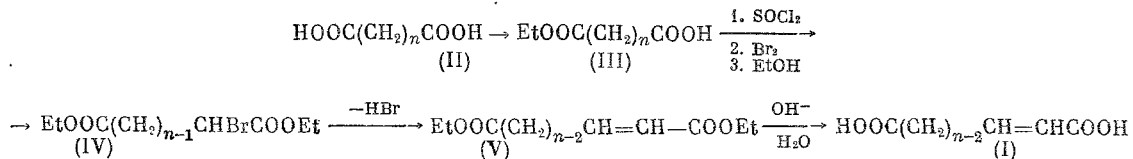


SYNTHESIS OF TRAUMATOIC (2E-DODECENEDIOIC) ACID FROM
DODECANEDIOIC ACID

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Traumatoic (2E-dodecenedioic) acid (Ic) is one of the plant hormones [1], and is also the starting compound for the one-step preparation of 2-(6-carbomethoxyhexyl)cyclopent-2-en-1-one or synthone in the synthesis of 11-deoxy-PGE₁ [2]. Several syntheses of acid (Ic) have been described [3-7]. We developed a simple method for obtaining (Ic) from the readily available 1,12-dodecanedioic acid (IIc) by the following scheme:



n = 7 (a), 8 (b), and 10 (c).

Acid (IIc) is converted in conventional manner to the monoethyl ester of dodecanedioic acid (IIIc), which when brominated as described in [8] gives the diethyl ester of 2-bromo-dodecanedioic acid (IVc). We found that the dehydrobromination of (IVc) to the diethyl ester of 2E-dodecenedioic acid (Vc) proceeds easily by treatment with dry NaHCO₃ in HMPA at 100-110°C. Previously this dehydrobromination method was used to obtain the higher cyclic α,β-unsaturated ketones from 2-bromocycloalkanones [9]. The hydrolysis of (Vc) with alcoholic caustic gives the pure acid (Ic). It should be mentioned that if the dehydrobromination of (Vc) is run with a large excess of NaHCO₃ and for a longer time, then the double bond undergoes partial isomerization from the α,β to the β,γ position. In a similar manner, from 1,10-dodecanedioic acid (IIb) we obtained 2E-decenedioic acid (Ib), which is a component part of mother's milk [5]. The dehydrobromination of the diethyl ester of 2-bromodecane-1,10-dioic acid (IVb), obtained from acid (II), to the diethyl ester of 2E-decenoic acid (Vb) proceeds easily by treatment either with NaHCO₃ in HMPA or with Li₂CO₃ in the presence of LiBr in DMF. The latter dehydrobromination method was used previously to obtain cyclic α,β-unsaturated ketones from cyclic α-haloketones [10]. The structure of ester (Vb) was confirmed via PMR. The alkaline hydrolysis of (Vb) leads to acid (Ib).

In a similar manner, we obtained 2E-nonenedioic acid (Ia) from 1,9-nonanedioic acid (IIa), and the ethyl ester of 2E-nonenoic acid (VI) from nonanoic acid.

EXPERIMENTAL

The GLC analysis of the compounds was run on a Tswett-4 chromatograph equipped with a katharometer, and using a 2 m × 2.5 mm column, packed with Silicone SE-30 (5%) deposited on Chromaton N-AW-HMDS, at 220°. The PMR spectrum was obtained on an NR-2309 instrument using HMDS as the internal standard. The monoethyl esters of the dicarboxylic acids were obtained by a modification of the method given in [11]. The ethyl ester of 2-bromononanoic acid was synthesized as described in [12].

