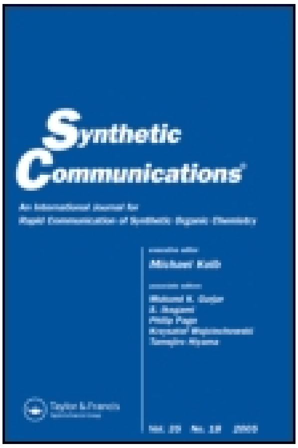

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KOLBE ELECTROSYNTHESIS OF 1,2-DI(BICYCLO[2.2.1]HEPTAN-2-YL)ETHANE AND 1,2-DIPHENYLETHANE

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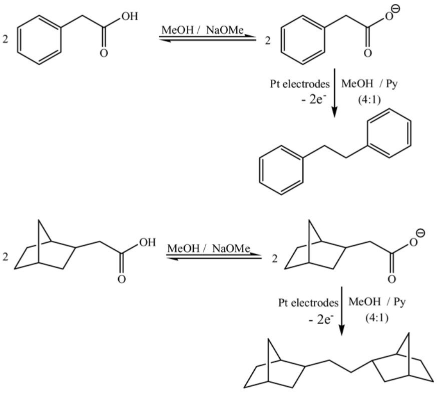
GRAPHICAL ABSTRACT



Abstract *Kolbe electrosynthesis, at low current densities, of 1,2-diphenylethane and 1,2-di(bicyclo[2.2.1]heptan-2-yl)ethane with 77 and 72% yields, respectively, is described.*

Keywords Dimerization; Kolbe electrosynthesis; oxidation; radical reactions

INTRODUCTION

The Kolbe synthesis[1] is considered to be the first electro-organic reaction of interest in the synthesis of natural products.[2] Recently, this reaction has been carried out by photochemistry,[3] sonoelectrosynthesis using a biphasic system as

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solvent,[4,5] solid polymer electrolyte (SPE) composite electrode,[6] and solid-phase organic synthesis.[7–9]

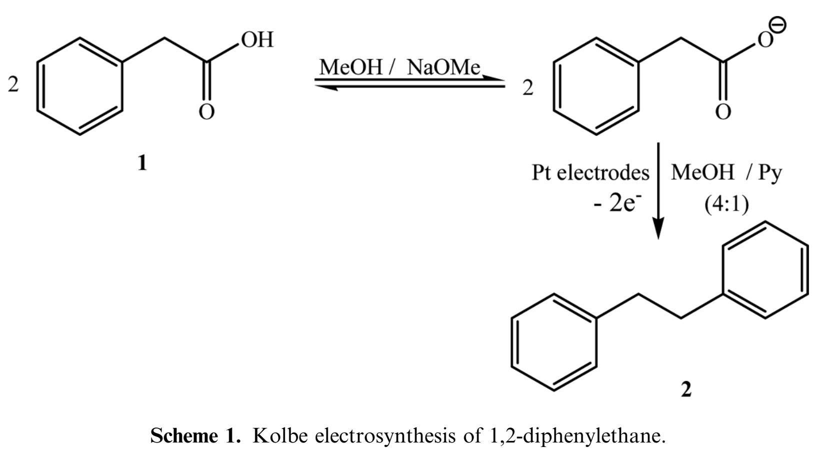
The Kolbe reaction consists of the oxidative decarboxylation of a carboxylic acid with the formation of a radical intermediate that can react in coupling reactions. Depending on the experimental conditions, the anodic decarboxylation of carboxylates, generated from carboxylic acids, can afford radicals (Kolbe electrolysis) or carbocations (non-Kolbe electrolysis)[10] at the anode, in a selective fashion. The radicals can be used in homo- and heterocoupling or in inter- and intramolecular addition reactions to double bonds.[11] The selectivity of the Kolbe synthesis is strongly dependent on the chemical structure of carboxylic acid(s) and on the experimental conditions.[10] The Kolbe reaction mechanism involves an initial electron transfer from the carboxylates at the anode, giving rise to a radical that can decarboxylate, and the radicals combine between them, producing the dimer.[12] If a cation is formed, it may react in a non-Kolbe reaction, namely by substitution, disproportionation, C-C bond cleavage or rearrangement, affording compounds such as alcohols, ethers, esters, and amides.[13] The best conditions to obtain the dimer are high current density, 0.25 V–1.0 A/cm^2, platinum electrodes, neutral or slightly acidic aqueous methanol as solvent, and temperatures less than 50 °C.[10]

