198. Electrochemical Synthesis of the Sex Attractant Pheromone of the Housefly: (*Z*)-9-Tricosene

by **Ashok K. Yadav** and **Paul Tissot***

Département de Chimie Minérale, Analytique et Appliquée, Université de Genève, CH-1211 Genève 4

(8.V.84)

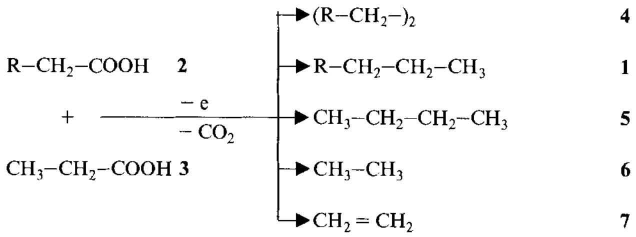
Summary

The electrochemical synthesis of muscalure, (*Z*)-9-tricosene(**1**), has been carried out by coelectrolysis of erucic acid (**2**) and propionic acid (**3**) in an undivided cell in methanol. To optimize the yield of the cross coupled product **1**, the reaction has been studied in detail by varying different parameters, *viz.*, electrode material, current density, molar ratio of **2** to **3**, degree of partial neutralization and quantity of water in methanol.

Introduction. – The isolation, identification and synthesis of **1** arising from a *Wittig* reaction between 1-bromotetradecane and nonanal, a sex attractant pheromone of the common housefly *Musca domestica L,* was reported by *Carlson et al.* [1]. Soon after this work, *Cargill & Rosenblum* [2] published a better and more convenient synthesis of **1** by reaction between a natural fatty acid (*viz.*, **2**) and MeLi followed by the reduction of the resulting ketone with hydrazine hydrate and KOH. Since both these syntheses involved the use of toxic reagents, *Cormier et al.* proposed a student synthesis of **1** from **2** with a 34% yield involving multiple steps [3]. Our work was stimulated by the recent interest in exploiting the novel application of the *Kolbe* electrolysis, a simple electrochemical method, for the synthesis of some pheromones [4–6]. A recent report [7], however, demonstrates that the method is unsuitable if γ, δ-unsaturated carboxylic acids are employed, because the double bond can isomerize at the alkenyl radical stage by a reversible cyclization *via* cyclopropylcarbinyl radicals. Here, we report the synthesis of **1** by anodic cross coupling between partially neutralized **2** and **3** in MeOH, a *Wurtz* extension [8] over the *Kolbe* electrosynthesis [9]. The effect of various parameters like electrode material, current density, degree of partial neutralization, molar concentration ratio of **2** and **3** and quantity of H_2O in MeOH has been studied in order to optimize the yield of the desired product **1**.

Results and Discussion. – The main aim of the synthesis of pheromones is to obtain the product configurationally pure, because its efficiency is greatly influenced by contamination with other isomers [10–12]. We have achieved this goal by coelectrolysing **2** and **3** partially neutralized by MeONa in MeOH, at a Pt anode. Our choice of **2** and **3** was mainly due to the easy availability and removal of the gaseous products arising from the ethyl radical, *viz.*, the dimer butane and disproportionation products *i.e.* ethane and ethylene, which, in principle are obtainable in anodic cross coupling. In

Scheme



$R = CH_3–(CH_2)_7–CH=CH–(CH_2)_{10}$

fact, we have isolated the dimer 9,33-dotetracontadiene (**4**) and detected butane (**5**), ethane (**6**) and ethylene (**7**) by gas chromatography, as shown in the *Scheme*.

In our results, we have not included quantitative analyses of **5**, **6** and **7** because of experimental limitations to the possibility of analyzing gases in the reactor. The analysis of **4** was also excluded as its nature changes during the isolation of **1** by distillation (see *Experimental*). However, we were able to study the reaction with regard to the desired product **1**. *Table 1* presents the results obtained with different molar ratios of the acids and different degrees of neutralization.

Table 1. *Coelectrolysis of* **2** *with* **3** *in MeOH*. Anode: Pt, cathode: Ti, anodic current density: 0.1 A·cm^{-2}.

Run	Molar ratio (2:3)	Current passed [F/mol of acids]	Neutralization degree [molar %]	Yield of **1**[a]) [%]
1	1:1	1	36	17
2	1:2	0.84	6	16
3	1:2	0.84	12	29
4	1:2	0.84	24	24
5	1:2	1	12	40
6	1:2	1	36	27
7	1:5	1	36	32
8	1:10	1	12	59
9	1:10	1	18	49
10	1:10	1	36	33

[a]) The yields are based on **2**, accuracy ± 1%.

