ELECTROCHEMICAL OXIDATIVE DIMERIZATION OF ACETOACETIC AND BENZOYLACETIC ESTERS IN THE PRESENCE OF METAL HALIDES

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Acetoacetic and benzoylacetic esters dimerize on electrolysis in the presence of metal halide mediators to form 2,5-dioxohexane-3,4-dicarboxylic and 1,4dioxo-1,4-diphenylbutane-2,3-dicarboxylic esters in yields up to 90%. Primarily the meso-form of the dimer is produced (up to 90%) under optimal conditions (NaI, -20°C) in acetone and acetonitrile. Diastereomers of the dimer are produced in comparable amounts in methanol and ethanol.

Electrolysis of malonic ester in a diaphragmless electrolyzer in the presence of iodides at temperatures greater than 50°C in alcohols and CH_3CN produces esters of ethane-1,1,2,2,tetracarboxylic acid in yields up to 85% [1]. We found earlier that this process occurs effectively over a wide temperature range from -20°C to 60°C [2]. The closest analog of malonic ester, acetoacetic ester (Ia), on electrolysis in the presence of KI in CH_3CN at 10°C converts into the ester of 1,2-diacetylethane-1,2-dicarboxylic acid (IIa) in yields of only 40% [3]. Compound IIa is obtained in 46% yield on oxidation of anion Ia by iodine in ether [4].

In continuation of our investigations of the electrochemical oxidation of organic compounds in the presence of mediators, metal halides [5, 6], in the present work we studied electrochemical oxidation of acetoacetic esters (Ia and Ib) and benzoylacetic ester (Ic):

 $\begin{array}{cccc} & & & & & & & \\ & & & & & \\ & & & & \\ & & & & \\ & &$

Solutions of Ia-c were oxidized electrochemically in a diaphragmless electrolyzer using direct current. Conditions were intentionally changed in order to obtain the maximal yield of dimer IIa-c (Table 1).

The conversion of Ia and the yield of IIa per converted Ia increased in all studied solvents in the presence of NaI as the electrolysis temperature was lowered. This indicates that the selectivity of the electrochemical oxidation of Ia increases and the fraction of Ia involved in competing condensation and polycondensation processes induced by electrolysis decreases as the temperature is lowered [5, 6]. At 50°C in acetone, the yield of the two isomeric forms of IIa was only 34% whereas the bulk of Ia was converted into resinous oligomeric products, the formation of which by electrolysis of Ia has been noted [3, 7].

The optimal solvent turned out to be acetone, which was not used earlier in electrolysis of C-H acids. Ester IIa is obtained in quantitative yield with more than 90% conversion of starting Ia.

Besides NaI, KI, and Bu_4NI are sufficiently effective as mediators in acetone at $-20^{\circ}C$. The yield of IIa is 91 and 67% with more than 80% conversion of Ia. If LiI in acetone at $-20^{\circ}C$ is used, the metallic Li generated at the cathode apparently reacts too slowly with Ia and the main process becomes oxidation of metallic Li by iodine generated at the anode. Use of NaBr in ethanol (the solubility of NaBr in acetone and CH_3CN is too low) was also unsuccessful. The conversion of Ia in this instance was practically unchanged from 20 to $-20^{\circ}C$

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Starting compound	Electrolyte	Solvent	т, ℃	Conver- sion of I, %	Reaction product	Yield, %	
						meso- form	d, l-form
(Ia)	NaI	Acetone	50	67	(IIa)	18	16
»	»	»	20	79	`»`	35	31
*	»	*	0	85	»	57	33
*	»	*	-20	91	»	90	9
»	»	MeCN	20	68	»	30	29
*	»	*	0	69) »	61	30
»	»	»	-20	74	»	77	19
»	»	EtOH	20	76	»	14	12
»	»	»	0	78	»	31	24
»	»	»	·-20	89	»	50	44
»	KI	Acetone	-20	85	»	76	15
»	LiI	»	-20	26	»	28	18
»	${ m Bu}_4{ m NI}$	»	-20	84	»	49	18
(lb)	NaI	» .	-20	100	(II b)	82	16
(lb)	»	MeOH	-20	72	(IIb)	47	46
(lc)	»	Acetone	-20	92	(IIc)	59	28
(Ic)	»	EtOH	-20	68	(IIc)	42	38

TABLE 1. Electrochemical Oxidation of Acetoacetic (Ia, b) and Benzoylacetic (Ic) Esters in the Presence of Metal Halides*

*Conditions: 32 mmoles ester (I), 8 mmoles electrolyte in 20 ml solvent, Fe cathode, Pt anode, 1.2 F of electricity passed per mole ester (I) at current density 110 mA/cm².

at 70% whereas the yield of IIa increased only insignificantly from 33 to 56%. The process in this instance is most probably complicated by electrochemical oxidation of ethanol catalyzed by NaBr [1] and condensation of the acetaldehyde that is forming with Ia [7].

Electrolysis of Ib and Ic was also carried out under the optimal conditions for electrochemical oxidation of Ia. Compounds IIb and IIc were obtained in high yields of 98 and 94%, respectively.