In this work, we describe the electrosynthesis of 1,2-diphenylethane and 1,2-di(bicyclo[2.2.1]heptan-2-yl)ethane at low current density. The synthesis of 1,2-diphenylethane at high current density was described previously.[14]

RESULTS AND DISCUSSION

Electrosynthesis of 1,2-Diphenylethane

A solution of phenylacetic acid **1** 0.8 M was electrolyzed at platinum electrodes using a current density of 15 mA · cm^{-2} in MeOH/Py, in the presence of 10% of sodium methoxide (NaOMe), which was used to neutralize the carboxylic acid at a controlled temperature of 19 °C (Scheme 1). The expected product, 1,2-diphenylethane **2**, was obtained in 2.5% yield (Table 1, entry 1). To improve the dimer yield, we studied the influence of the concentration of NaOMe. We found that an increase



Scheme 1. Kolbe electrosynthesis of 1,2-diphenylethane.

Table 1. Electrosynthesis of 1,2-diphenylethane by electrolysis of phenylacetic acid (0.8 M) at platinum electrodes and at constant current density (15 mA · cm^{-2}) in MeOH/Py (4:1)

Entry	NaOMe (%)	Electrodes (cm^2)	Time (h)	Temperature (°C)	Charge (C)	n[a]	Product **2** (%)	
							η_m	η_c
1[b]	10	1.1 × 1.1	7.00	5	915	0.5	2.5	3.4
2[b]	50	1.1 × 1.1	7.47	5	976	0.5	0.4	0.4
3[c]	10	2.5 × 2.5	9.37	19	6325	1.6	77	29

[a] Number of electrons involved per molecule of phenylacetic acid.

[b] Total volume of electrolyte solution was 25 cm^3.

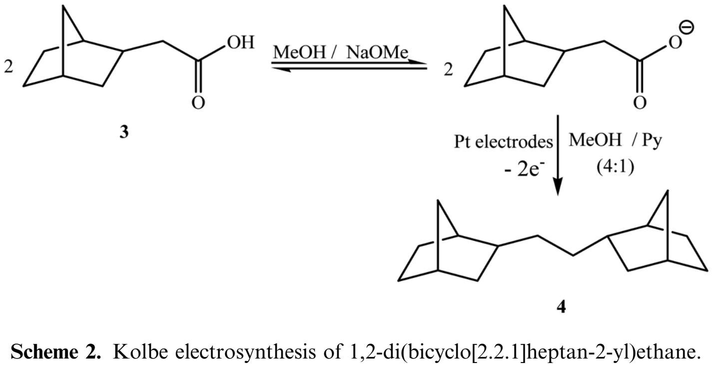
[c] Total volume of electrolyte solution was 50 cm^3.

Note. η_m = [obtained mass of dimer (g) / theoretical mass of dimer (g)] × 100; η_c = [moles of product obtained by a charge *c* / theoretical moles of product obtained by a charge *c*] × 100.