Monoethyl Esters of Dicarboxylic Acids (III). A stirred mixture of 0.2 mole of 1,12-dodecanedioic acid (IIc), 0.2 mole of the diethyl ester of acid (IIc), 0.4 mole of abs. EtOH, and 0.01 mole of H₂SO₄ (sp. gr. 1.83) was refluxed for 4-6 h. The excess EtOH was removed in vacuo, and the residue was poured into cold water and extracted with ether. The ether extract was washed with a small amount of NaHCO₃ solution, then with water, and dried over Na₂SO₄. Vacuum-distillation gave 0.14 mole (72%) of ester (IIIc), bp 182-186° (1 mm), mp 48-50°, cf. [11]. In a similar manner were obtained: ester (IIIb) in 65% yield, bp 158-160° (1 mm), mp

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35-36°, cf. [13], and ether (IIIa) in 62% yield, bp 150-152° (1.5 mm), mp 25-26°, cf. [14].

Diethyl Esters of 2-Bromodicarboxylic Acids (IV). A mixture of 0.1 mole of esters (IIIc) in 50 ml of SOCl_2 was refluxed for 3-4 h. Then, under gentle reflux, 0.105 mole of Br_2 was gradually added at such a rate that the amount of Br_2 vapors in the upper part of the condenser was negligible. At the end of Br_2 addition the reaction mixture was heated under gentle reflux until nearly all of the bromine had disappeared (4-6 h), after which the excess SOCl_2 was vacuum-distilled. The residue was treated carefully with 20 ml of abs. EtOH and the mixture was refluxed for 0.5-1 h, cooled, poured into cold water, and extracted with ether. The ether extract was washed with water, then with NaHCO_3 solution, and dried over Na_2SO_4 . The ether was removed and the residue was vacuum-distilled to give 76% of (IVc), bp 174-176° (1 mm). Found: C 52.99; H 7.98%. $\text{C}_{16}\text{H}_{29}\text{BrO}_4$. Calculated: C 52.61; H 8.00%; in a similar manner were obtained: diester (IVb) (70%), bp 160-162° (1 mm), cf. [8], and ester (IVa) (64%), bp 150° (1 mm), cf. [15].

Diethyl Ester of 2E-Dodecene-1,12-dioic Acid (Vc). A stirred mixture of 20 g of bromoester (IVc), 70 ml of dry HMPA, and 6 g of dry NaHCO_3 was heated for 5 h at 100-110°. The reaction course was checked by GLC. The heating and stirring were stopped when the isomerized unsaturated diester appeared in the reaction product. Then most of the HMPA was vacuum-distilled from the reaction mass, the residue was treated with hexane, and the mixture was poured into water. The hexane solution was washed twice with water and dried over Na_2SO_4 . Vacuum-distillation gave 13.3 g (87%) of (Vc), bp 155-156° (1 mm). Found: C 68.25; H 10.35%. $\text{C}_{16}\text{H}_{28}\text{O}_4$. Calculated: C 67.57; H 9.92%.

Traumatolic (2E-Dodecene-1,12-dioic) Acid (Vc). A solution of 13 g of (Vc) in a mixture of 7 g of KOH, 50 ml of EtOH, and 14 ml of H_2O was refluxed for 2 h. Most of the alcohol was vacuum-distilled and then water was added to the residue. The obtained solution was filtered and the filtrate was acidified with concentrated HCl. The obtained acid was filtered, washed on the filter with water, and dried. We obtained 9.5 g (91%) of (Ic), mp 163-165° (EtOAc). Found: C 62.98; H 8.71%. $\text{C}_{12}\text{H}_{20}\text{O}_4$. Calculated: C 63.14; H 8.38%; cf. [7].

