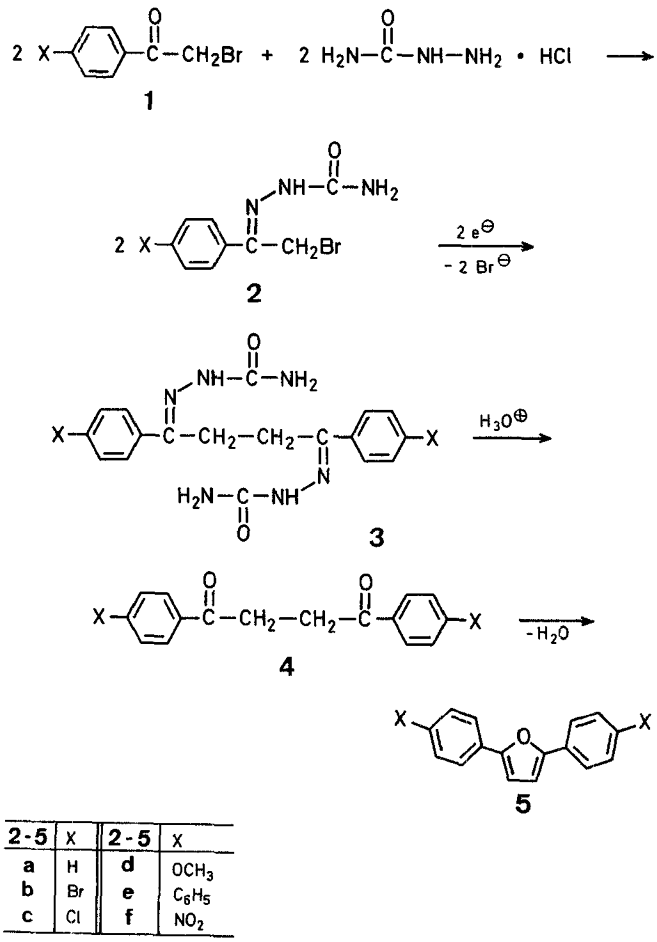
Synthesis of 2,5-Diarylfurans from Phenacyl Bromides

Fructuoso BARBA*, M. Desamparados VELASCO, Antonio GUIRADO

Department of Organic Chemistry, University of Murcia, Murcia, Spain

We have previously reported the electrochemical synthesis of 2,4-diarylfurans by the direct cathodic reduction of phenacyl bromides[1]. The reduction generates enolate anions which undergo addition reactions with the carbonyl groups[2]. We now describe the synthesis of 2,5-diarylfurans (5) from the same starting materials, the carbonyl groups being protected by semicarbazone formation prior to the electrochemical reduction.



2-5	X	2-5	X
a	H	d	OCH_3
b	Br	e	C_6H_5
c	Cl	f	NO_2

The reaction of phenacyl bromides (1) with semicarbazide gives the corresponding semicarbazones (2) which are isolated as crystalline solids. Cathodic reduction of compounds 2 affords the dimeric products 3 in practically quantitative yields. Acid hydrolysis of 3 gives 1,4-diaryl-1,4-butanediones (4) which are dehydrated to give the 2,5-diarylfurans 5. In some cases, hydrolysis of 3 leads directly to the furans. The conversion 2 → 3 involves nucleophilic attack of the electrochemically generated carbanion (derivative of 2) on an unreduced molecule of 2.

Several methods for the synthesis of 2,5-diarylfurans have been reported[3,4,5]. Advantages of the present route are: unambiguous position of the substituents; good yields; easy availability of starting materials.

ω-Bromoacetophenone Semicarbazones (2); General Procedure:
To a solution of semicarbazide hydrochloride (10 g, 90 mmol) in water (50 ml), the appropiate phenacyl bromide (**1**; 20 mmol) in methanol (50 ml) is added under vigorous stirring. The quantitatively precipitated solid **2** is isolated by suction and recrystallized from ethanol (Table 1).

