Tetrahedron Letters, Vol. 33, No. 27, pp. 3911-3914, 1992
Printed in Great Britain

0040-4039/92 $5.00 + .00
Pergamon Press Ltd

Electrosynthesis of 4-Aryl-2-Methylfurans

Fructuoso Barba* and José Luis de la Fuente
Department of Organic Chemistry, University of Alcalá de Henares, Madrid, Spain

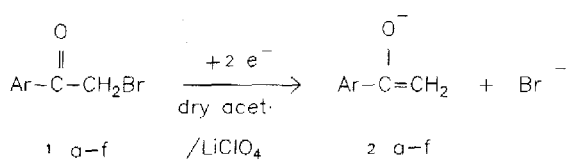
Abstract: *The electrochemical reduction on Hg cathode of a dropping solution of phenacyl bromides in dry acetone-$LiClO_4$ yields 4-aryl-2-methylfurans and acetophenones. In this process the acetone plays a dual role, as solvent and reagent.*

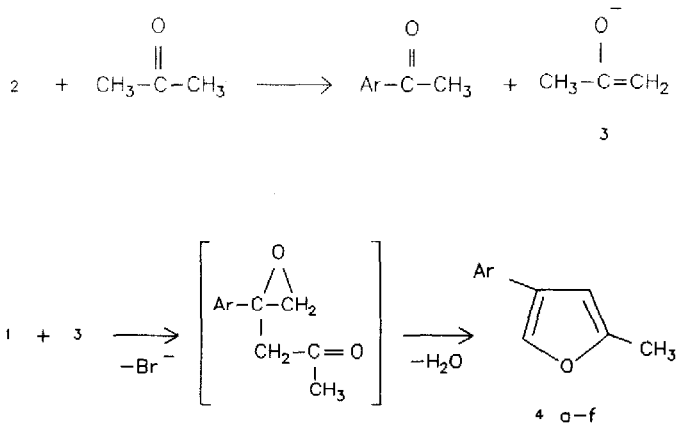
The furan ring system continues to be of interest to synthetic chemists, since many furans exist in nature and some of them exhibit interesting biological activities[1].

However, the synthesis of 4-aryl-2-methylfurans have not been developed at present with practical methods that involve at the same time, good yields, easy starting materials and facile work up. Only some attempts have been published in the literature for the synthesis of 2-methyl-4-phenylfuran[2-10]. We have developed a novel alternative to the classic furan synthesis.

Previosly, we have described how the cathodic reduction of phenacyl bromides leads to the generation of the intermediate anions. These negatively charged species may function as nucleophiles, giving 2,4-diarylfurans[11,12] or as electrogenerated bases (EGBs), leading to *(E)*-4-bromo-1,3-diaryl-2,3-epoxybutan-1-one[13]. The outcome depends mainly on the substrate concentration in the reaction medium.

In this paper we report our results on the suppression of the anion's potency as a nucleophile by running the electrochemical reaction at a very low concentration in dry acetone as solvent, as outlined in Scheme 1.





1-2-4	Ar	Product	Yield(%)[a]	m.p.(°C)[b]
a	C_6H_5	4a	78	60-61
b	4-Br-C_6H_4	4b	64	90-91
c	4-Cl-C_6H_4	4c	66	84-85
d	4-CH_3-C_6H_4	4d	62	58-59
e	4-CH_3O-C_6H_4	4e	44	106-107
f	4-C_6H_5-C_6H_4	4f	84	164-166

a. Yield was calculated according to the stoichiometry.

b. Uncorrected.

Scheme 1

According to Scheme 1, the electrogenerated anion **2** cannot react with another adsorbed molecule, because the concentration of **1** adsorbed onto the mercury electrode is low compared to the concentration of the solvent. The enolate reacts in solution with a molecule of acetone by abstracting a proton (the enolate is a hard base) to give a new anion **3** and arylmethylketone. This anion then adds to the carbonyl group of another molecule of the substrate and finally cyclises to give 4-aryl-2-methylfurans **4**.

The advantages of the present route are: unambiguous position of the substituents, good yields and easy availability of starting materials. The only drawback of the method is that half of the phenacyl bromide is converted into acetophenone.

