsulfuranylidene)acetate (EDSA, **1**) and α,β-unsaturated compounds in aprotic solvents to produce substituted cyclopropanes was recently reported.[1] We now report that reaction of EDSA with certain α,β-unsaturated esters in ethanol solution leads not to cyclopropanes but rather to open-chain products of varying complexity.

Results and Discussion

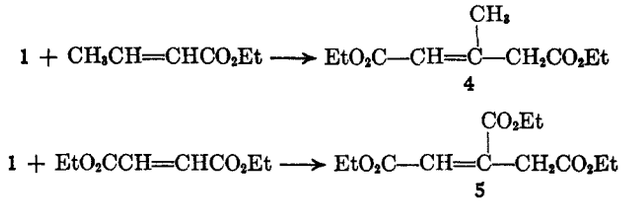
Reaction of EDSA with 4 molar equiv of ethyl acrylate in ethanol at 30–35° afforded a 69% yield (based on EDSA) of triethyl 2-pentene-1,3,5-tricarboxylate (**2**) along with a 20% yield of triethyl 3-(2-ethoxycarbonylethyl)-1-pentene-1,3,5-tricarboxylate (**3**). Tetraester



3 was subsequently prepared in 40% yield as the sole product obtained from ethyl acrylate and EDSA when the latter was generated slowly *in situ* by reaction of carbethoxymethyl dimethylsulfonium bromide with anhydrous potassium carbonate.



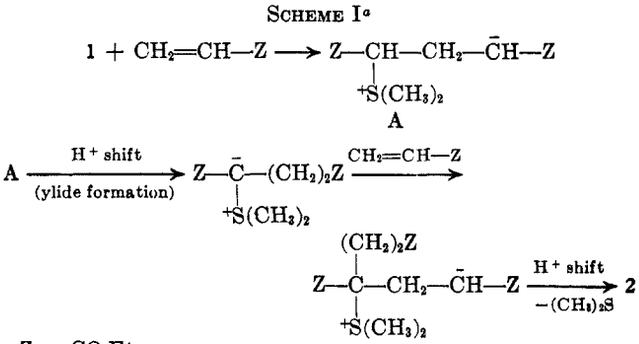
Ethyl crotonate and EDSA afforded a 75% yield of diethyl 3-methylglutaconate (**4**) as a 50:50 mixture of *cis–trans* isomers while EDSA and diethyl fumarate gave triethyl aconitate (**5**) in 87% yield as a 70:30 mixture of *trans–cis* isomers.



Compound **2** was identified by elemental and nmr analyses and by hydrogenation followed by saponification to the known 1,3,5-pentanetricarboxylic acid. Structure **3** was assigned on the basis of elemental and nmr analyses. Saponification of **4** gave the known 3-methylglutaconic acid as a mixture of *cis–trans* isomers, and **5** was identified by comparison with an authentic sample of triethyl aconitate.

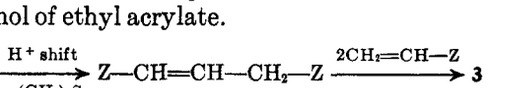
The formation of **2** has been rationalized according to Scheme I.

SCHEME I[a]

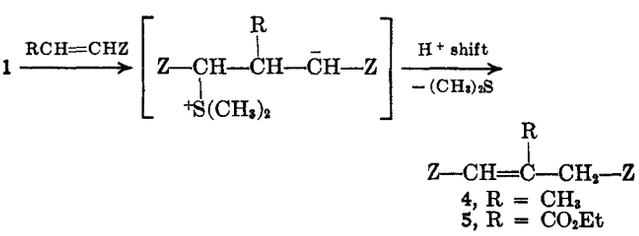


[a] Z = CO_2Et

Compound **3** can be visualized as being formed *via* intermediates A and B by Michael reaction of the latter with 2 mol of ethyl acrylate.



The conversions of ethyl crotonate into **4** and diethyl fumarate into **5** are believed to occur by the same mechanism.



Experimental Section[2]

Reaction of EDSA with Ethyl Acrylate.—To a solution of 20.0 g (0.20 mol) of ethyl acrylate in 50 ml of absolute ethanol was

(1) G. B. Payne, *J. Org. Chem.*, **32**, 3351 (1967).

(2) Melting points are corrected; boiling points are uncorrected. Nmr spectra were obtained in $CDCl_3$ with a Varian A-60 spectrometer using tetramethylsilane as an internal standard. Glpc analyses were done with an F & M Model 720 instrument using a column packed with 5% of XF-1150 on Chromosorb W.