Table 1. ω-Bromoacetophenone Semicarbazones **(2)**

2	Yield	m.p.[a] [°C]	Molecular Formula[b] or Lit. m.p. (°C)	
a	nearly	145°	146°[6]	
b	quanti-	156°	$C_9H_9Br_2N_3O$	(335.1)
c	tative	151°	$C_9H_9BrClN_3O$	(290.6)
d		148–150°	$C_{10}H_{12}BrN_3O_2$	(286.1)
e		185°	$C_{15}H_{14}BrN_3O$	(332.2)
f		181–182°	$C_9H_9BrN_4O_3$	(301.1)

[a] Uncorrected.

[b] Satisfactory microanalyses obtained: C, ±0.43; H, ±0.21; N, ±0.32.

1,4-Diaryl-1,4-butanedione Semicarbazones (3); General Procedure:
Anode: Platinum.
Anolyte: Lithium perchlorate (4 mmol) in dry dimethylformamide (20 ml).
Cathode: Mercury pool.
Catholyte: ω-Bromoacetophenone semicarbazone **2** (5 mmol) and lithium perchlorate (6 mmol) in dry dimethylformamide (30 ml).
Electrolysis Cell: Divided cell thermostated at 20 °C, equipped with a magnetic stirrer containing a piece of glass tubing with glass frit of medium porosity at one end to serve as auxiliary electrode (anode compartment).

The electrolysis is carried out under a controlled potential of −1 V (vs saturated calomel electrode) using an Amel potentiostat model 557 with an electronic integrator Amel model 558.

Solid sodium thiosulphate (2 g) and sodium carbonate (3 g) are added to the anode compartment for *in situ* neutralization of the bromine and acid generated. The electrolysis is continued until the current decreases to less then 1% of the starting value. The amount of charge passed is equivalent to 1 electron consumed per molecule of substrate. The cathode solution is worked up by evaporation of the solvent to dryness at 60 °C under reduced pressure. The residue is extracted with water (2 × 50 ml) to remove inorganic salts, then washed with cold methanol, and recrystallized from dimethyl sulphoxide/methanol to give the product **3** (Table 2).

Table 2. 1,4-Diaryl-1,4-butanedione Bis-semicarbazones **(3)**

3	Yield[a] [%]	m.p.[b] [°C]	Molecular Formula[c]	
a	97	215–217°	$C_{18}H_{20}N_6O_2$	(352.4)
b	98	227–228°	$C_{18}H_{18}Br_2N_6O_2$	(510.2)
c	94	221°	$C_{18}H_{18}Cl_2N_6O_2$	(421.3)
d	95	215–216°	$C_{20}H_{24}N_6O_4$	(412.5)
e	96	270° (dec)	$C_{30}H_{28}N_6O_2$	(504.6)
f	94	240° (dec)	$C_{18}H_{18}N_8O_6$	(442.4)

[a] Yield of pure isolated product.

[b] Not corrected.

[c] Satisfactory microanalyses obtained: C, ±0.24; H, ±0.14; N, ±0.17.

1,4-Diaryl-1,4-butanediones (4); General Procedure:
The semicarbazone **3** (5 mmol) is hydrolyzed with 15% hydrochloric acid (50 ml) containing mercury (II) chloride (5%) under reflux for 6 h. The mixture is added to crushed ice (100 g) and the precipitate is crystallized from acetic acid or ethanol. The hydrolysis of **3f** is carried out by a similar procedure, using concentrated hydrochloric acid.

1,4-Bis[4-bromophenyl]-1,4-butanedione (**4b**); yield: 1.6 g (81%); colourless flakes from acetic acid, m.p. 182–183 °C (Ref.[7], m.p. 180–181 °C).

$C_{16}H_{12}Br_2O_2$	calc.	C 48.52	H 3.05
(396.1)	found	48.39	3.16

M.S.: *m/e* (relative intensity) = 398(2), 396(4), 394(M$^+$, 2), 185(97), 183(100), 157(35), 155(35), 104(11), 76(32), 75(26), 50(21).

I.R. (Nujol): ν = 1670, 1588, 1330, 1195, 1079, 1005, 852, 832, 798, 790 cm^{-1}

1,4-Bis[4-chlorophenyl]-1,4-butanedione (**4c**); yield 1.3 g (85%); colourless flakes from ethanol; m.p. 151–152 °C (Ref.[8], m.p. 151 °C).