As expected [13], the yield of **1** increases with the proportion of the lower molecular weight acid (runs 1, 6, 7, 10). We have not used a ratio lower than 1:10. These results may be explained in the light of the proposition of *Eberson* [14] [15] and *Muck et al.* [16]; the carboxylate ion approaches the suitably conditioned electrode (*i.e.* covered by an oxide layer) and is weakly adsorbed assuming certain orientations (the short chain carboxylate ($\leqq C_6$) approaches in a more or less random fashion, while the long chain ($> C_6$) does so in an orientation perpendicular to the electrode surface). Subsequently, both undergo electron transfer to the electrode with simultaneous cleavage of C-COO to give radicals, usually separated by a width corresponding to that of CO_2 molecules ($\approx$ 6Å). The products thus mainly depend upon the electrode material and the length of the carbon chain of the carboxylate, which direct the reactants to undergo either another electron transfer or further chemical reactions. The two radicals formed in our case are very different with regard to their size, the mobility and the reactivity of ethyl radicals being higher. These radicals undergo unsymmetrical dimerization to give **1** and symmetrical dimerization to give **4** and **5**. Besides these reactions, the ethyl radicals also undergo disproportionation to give **6** and **7** [17]. Though we have not analyzed quantitatively the dimer **4** of the erucic acid, it seems that the quantities obtained are never very significant. Thus, increasing the molar proportion of **3** results in the higher yield of **1** *(Table 1)* simply by providing more ethyl radicals for unsymmetrical dimerization.

If one considers the degree of neutralization of the acids with MeONa (rund 2, 3, 4; 5, 6; 8, 9, 10), it is clear that the yield of **1** increases with the diminution of the base. The optimum percentage of neutralization is 12%; a lower quantity of MeONa (run 2) decreases the yield. During the course of the electrolysis the pH increases, so that we have not passed more than 1F per mol of acids to avoid a pH greater than 8, which is not favourable for the one electron oxidation process [18].

With the help of the above studies, we have synthesized **1** with a 59% yield (run 8). It seems that it is difficult to enhance the yield significantly further, probably due to the preferential orientations for adsorption and then competitive desorption, resulting from the difference of chain sizes. We have investigated the effect of current density on the unsymmetrical coupling process for our system and the results are presented in *Table 2*.

Table 2. *Effect of Current Density on the Yield of* **1**. Conc. of **2**: 10^{-2} mol; of **3**: 2×10^{-2} mol; anode: Pt; cathode: Ti; current passed: 0.536 A h, 0.84 F/mol of acids; neutralization degree: 12%.

Current density [A·cm^{-2}]	Yield of **1** [%]	Current density [A·cm^{-2}]	Yield of **1** [%]
0.05	20	0.12	27
0.08	28	0.14	26
0.10	29	0.20	25

It is evident from these results that the optimum yield is obtainable at a current density 0.10 A cm^{-2}. A lower current density decreases the yield of **1** appreciably, while its increase causes little change. Addition of H_2O to MeOH in a typical experiment ($MeOH/H_2O$, 9:1) reduces the yield of **1** from 29% to 15%, which may be due to the low solubility of sodium erucate in H_2O.

We have also studied the reaction at gold and Ir anodes (**1**, 1×10^{-2}M. **2**, 1×10^{-2}M, current density 0.10 A cm^{-2}, degree of neutralization, 12%) and obtained **1** in 26% and 25.5%, respectively (under similar conditions Pt gave 29%). Gold was not suitable as it eventually crumbled, but Ir seems to be unaffected.

Experimental. – *General.* Melting points are uncorrected. The refractive index was determined using a *Carl Zeiss* refractometer. IR spectra were recorded on a *Perkin Elmer 681* grating IR spectrophotometer. NMR spectra were run on a *Bruker WH-360* spectrometer and the chemical shifts are given in ppm relative to TMS (= 0 ppm). Erucic acid (*Riedel-de Haën*, 90% (Z)-product(*(Z)-13-docasenoic acid*)), propionic acid *(Fluka)* and MeOH *(Merck)* were used without further purification.

Cell Assembly. The electrolysis apparatus consisted of a 100 ml double-wall cell closed with a teflon cover. Cold water was circulated through the cooling mantle to maintain the temp. of the electrolyte between 15° at the beginning of the electrolysis and 25–35° at the end. A Pt-plate anode, with a surface area of 10 cm^2, was flanked symmetrically by two titanium cathodes, each with a surface area of 10 cm^2. The distance between the anode and the cathodes was 0.8 cm. Constant current was supplied by a d.c. regulated power supply. The electrolyte was stirred magnetically.

Electrolysis. – a) *Anodic Coupling of* **2**. Erucic acid (**2**, 3.38 g, 10^{-2} mol) partially neutralized with MeONa in MeOH (0.083 g of Na in 80 ml of MeOH, 36% of acid neutralized) was electrolyzed for 16 min at 1 A (1F/mol).

b) *Anodic Coupling between* **2** *and* **3** *(cf.* Run 8, *Table 1).* Erucid acid (**2**) (0.61 g, 0.182×10^{-2} mol) and propionic acid (**3**, 1.34 g, 1.82×10^{-2} mol) partially neutralized with MeONa in MeOH (0.055 g of Na in 80 ml of MeOH, 12% of acids neutralized) were electrolyzed for 32 min at 1 A (1F/mol of acids).