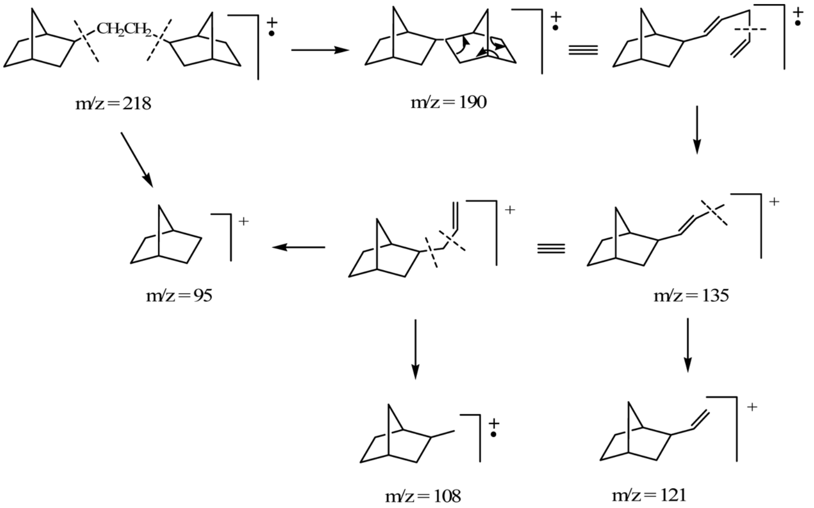
on the concentration from 10% to 50% led to a decrease in the yield of **2** to 0.4% (Table 1, entry 2). The influence of the electrode's size was also explored, and an increase from 1.1 × 1.1 cm^2 to 2.5 × 2.5 cm^2 in the presence of 10% NaOMe led to a mass yield (η_m) of 77% with a current efficiency (η_c) of 29% (Table 1, entry 3). A higher current efficiency (55%) using a current density of 128 mA · cm^{-2} was reported.[13] The dimer **2** was identified by nuclear magnetic resonance spectra (^{1}H and ^{13}C), and its melting point is in good agreement with that reported.[14] The number of electrons obtained in the formation of the dimer was 1.6 e− instead of 1. This is because of the formation of by-products from non-Kolbe reactions, observed as high-polarity compounds in thin-layer chromatography (TLC).

Electrosynthesis of 1,2-Di(bicyclo[2.2.1]heptan-2-yl)ethane

The electrosynthesis of 1,2-di(bicyclo[2.2.1]heptan-2-yl)ethane **4** (Scheme 2) starting with 0.8 M 2-norbornaneacetic acid **3** was also carried out at constant current with a density of 15 mA · cm^{-2} in MeOH/Py (4:1) in the presence of 10% of sodium methoxide, at a constant temperature (19 °C) at platinum electrodes (2.5 × 2.5 cm^2). The number of electrons involved in the reaction per molecule of 2-norbornaneacetic acid was equal to 2. Again, as in the electrosynthesis of 1,2-diphenylethane, this value is a result of the formation of by-products by non-Kolbe



Scheme 2. Kolbe electrosynthesis of 1,2-di(bicyclo[2.2.1]heptan-2-yl)ethane.



Scheme 3. Partial sequence of fragmentation for compound **4**.

reactions, observed as polar compounds in TLC. The expected product, 1,2-di(bicyclo[2.2.1]heptan-2-yl)ethane (**4**), was obtained in a mass yield of 72% and a current efficiency of 71%. ^{1}H NMR, ^{13}C NMR, ^{1}H–^{1}H correlation spectroscopy (COSY), heteronuclear single quantum coherence (HSQC), heteronuclear multiple-bond correlation (HMBC), and mass spectrometry (MS) data (Scheme 3) were consistent with the dimer **4** structure.

CONCLUSIONS

These results demonstrate that Kolbe synthesis can be carried out under experimental conditions that are not favorable to dimer formation. In fact, it is reported[10] that high current densities are needed to obtain the desired dimer. However, the dimers, 1,2-diphenylethane and 1,2-di(bicyclo[2.2.1]heptan-2-yl)ethane, were obtained from the electro-oxidation of phenylacetic and 2-norbornaneacetic acids, respectively, in yields better than 70% at low current density and at room temperature. Thus, we have developed a "green" methodology that enables the reaction to be carried out under mild conditions, operating at room temperature using low current densities. Moreover, the product, 1,2-di(bicyclo[2.2.1]heptan-2-yl)ethane, is new, and this work describes it for the first time.