General Procedure:

Anode: Platinum.

Anolyte: Lithium perchlorate (4 mmol) in dry acetone (20 mL).

Cathode: Mercury pool.

Catholyte: Lithium perchlorate (6 mmol) in dry acetone (30 mL).

Electrolysis cell: Divided cell thermostated at 15 °C, equipped with a magnetic stirrer containing a piece of glass tubing with a glass frit of medium porosity at one end (anode compartment). Solid sodium carbonate (2.0 g) was added to the anode compartment for *in situ* neutralization of the acid generated.

All reagents were purchased from the Fluka Chemical Co. and the Aldrich Chemical Co.. The acetone was dried at least 24 hours over anhydrous K_2CO_3 and then distilled according to the procedure of Weissberger and Proskauer[14].

The solution of **1** (5 mmol in 15mL of dry acetone) was dropped slowly onto the cathodic compartment and a potential of -1.0 v vs ECS was applied. A new drop was added when the current approached zero. The consumed charge was 1.0 $Fmol^{-1}$. The electrolysis was carried out using an Amel potentiostat model 552 with an electronic integrator Amel model 721.

The cathode solution was worked up by evaporation of the solvent to dryness at 30 °C under reduced pressure. The residue was extracted with ether and washed with water (2x50 mL) to remove inorganic salts. The extract was dried (anhydrous Na_2SO_4) and then evaporated to dryness under reduced pressure. The crude reaction products were chromatographed on a silica gel column (14 cm x 2 cm, 230-400 mesh) using CH_2Cl_2-hexane (1:1) as eluent for **4a**, **4d** and **4e** and (1:3) for **4b** and **4c**. Colourless crystals were obtained after crystallization from methanol. When **1f** is the substrate, the crude reaction product was obtained by removing the acetone and adding water to dissolve the electrolyte, leaving a white solid **4f**, which was collected by vacuum filtration and then crystallized from $CHCl_3$.

2-Methyl-4-phenylfuran (**4a**):

The physical and spectroscopic data are in accordance with that described in the literature[4].

4-(4'-Bromophenyl)-2-methylfuran (**4b**):

M.S. (70 eV), m/z (rel. int.): 238 (M^++2,71), 236 (M^+,75), 209 (11), 207 (12), 129 (45), 128 (100), 127 (33), 126 (10), 102 (15), 77 (10), 75 (14). IR (KBr)√: 1564, 1547, 1483, 1409, 1130, 1074, 1007, 919, 829, 800, 763 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 7.56 (1H, s, 5H); 7.48-7.29 (4H, m, $H_{arom.}$); 6.25 (1H, s, 3H); 2.33 (3H, s, CH_3). Anal. Calcd. for $C_{11}H_9BrO$: C, 55.72; H, 3.82. Found: C, 55.91; H, 3.74.

4-(4'-Chlorophenyl)-2-methylfuran (**4c**):

M.S. (70 eV), m/z (rel. int.): 194 (M^++2,29), 192 (M^+,100), 163 (18), 149 (6), 129 (53), 128 (56), 127 (33), 126 (8), 102 (7), 101 (8), 77 (8), 75 (14). IR (KBr)√: 1544, 1486, 1412, 1131, 1095, 922, 832, 799, 763 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 7.56 (1H, s, 5H); 7.38-7.29 (4H, m, $H_{arom.}$); 6.26 (1H, s, 3H); 2.33 (3H, s, CH_3). Anal. Calcd. for $C_{11}H_9ClO$: C, 68.59; H, 4.71. Found: C, 68.77; H, 4.62.

2-Methyl-4-(4'-methylphenyl)furan (**4d**):

M.S. (70 eV), m/z (rel. int.): 173 (M^++1,12), 172 (M^+,100), 143 (29), 129 (55), 128 (58), 127 (16), 115 (25), 91 (8), 89 (7), 77 (10), 65 (8), 63 (14), 51 (11). IR (KBr)√: 1556, 1504, 1443, 1214, 1183, 1126,

917, 804, 756 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 7.54 (1H, s, 5H); 7.35-7.14 (4H, m, $H_{arom.}$); 6.28 (1H, s, 3H); 2.35 (3H, s, CH_3-Ph); 2.33 (1H, s, CH_3). Anal. Calcd. for $C_{12}H_{12}O$: C, 83.70; H, 7.02. Found: C, 83.92; H, 6.90.