Compounds IIa-c were isolated. They exist in solutions as isomeric meso- and d,l-diketo forms. The meso- and d,l-forms of IIc have been described earlier [8]. The meso- and d,l-forms of IIa were identified by PMR spectroscopy. The singlet for the proton of the C-H group splits into two lines with $\Delta = 1$ Hz (cf. Experimental) in the PMR spectrum of the d,l-form of IIa in the presence of (+)-(MeO)(CF₃)C(Ph)CO₂H.[†]

Primarily the meso-form (IIa-c) is formed in acetone and CH_3CN at -20°C. For IIa, the meso- and d,L-forms can be obtained in the ratio 10:1.

Both forms are formed in comparable amounts in ethanol (methanol for Ib), acetone, and CH_3CN at temperatures greater than 20°C.

The stereochemical results most probably indicate that primarily the meso-form of IIa-c is formed by electrolysis under kinetic control. The meso- and d, ℓ -forms of IIa-c are formed in about equal amounts under thermodynamic control. Conditions for thermodynamic control in alcohols probably result from generation of alcoholate anions at the cathode that cause the meso-forms of IIa-c to isomerize. The fact that meso-IIa isomerizes by 36% into d, ℓ -IIa in 0.5 M MeONa in MeOH after 2 h (standard electrolysis time) at 20°C supports this hypothesis.

An alternative explanation could be that the anion of Ia-c, which is poorly soluble in acetone and CH_3CN , adsorbs on the cathode surface before reacting at negative temperatures with iodine. As the temperature is raised this process occurs in solution. In this instance, the result of the reaction in alcohols is explained by the high solubility of anions Ia-c in this solvent.

On the basis of the results and literature data [1, 3], the following reaction mechanism is proposed:

[†]The authors thank Yu. A. Strelenko for supplying the optically active acid and recording the PMR spectrum.

At the anode $2I^- - 2e \longrightarrow I_2$ At the cathode $2M^+ + 2e \longrightarrow 2M$ (M = Li, Na, K) $2(1) + 2M \longrightarrow 2R^{1}CCH(COOR^{2}) + H_{2} + 2M^{+}$ 0 or $2(1) + 2\varepsilon \longrightarrow 2R^1C\bar{C}H(COOR^2) + H_2$ 0 In alcohols preferentially: $2ROH + 2e \longrightarrow 2RO^{-} + H_2$ $2(1) + 2RO^{-} \longrightarrow 2B^{1}C\bar{C}H(COOR^{2}) + 2ROH$ 0 In solution: $\mathbb{R}^{1}CCH(COOR^{2}) + I_{2} \longrightarrow \mathbb{R}^{1}CCHI(COOR^{2}) + I^{-}$ || 0 0 Ω $R^{1}CCH_{I}(COOR^{2}) + R^{1}CCH_{I}(COOR^{2}) \longrightarrow R^{1}CCH_{I}CH_{I} + I^{-}$ R2OOC COOR2 (II)

Further oxidative conversions of dimer II in the mediator system used, in contrast to oxidation of the dimer of malonic ester [2, 9, 10], occurs very nonselectively. This is apparently explained by the presence in II of additional electrochemically and chemically very reactive centers, the two carboxylic groups.

EXPERIMENTAL

Bruker M-250 (250 MHz), Bruker AM-300 (300 MHz), and JEOL FX 90 (90 MHz) instruments were used to record ¹H and ¹³C NMR of the compounds in CDCl₃ solutions. The chemical shifts are represented as δ values using TMS as an internal standard.

Pure grade KI, NaBr, NaI, and LiI wre dried under vacuum before use. Pure grade Bu_4NI was recrystallized from THF.

Pure grade ethyl ester of acetoacetic acid (Ia) was distilled under vacuum before use. The methyl ester of acetoacetic acid was prepared by transesterification of Ia in methanol. The ethyl ester of benzoylacetic acid was prepared from Ia and benzoyl chloride by the literature method [11].

Electrolysis of Ia-c in the Presence of Metal Halides. General Method. Ester (Ia-c, 32 mmoles) and mediator metal halide (8 mmoles) were placed into a diaphragmless cell equipped with an Fe cathode, Pt anode (~5 mm between electrodes), external cooling, magnetic stirrer, thermometer, and reflux condenser. The electrolysis was carried out at a current density of 110 mA/cm². A total of 1.2 F of electricity per mole of ester Ia-c was passed. The reaction mixture was evaporated and extracted with CHCl₃. The CHCl₃ was distilled. The conversion of Ia-c and yield of IIa-c were quantitatively determined by PMR spectroscopy using 1,4-dichlorobenzene as internal standard. Esters IIa-c were then isolated by recrystallization from an acetone-pentane mixture. Under the optimal conditions, the CHCl₃ extract was washed with an aqueous solution of thiosulfate and dried over Na_2SO_4 before the CHCl₃ was removed. Practically pure IIa-c were obtained after washing the solid residue on the filter with hexane.