$C_{16}H_{12}Cl_2O_2$	calc.	C 62.56	H 3.94
(307.2)	found	62.21	4.03

M.S.: *m/e* (relative intensity) = 308(2), 306(M$^+$, 3), 167(8), 141(31), 139(100), 113(10), 111(31), 75(16).

I.R. (Nujol): ν = 1667, 1581, 1568, 1482, 1320, 1186, 1090, 1002, 852, 785 cm^{-1}.

1,4-Bis[4-methoxyphenyl]-1,4-butanedione (**4d**); yield 1.1 g (74%); colourless crystals from acetic acid; m.p. 151 °C; (Ref.[7], m.p. 150–151 °C).

$C_{18}H_{18}O_4$	calc.	C 72.47	H 6.08
(298.3)	found	72.70	6.22

M.S.: *m/e* (relative intensity) = 298(M$^+$, 2), 163(6), 136(9), 135(100), 107(10), 92(14), 77(22), 64(7).

I.R. (Nujol): ν = 1668, 1600, 1573, 1504, 1260, 1238, 1172, 1181, 1029, 990, 838 cm^{-1}.

1,4-Bis[4-biphenylyl]-1,4-butanedione (**4e**); yield 1.5 g (77%); colourless crystals from acetic acid, m.p. 265–267 °C.

$C_{28}H_{22}O_2$	calc.	C 86.13	H 5.68
(390.5)	found	85.87	5.83

M.S.: *m/e* (relative intensity) = 390(M$^+$, 7), 182(14), 181(100), 153(25), 152(39).

I.R. (Nujol): ν = 1647, 1674, 1232, 1200, 1184, 990, 841, 729, 690 cm^{-1}.

Hydrolysis of the semicarbazones **3a** and **3f** gives the furans **5a** and **5f** directly.

2,5-Diarylfurans (5); General Procedures:
In the cases in which the furans are not obtained directly from the hydrolysis step, cyclodehydration of diketones **4** is carried out by one of following methods:

Method A: The diketone **4** (10 mmol) and polyphosphoric acid (8 g) are stirred and heated at 140 °C for 1.5 h. Then, crushed ice (100 g) is added. The crystalline furan is isolated by suction and recrystallized from ethanol or chloroform.

Method B: Polyphosphoric acid (0.5 g) is added to a stirred mixture of diketone **4** (10 mmol) and acetic anhydride (75 ml) and stirring at room temperature is continued for 30 min. The solution is poured into ice/water and the mixture ist stirred for 2 h. The furan is isolated by suction and recrystallized from ethanol.

2,5-Diphenylfuran (**5a**); this compound is obtained by hydrolysis of 1,4-diphenyl-1,4-butanedione semicarbazone (**3a**); yield: 1.7 g (77%); colourless crystals from ethanol, m.p. 88 °C (Ref.[9], m.p. 88–89 °C).

$C_{16}H_{12}O$	calc.	C 87.25	H 5.49
(220.3)	found	87.04	5.61

M.S.: *m/e* (relative intensity) = 221(M$^+$ + 1, 18), 220(M$^+$, 100), 191(18), 115(59), 110(18), 105(32), 89(13), 77(43), 51(17).

I.R. (Nujol): ν = 1608, 1022, 929, 798, 766, 760, 697, 676 cm^{-1}.

2,5-Bis[4-bromophenyl]-furan (**5b**); dehydration Method A; yield: 3.1 g (82%); colourless flakes from ethanol, m.p. 201 °C (Ref.[9], m.p. 201–202 °C).

$C_{16}H_{10}Br_2O$	calc.	C 50.83	H 2.67
(378.1)	found	51.01	2.75

M.S.: *m/e* (relative intensity) = 380(40), 378(79), 376(M$^+$, 41), 189 (100), 157(44), 155(45), 114(68), 94(83), 76(50), 75(50).

I.R. (Nujol): ν = 1588, 1077, 1011, 1007, 926, 830, 818, 794 cm^{-1}.