4-(4'-Methoxyphenyl)-2-methylfuran **(4e)**:

M.S. (70 eV), m/z (rel. int.): 189 (M^+ + 1,12), 188 (M^+,100), 173 (76), 159 (11), 145 (22), 128 (10), 127 (9), 117 (13), 116 (15), 115 (52), 91 (18), 89 (11), 63 (14). IR (KBr)✓: 1556, 1502, 1252, 1180, 1123, 1030, 835, 805, 756 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 7.50 (1H, s, 5H); 7.39-7.26 (4H, m, $H_{arom.}$); 6.25 (1H, s, 3H); 3.82 (3H, s, CH_3O); 2.32 (3H, s, CH_3). Anal. Calcd. for $C_{12}H_{12}O_2$: C, 76.58; H, 6.42. Found C, 76.76; H, 6.32.

2-Methyl-4-(4'-phenylphenyl)furan **(4f)**:

M.S. (70 eV), m/z (rel. int.): 235 (M^+ + 1,17), 234 (M^+,100), 205 (20), 203 (13), 202 (14), 191 (22), 189 (14), 165 (13), 128 (13), 101 (10), 77 (11), 76 (10). IR (KBr)✓: 1559, 1485, 1154, 1126, 839, 833, 807, 754, 688 cm^{-1}. ^1H NMR (DMSO-d_6) δ: 8.00 (1H, s, 5H); 7.62-7.34 (9H, m, $H_{arom.}$); 6.62 (1H, s, 3H); 2.34 (3H, s, CH_3). Anal Calcd. for $C_{17}H_{14}O$: C, 87.14; H, 6.02. Found: C, 87.36; H, 5.90.

Acknowledgements:

This study was financed by DGICYT PB88-0153 and the Autonomous Community of Madrid N° C018/90.

REFERENCES:

(1) Padwa, A.; Murphree, S.S.; Yeske, P.E. *J. Org. Chem.* **1990**, *55*, 4241 and references cited therein.

(2) Raties, M.; Drouillard, S; Trouve, B.; Duboudin, J.G. *Synth. Commun.* **1986**, *16*, 1509.

(3) Okazaki, R.; Negishi, Y.; Inamoto, N. *J. Org. Chem.* **1984**, *49*, 3819.

(4) Pri-Bar, I.; Pearlman, P.S.; Stille, J.K. *J. Org. Chem.* **1983**, *48*, 4629.

(5) Kosugi, H.; Takano, I.; Hoshino, I.; Migita, T. *J. Chem. Soc. Chem. Commun.* **1983**, 989.

(6) Okazaki, R.; Negishi, Y; Inamoto, N. *J. Chem. Soc. Chem. Commun.* **1982**, 1055.

(7) Nishio, T.; Sugawara, M.; Omote, Y. *J. Heterocyclic. Chem.* **1979**, *16*, 815.

(8) Schreurs, P.H.M.; de Jong, A.J.; Brandsma, L. *Rec. Trav. Chim.* **1976**, *95*, 75.

(9) Miller, D. *J. Chem. Soc. (C).* **1969**, 12.

(10) Morel Th.; Verkade, P.E. *Rec. Trav. Chim.* **1951**, *70*, 35.

(11) Barba, F.; Velasco, M.D.; Guirado, A. *Synthesis.* **1981**, 625.

(12) Barba, F.; Velasco, M.D.; Guirado, A. *Electrochim. Acta.* **1983**, *28*, 259.

(13) Barba, F.; Velasco, M.D.; López, M.I.; Zapata, A.; Aldaz, A. *J. Chem. Research(s).* **1988**, 44.

(14) Weissberger, A.; Proskauer, E. *Organic Solvents.* (ed.), Oxford Press, London. 1935, p.143.

(Received in UK 7 April 1992)