Workup and Physicochemical Data. – a) *Anodic Coupling of* **2**. The volume of the electrolyte was reduced to 25 ml by distilling off MeOH under reduced pressure (15 Torr) followed by cooling to 10°, whereby a white product separated out. It was filtered, washed with MeOH and dried. This product was identified as **4**. Yield: 2.7 g (92%); m.p. 33°. IR (KBr): 3010, 2925, 2845, 1560, 1465, 1445, 1425, 720 and 700. ^{1}H-NMR (360 MHz, $CDCl_3$): 0.90 (*t*, 6H, 2 CH_3); 1.20–1.40 (*m*, 64H, 32 CH_2, non-allylic); 1.95–2.10 (*m*, 8H, 4 CH_2, allylic); 5.36 (apparent *t*, *J* = 5, 4H, olefinic).

b) *Anodic Cross-coupling.* The electrolyte was neutralized with AcOH and the solvent, the unreacted **3** and AcOH were removed by distillation under reduced pressure (15 Torr). The white viscous mass (0.97 g) thus obtained was purified by bulb-to-bulb distillation in a *Büchi GKR-50* assembly giving **1** (0.34 g, 59%); $n_D^{25.5} = 1.4536$ ([1]: $n_D^{26} = 1.4517$; [2]: $n_D^{23} = 1.4532$); b.p.: 156–158°/0.1 Torr ([1]: 157–158°/0.1 Torr). IR (neat): 3010, 2925, 2850, 1460, 1380 und 720. ^{1}H-NMR (360 MHz, $CDCl_3$): 0.88 (*t*, 6H, 2 CH_3); 1.24–1.34 (*m*, 34H, 17 CH_2, non-allylic); 2.98 (*m*, 4H, 2 CH_2, allylic); 5.38 (apparent *t*, *J* = 5, 2H, olefinic); *cf.* the data in [1–3].

The residue from the distillation, shaken with H_2O, filtered and repeatedly washed with H_2O to remove the sodium salts, afforded 0.21 g of a white product which was formed during the distillation by the partial decomposition of **4**.

Technical assistance from Miss *H. Lartigue* is gratefully acknowledged.

REFERENCES

[1] *D.A. Carlson, M.S. Mayer, D.L. Silhacek, J.D. James, M. Beroza & B.A. Bierl,* Science *174,* 76 (1971).
[2] *R.L. Cargill & M.G. Rosenblum,* J. Org. Chem. *37,* 3971 (1972).
[3] *R.A. Cormier, M. Duc Phan, T. Graddis & R. Singer,* J. Chem. Educ. *56,* 345 (1979).
[4] *H.J. Schäfer,* Chem. Phys. Lipids *24,* 321 (1979).
[5] *H. Klünenberg & H.J. Schäfer,* Angew. Chem. *90,* 48 (1978); ibid. Int. Ed. *17,* 47 (1978).
[6] *U. Jensen & H.J. Schäfer,* Chem. Ber. *114,* 292 (1981); Justus Liebigs Ann. Chem. *1982,* 1532.
[7] *M. Huhtasaari, H.J. Schäfer & H. Luftmann,* Acta Chem. Scand., Ser. B *37,* 537 (1983).
[8] *A. Wurtz,* Ann. Chim. Phys. *44,* 291 (1855); Jahresbericht *1855,* 575.
[9] *H. Kolbe,* Ann. Chem. *69,* 257 (1849).
[10] *W.L. Roelofs & A. Comeau,* Nature (London) *220,* 600 (1968).
[11] *M. Jacobson,* Science *163,* 190 (1969).
[12] *H.H. Shorey & J.J. Mckelvey,* Jr., eds., 'Chemical Control of Insect Behavior', Wiley, Chichester-New York, 1977.
[13] *W.S. Greaves, R.P. Linstead, B.R. Shephard, S.L.S. Thomas & B.C.L. Weedon,* J. Chem. Soc. *1950,* 3326.
[14] *L. Eberson,* Acta Chem. Scand. *17,* 2004 (1963).
[15] *L. Eberson,* Electrochim. Acta *12,* 1473 (1967).
[16] *D.L. Muck & E.R. Wilson,* J. Electrochem. Soc. *117,* 1358 (1970).
[17] *B.C.L. Weedon,* in 'Advances in Organic Chemistry', Vol. 1, eds. R.A. Raphael, E.C. Taylor and H. Wynberg, Interscience, New York, 1960, p. 5.
[18] *J.H.P. Utley,* in 'Technique of Electroorganic Synthesis', Part 1, ed. N.L. Weinberg, John Wiley, New York, 1974, p. 802.