Diethyl ester of meso-2,5-dioxohexane-3,4-dicarboxylic acid (IIa), mp 90-91°C. Found, %: C 55.69; H 6.81. $C_{12}H_{18}O_6$. Calculated, %: C 55.81; H 6.97. PMR spectrum (δ , ppm): 1.24 t (6H, CH₃), 2.42 s (6H, CH₃), 4.14 q (4H, CH₂O), 4.49 s (2H, CH). ¹⁹C NMR spectrum (δ , ppm): 13.9 q (CH₃), 30.7 q (CH₃), 50.8 d (CH), 62.0 t (CH₂O), 167.0 (CO₂), 201.4 s (C=O).

 $\begin{array}{c} \underline{\text{Dimethyl ester of meso-2,5-dioxohexane-3,4-dicarboxylic acid (IIb), mp 146-147°C.} \\ \text{Found, $\%$: C 52.37; H 6.09. $C_{10}H_{14}O_6$. Calculated, $\%$: C 52.17; H 6.09. $PMR spectrum ($\delta$, $ppm)$: 2.44 s (6H, CH_3), 3.72 s (6H, OCH_3), 4.50 s (2H, CH). $^{13}C $NMR spectrum ($\delta$, $ppm)$: 30.7 q (CH_3), 52.9 q (CH_3O$), 57.6 d ($CH$), 167.6 s ($CO_2$), 201.3 s ($C=0$). \\ \end{array}$

<u>Mixture of dimethyl esters of meso- and d,l-2,5-dioxohexane-3,4-dicarboxylic acids</u> <u>in a l:l ratio (IIb)</u>, mp 115-117°C. Found, %: C 52.23; H 6.07. $C_{10}H_{14}O_6$. Calculated, %: C 52.17; H 6.09. PMR spectrum (δ , ppm): 2.36 s, 2.44 s (6H, CH₃); 3.68 q, 3.72 q (6H, OCH₃); 4.48 s, 4.50 s (2H, CH).

Diethyl ester of meso-1,4-dioxo-1,4-diphenylbutane-2,3-dicarboxylic acid (IIc), mp 130-131°C. Found, %: C 69.33; H 5.68. $C_{22}H_{22}O_6$. Calculated, %: C 69.10; H 5.76. PMR spectrum (δ , ppm): 1.22 t (6H, CH₃), 4.21 q (4H, CH₂O), 5.61 s (2H, CH), 7.3-8.2 m (10H, ArH). ¹³C NMR spectrum (δ , ppm): 13.6 q (CH₃); 53.3 d (CH); 62.0 t (CH₂O); 128.6, 129.4, 133.7, 136.3 (C_6H_5); 167.1 (CO₂); 194.0 (C=O).

<u>Mixture of diethyl esters of meso- and d, l-1, 4-dioxo-1, 4-diphenylbutane-2, 3-dicarboxylic acids in a l:l ratio (IIc), mp 78-80°C.</u> Found, %: C 69.37; H 5.82. $C_{22}H_{22}O_6$. Calculated, %: C 69.10; H 5.76. PMR spectrum (δ , ppm): 1.20 t, 1.22 t (6H, CH₃); 4.19 q, 4.21 q (4H, CH₂0); 5.53 s, 5.61 s (2H, CH); 7.3-8.2 m (10H, ArH).

A mixture of meso- and d,l-IIa in a 2:1 ratio (0.1 g) and (+)-(MeO)(CF_3)C(Ph)CO₂H (0.3 g) was dissolved in CdCl₃ (0.5 ml). The solution was used to determine the configuration of the isomers by PMR spectroscopy.

LITERATURE CITED

- 1. D. A. White, J. Electrochem. Soc., 124, No. 8, 1177 (1977).
- M. N. Élinson, S. K. Fedukovich, and G. I. Nikishin, Izv. Akad. Nauk SSSR, Ser. Khim., No. 11, 2534 (1988).
- 3. T. Okubo and S. Tsutsumi, Bull. Chem. Soc. Jpn., <u>37</u>, No. 12, 1794 (1964).
- 4. J. A. Bilton and R. P. Linstead, J. Chem. Soc., 924 (1937).
- 5. M. N. Elinson, S. K. Fedukovich, S. V. Lindeman, et al., Izv. Akad. Nauk SSSR, Ser. Khim., No. 7, 1603 (1989).
- M. N. Elinson, I. V. Makhova, and G. I. Nikishin, Izv. Akad. Nauk SSSR, Ser. Khim., No. 1, 122 (1991).
- 7. T. D. Binns and R. Brettle, J. Chem. Soc. C, No. 3, 336 (1966).
- 8. N. B. Galstukhova and M. N. Shchukina, Zh. Obshch. Khim., 27, No. 3, 1857 (1957).
- 9. M. N. Elinson, S. K. Fedukovich, and G. I. Nikishin, Izv. Akad. Nauk SSSR, Ser. Khim., No. 1, 96 (1988).
- M. N. Élinson, S. K. Fedukovich, and G. I. Nikishin, Izv. Akad. Nauk SSSR, Ser. Khim., No. 2, 352 (1989).
- 11. Syntheses of Organic Compounds [Russian translation], No.2, Izd. IL, Moscow (1949), p. 584.