Diethyl Ester of 2E-Decene-1,10-dioic Acid (Vb). a) A stirred mixture of 15 g of bromoester (IVb), 40 ml of dry HMPA, and 5 g of dry NaHCO_3 was heated for 4 h at 105-110°. The reaction course was checked by GLC. After the usual workup we obtained 8.8 g (85%) of (Vb), bp 122-124° (1 mm).

b) A stirred mixture of 4.8 g of bromoester (IVb), 30 ml of dry DMF, 1.5 g of Li_2CO_3 , and 1.2 g of LiBr was heated for 4 h at 135-140°. The reaction course was checked by GLC. Most of the DMF was removed in vacuo, and then water and hexane were added to the cooled residue. The hexane solution was washed twice with water and dried over MgSO_4 . Vacuum-distillation gave 3.3 g (90%) of (Vb), bp 139-140° (4 mm). PMR spectrum (CCl_4 , δ , ppm): 1.19 and 1.24 m (6H, $J = 7$ Hz, $2\text{CH}_3\text{CH}_2\text{O}$), 1.32 m (8H, $\text{CH}_2(\text{CH}_2)_4\text{CH}_2$), 2.16 m (4H, $\text{CH}_2(\text{CH}_2)_4\text{CH}_2$), 3.94 and 3.99 q (4H, $J = 7$ Hz, $2\text{CH}_3\text{CH}_2\text{O}$), 5.59 and 6.69 (2H, $J_{\text{AB}} = 16$ Hz (trans), $J_{\text{B-CH}_2} = 7$ Hz, $\text{CH}=\text{CH}$). Found: C 65.55; H 9.50%. $\text{C}_{14}\text{H}_{24}\text{O}_4$. Calculated: C 65.62; H 9.37%.

2E-Decene-1,10-dioic Acid (Ib). A solution of 8 g of ester (Vb) and 5 g of KOH in 30 ml of EtOH and 10 ml of H_2O was refluxed for 2 h. After the usual workup we isolated 6.6 g (94%) of (Ib), mp 170-171° (H_2O), cf. [2].

2E-Monene-1,9-dioic Acid (Ia). A stirred mixture of 10 g of bromoester (IVa) and 5 g of dry NaHCO_3 in 30 ml of HMPA was heated for 4 h at 105-110°. After the usual workup we obtained 6.5 g (86%) of the diethyl ester of 2E-monene-1,9-dioic acid (Va), bp 118-120° (1 mm). Found: C 64.56; H 9.10%. $\text{C}_{13}\text{H}_{22}\text{O}_4$. Calculated: C 64.46; H 9.10%. A solution of 5 g of diester (Va) and 3 g of KOH in 20 ml of EtOH and 6 ml of H_2O was refluxed for 2 h. After the usual workup we obtained 4.2 g (91%) of (Ia), mp 104-106°, cf. [10].

Ethyl Ester of 2E-Nonenoic Acid (VI). A stirred mixture of 20 g of ethyl 2-bromononanoate, 50 ml of dry HMPA, and 5 g of dry NaHCO_3 was heated for 3 h at 100°. After the above described workup we obtained 12.5 g (90%) of (VI), bp 112-114° (10 mm), cf. [16]. Found: C 70.61; H 10.76%. $\text{C}_{11}\text{H}_{20}\text{O}_2$. Calculated: C 71.70; H 10.92%.

CONCLUSIONS

1. The synthesis of traumatolic (2E-dodecanedioic) acid from 1,12-dodecanedioic acid via the diethyl ester of 2-bromododecanedioic acid was proposed.

2. The diesters of α -bromodicarboxylic acids were dehydrobrominated to the diesters of α,β -unsaturated dicarboxylic acids by using either NaHCO_3 in HMPA or Li_2CO_3 in DMF.