2,5-Bis[4-chlorophenyl]-furan (**5c**; X = Cl); dehydration Method A; yield: 2.1 g (73%); colourless needles from ethanol, m.p. 167–168 °C (Ref.[9], m.p. 168–169 °C, Ref.[11], m.p. 169–170 °C).

$C_{16}H_{10}Cl_2O$	calc.	C 66.46	H 3.49
(289.2)	found	66.78	3.66

M.S.: *m/e* (relative intensity) = 290(65), 288(M$^+$, 100), 225(24), 189(22), 151(22), 149(66), 139(57), 111(51), 94(34), 75(30).

I.R. (Nujol): ν = 1110, 1098, 1024, 1006, 928, 835, 797 cm^{-1}.

2,5-Bis[4-methoxyphenyl]-furan (**5d**); dehydration Method B; yield: 2.1 g (75%); colourless crystals from ethanol, m.p. 195–196 °C (Ref.[10], m.p. 195–196 °C).

$C_{18}H_{16}O_3$	calc.	C 77.12	H 5.75
(280.3)	found	76.97	5.90

M.S.: *m/e* (relative intensity) = 281(M$^+$ + 1, 20) 280(M$^+$, 100), 266(19), 265(93), 222(12), 194(25), 165(18), 140(50), 118(17), 77(13), 76(10).

I.R. (Nujol): ν = 1500, 1289, 1250, 1029, 839, 788 cm^{-1}.

2,5-Bis[4-biphenylyl]-furan (**5e**); dehydration Method A; yield. 3.2 g (86%); colourless crystals from chloroform, m.p. 284–286 °C.

$C_{28}H_{20}O$	calcd.	C 90.29	H 5.41
(372.5)	found	89.93	5.49

M.S.: *m/e* (relative intensity) = 373(M$^+$ + 1, 32), 372(M$^+$, 100), 191(30), 186(42), 152(36).

I.R. (Nujol): ν = 1600, 849, 792, 767, 728, 697 cm^{-1}.

2,5-Bis[4-nitrophenyl]-furan (**5f**); obtained by hydrolysis of **3f**; yield: 2.5 g (80%); red crystals from acetic acid, m.p. 210 °C (dec).

$C_{16}H_{10}N_2O_5$	calcd.	C 61.94	H 3.25	N 9.03
(310.3)	found	62.21	3.37	8.86

M.S.: *m/e* (relative intensity) = 311(M$^+$ + 1, 19), 310(M$^+$, 100), 280 (16), 264(13), 234(17), 218(10), 190(18), 189(53), 76(8).

I.R. (Nujol): ν = 1596, 1507, 1340, 1330, 1110, 933, 855, 795, 755, 699 cm^{-1}.

Received: October 19, 1983

---

* Address for correspondence.

[1] F. Barba, M.D. Velasco, A. Guirado, *Synthesis* **1981**, 625.

[2] F. Barba, M.D. Velasco, A. Guirado, *Electrochim. Acta* **28**, 259 (1983).

[3] P. Bosshard, C.H. Eugster, *Adv. Heterocyclic Chem.* **7**, 377 (1966).

[4] K. Gump, S.W. Moje, C.E. Castro, *J. Am. Chem. Soc.* **89**, 6770 (1967).

[5] A. Kiyosi, M. Masakatsu, *Chem. Lett.* **1974**, 701.

[6] *Handbook of Tables for Organic Compound Identification*, 3rd Ed., CRC Press, Inc., Florida, 1980, p. 173.

[7] E.E. Campaigne, W.O. Foye, *J. Org. Chem.* **17**, 1405 (1952).

[8] *Beilstein Handbuch der Organischen Chemie*, VII.

[9] G. Nowlin, *J. Am. Chem. Soc.* **72**, 5754 (1950).

[10] Ph.S. Bailey, H.M. White, *J. Org. Chem.* **30**, 487 (1965).

[11] A.A. Gorman, G. Lovering, M.A.J. Rodgers, *J. Am. Chem. Soc.* **101**, 3050 (1979).