EXPERIMENTAL

Phenylacetic acid (Merck, >99%), 2-norbornaneacetic acid (2-(bicyclo[2.2.1]heptan-2-yl)acetic acid) (Sigma-Aldrich, >98%), pyridine (Sigma-Aldrich, >99%), sodium methoxide (Fluka, ≥97%), and methanol (Sigma-Aldrich, >98%) were used as received. TLC was carried out on Merck silica-gel 60 F254 TLC plates. Melting points were measured on a Büchi melting-point B-540 apparatus. Electron impact mass spectrometry (EIMS) was carried out on a VG Autospec M and recorded at

70 eV; ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC 250P spectrometer or a Bruker Avance II, at 600 MHz (^{1}H NMR) and 150.9 MHz (^{13}C NMR) in $CDCl_3$. Chemical shifts are given in parts per million (ppm) and were measured versus residual peak of the solvent, 7.26 ppm for ^{1}H and 77.0 ppm for ^{13}C. Two-dimensional experiments (^{1}H–^{1}H COSY, HSQC, HMBC) were performed with standard Bruker software and were carried out for complete assignment of proton and carbon signals in the NMR spectra.

Constant-Current Electrolysis

Electrolyses were carried out in a single-compartment glass cell with two Pt foil electrodes separated by 5 mm, under magnetic stirring at a constant current of 15 mA/cm^2 using a dc power supply (Good Will Instruments GSP-3030D). Electrolyte solution volumes were 25 cm^3 or 50 cm^3, using 1.1×1.1 cm^2 or 2.5×2.5 cm^2 electrodes, respectively. The carboxylic acid was dissolved in MeOH/Py (4:1) and partially neutralized with NaOMe. The electrolysis was carried out at room temperature, until the pH of electrolyte solution was approximately 8. During the reaction, every 30 min, the polarity inversion was performed to avoid electrode passivation. After the electrolysis, the reaction mixture was extracted with chloroform (3×20 cm^3) and washed with water. The combined organic extracts were dried (Na_2SO_4) and concentrated. The crude residue was submitted to column chromatography over silica gel G (230–400 mesh) using n-hexane/ethyl acetate gradients of increasing polarity as solvent.

1,2-Diphenylethane (2)

White crystals; mp 50.1–51.3 °C; IR (nujol) 3086, 3064, 3031 (υ arC-H), 2960, 2927, 2856 (υ C-H), 1947, 1881, 1810, 1775 (comb monosubst.), 1599, 1487 (υ arC-C), 1146, 1027, 968 (δip arC-H), 909, 752, 699 (δoop) cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$), δ 2.95 (s, 4H, H-1 and H-2), 7.15–7.24 (m, 7H, H aromatic), 7.28–7.35 (m, 3H, H-aromatic); ^{13}C NMR (63 MHz, $CDCl_3$), δ 38.1 (C-1 and C-2), 126.4 (C-4′ and C-4″), 128.6 (C-2′, C-6′, C-2″ and C-6″), 128.9 (C-3′, C-5′, C-3″ and C-5″), 141.9 (C-1′ and C-1″).

1,2-Di(Bicyclo[2.2.1]heptan-2-yl)ethane (4)

White crystals; mp 98.3–99.2 °C; IR (nujol) 2952, 2933, 2873, 2854 (υ C-H), 1455 (δ CH2) cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$), δ 1.17–1.21 and 0.97–1.04 (m, 4H, H-6′ and H-6″), 1.23–1.28 (m, 2H, H-2′ and H-2″), 1.24–1.28 (m, 4H, H-1 and H-2), 1.34–1.41 and 0.93–1.00 (m, 4H, H-7′ and H-7″), 1.39–1.46 and 1.04–1.10 (m, 4H, H-3′ and H-3″), 1.42–1.46 and 1.08–1.12 (m, 4H, H-4′ and H-4″), 1.89–1.94 (m, 2H, H-1′, H-1′), 2.11–2.16 (m, 2H, H-5′, H-5″); ^{13}C NMR (150.9 MHz, $CDCl_3$), δ 28.9 (C-3′ and C-3″), 30.2 (C-4′ and C-4″), 35.3 (C-6′ and C-6″), 35.3 and 35.4 (C-1 and C-2), 36.6 (C-5′ and C-5″), 38.4 (C-7′ and C-7″), 41.2 (C-1′ and C-1″), 42.5 (C-2′ and C-2″); EIMS (%) *m/z* 218 (5) [M]$^{+}$, 190 (11), 135 (8), 121 (10), 108 (15), 95 (100).

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