LITERATURE CITED

1. J. English, J. Bonner, and A. J. Haagen-Smit, *J. Am. Chem. Soc.*, **61**, 3434 (1939).
2. A. S. C. Prakasa Rao and U. R. Dev. Sukh. Nayak, *Synthesis*, 608 (1975).
3. J. English, *J. Am. Chem. Soc.*, **63**, 942 (1941).
4. W. M. Lauer and W. J. Gensler, *J. Am. Chem. Soc.*, **67**, 1171 (1945).
5. W. H. Brown and R. J. Freure, *Can. J. Chem.*, **37**, 2042 (1959).
6. S. Doležal, *Collect. Czech. Chem. Commun.*, **35**, 1932 (1970).
7. P. H. M. Schreurs, P. P. Montijn, and S. Hoff, *Rec. Trav. Chim.*, **90**, 1331 (1971).
8. E. Schwenk and D. Papa, *J. Am. Chem. Soc.*, **70**, 3626 (1948).
9. T. Kato, H. Kondo, and G. Hata, *Japan Patent* 48,635 (1976); *C. A.*, **85**, P123437k (1976).
10. R. Joly, J. Warnant, J. Nomini, and D. Bertin, *Bull. Soc. Chim. France*, 551 (1961).
11. V. M. Andreev, S. G. Polyakova, V. I. Bazhulina, Z. S. Khrustova, V. V. Smirnova, V. P. Gorbunkova, and M. M. Shchedrina, *Zh. Org. Khim.*, **17**, 86 (1981).
12. H. Reinheckel, *Chem. Ber.*, **93**, 2227 (1960).
13. Ch. Swann, R. Eler, and R. Buswell, *Organic Syntheses*, [Russian translation], Vol. 2 (1949), p. 345.
14. H. McKennis and V. Vigneaud, *J. Am. Chem. Soc.*, **68**, 833 (1946).
15. B. Teimann, *Acta Chim. Acad. Sci. Hung.*, **41**, 331 (1964).
16. C. J. Martin, A. I. Schepartz, and B. F. Daubert, *J. Am. Chem. Soc.*, **70**, 2301 (1948).

 RADIATION-CHEMICAL REDUCTION OF 12-MOLYBDOVANADOPHOSPHATES
 IN AQUEOUS SOLUTION

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The transformations of heteropoly acids (HPA) when irradiated have received little study. We studied the reduction of concentrated aqueous solutions of some Na salts, which are used in the oxidative catalysis [1] of the acids $H_{3+n}PMo_{12-n}^{VI}V_n^{V}O_{40}$ (HPA-n, n = 0-6), when exposed to γ and β radiation.

EXPERIMENTAL

The aqueous solutions of the salts of composition $Na_nH_3PMo_{12-n}V_nO_{40}$ were prepared by reacting stoichiometric amounts of cp $NaVO_3$, $H_3PMo_{12}O_{40}$, and H_3PO_4 in bidistilled water. The pH value was controlled by adding H_2SO_4 and $NaOH$. We used the γ radiation of ^{60}Co at a dose rate of 0.5 Mrad/h and the β radiation of an ILU-6 linear pulse accelerator with an energy of 1.6 MeV and an average dose rate of 1 Mrad/sec. We irradiated aerated aqueous solutions of HPA-n (0.20 mole/liter, d = 1.29-1.35 g/ml, weight of sample 3-4 g) at 20°C, and pH 1.3 and 5.0, in sealed ampuls made from Mo glass. The accumulation of V^{IV} , formed during the reduction of the HPA-n [1], was followed by EPR (EPR-3 spectrometer), by taking samples of the irradiated solutions (~ 0.08 g). The spectra were recorded at 77°K. As standards we used $VOSO_4$ solutions of known concentration and a $CuCl_2 \cdot 2H_2O$ monocrystal. At sufficiently high degrees of reducing the HPA-n (~ 1 eper molecule) the $[V^{IV}]$ was determined by potentiometric titration with $KMnO_4$.

DISCUSSION OF RESULTS

The intense β irradiation of HPA-n (n = 0-6) solutions with a dose D = 100-600 Mrad leads to their noticeable reduction (0.3-0.6 e/molecule at pH 1.3). In the presence of organic compounds (alcohols, aldehydes, ketones, carboxylic acids, etc.) both the rate and the degree of reducing the HPA increase; the process is accompanied by the oxidation of the additives.

The reduction of HPA-6, induced by γ radiation, was studied in greatest detail. The $PMo_6V_6^{VI}$ polyanions are stable in the pH range 2.5-5.5 [2]. At pH 1.3 they dissociate with

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