Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Synthesis of 3-Alkoxy-, 3-Aryloxy- and 3-Substituted Amino-2,5-Diarylfurans by Reductive-Furanization of α,β-Unsaturated-1,4-Diketones

Arvind Kumar [a] & David W. Boykin [a]

[a] Department of Chemistry , Georgia State University Atlanta , Georgia, 30303-3083, USA

To cite this article: Arvind Kumar & David W. Boykin (1995) Synthesis of 3-Alkoxy-, 3-Aryloxy- and 3-Substituted Amino-2,5-Diarylfurans by Reductive-Furanization of α,β-Unsaturated-1,4-Diketones, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 25:14, 2071-2078, DOI: 10.1080/00397919508015888

To link to this article: http://dx.doi.org/10.1080/00397919508015888

SYNTHETIC COMMUNICATIONS, 25(14), 2071-2078 (1995)

SYNTHESIS OF 3-ALKOXY-, 3-ARYLOXY- AND 3-SUBSTITUTED AMINO-2,5-DIARYLFURANS BY REDUCTIVE-FURANIZATION OF α,β-UNSATURATED-1,4-DIKETONES

Arvind Kumar and David W. Boykin*

Department of Chemistry
Georgia State University
Atlanta, Georgia 30303-3083 USA

ABSTRACT: The use of phosphorus trichloride for synthesis of 3-alkoxy, 3-aryloxy and 3-substitutedamino-2,5-diarylfurans from α,β-unsaturated-1,4-diketones by reductive-furanization is reported.

INTRODUCTION: Furans substituted with strong electron donors are often difficult to obtain.[1,2,3,4] Syntheses of alkoxydiarylfurans have been reported by reductive-furanization of alkoxydibenzoylethylenes using several reducing agents including Zn/HOAc, $Na_2S_2O_4$ and $CrCl_2$.[5-7] Alkoxydiarylfurans have also been prepared by acid catalyzed addition of alcohols to dibenzoylethylenes followed by ring closure[7,8]. However, these approaches are often limited by competing reactions. In the case of reductive-furanization of unsaturated 1,4-diketones frequently the carbon-carbon double bond is reduced and the corresponding saturated-1,4-ketone is formed.[5,6] There are a more limited number of methods to prepare amino substituted furans.[1,2,4] These include cyclodehydration of α-amino substituted 1,4-diketones, which in some cases result in

---

*To whom correspondence should be addressed elimination of the amino functional group to yield α,β-unsaturated-1,4-diketones rather than aminofurans.[9]

In a study of the reduction of *cis*-dibenzoylstilbene with phosphorus trichloride which formed 2,3,4,5-tetraphenylfuran it was concluded that reductive-furanization with this reagent required two substituents on the carbon-carbon double bond of the dibenzoylethylene system.[10] However, more recently it has been reported, without experimental detail, that α-N-morpholinodibenzoylethylene slowly undergoes reductive-furanization with phosphorus trichloride to form 3-(N-morpholino)-2,5-diphenylfuran.[11] In connection with other work, we required an effective method for synthesis of both alkoxy and aminosubstituted furans and we have explored the reaction of phosphorus trichloride with α-alkoxy-, α-aryloxy- and α-substitutedaminodibenzoylethylenes.

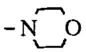
RESULTS AND DISCUSSION: The α-alkoxy-, α–aryloxy- and α-substituted amino-dibenzoylethylenes required for study of the reductive-furanization reaction were generally conveniently obtained by reaction of the appropriate alkyloxide, aryloxide or substituted amine with a 1,2-dibromo-1,2-dibenzoylethane following well established procedures.[5,9] Data for the dibenzoylethylenes investigated are listed in Table 1. Table 2 summarizes the results for the phosphorus trichloride reductive-furanization of several α-substituted-1,2-dibenzoylethylenes. Use of the change in ^{1}H- NMR signal at approximately 6.5 ppm served as a convenient method to monitor the conversion of the 1,2-dibenzoylethylenes into furans(see Table 1 and Table 2) . The phosphorus trichloride induced reductive-furanization of the alkyloxy and aryloxy-1,2-dibenzoylethenes was readily accomplished, in reasonable yields, after two to four hour reflux.

In contrast, the phosphorus trichloride reduction of α-substitutedamino-1,2-dibenzoylethylenes did not prove to be an efficient approach for formation of the corresponding 3-amino-2,5-diarylfurans. Longer reflux times, 6 to 8 hours, provided only modest yields of the 3-substitutedamino-2,5-diarylfurans. Even longer reflux times resulted in formation of significant amounts of apparently polymeric material.

Table 1

α-Substituted Dibenzoylethylenes.

$X(p)C_6H_4COCH{=}C(R)COC_6H_4(p)X$

Comp. No.	R	X	mp. (°C)	% yield	$\delta H\alpha^a$
1	OCH_3	H	106-107 (lit.[5] 108)[b]	91	6.54
2	OCH_3	Br	153-154 (lit. [12] 155)[c]	69	6.47
3	OC_6H_5	H	89-91 (lit.[5] 92)[d]	76	6.40
4	OC_6H_4 (*p*)CH_3	Br	137 -138	50	6.40
5	OC_6H_4 (*p*)CO_2Et	Br	148-149	70	6.40
6		H	164-167 (lit.[13] 169-173)[e]	86	6.00
7		Br	184-185	72	6.09

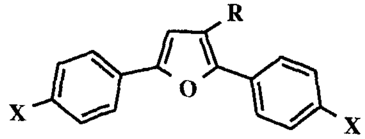
a) 1H NMR taken in $CDCl_3$ solution; see experimental section for detailed physical data on previously unreported compounds. b) MS molecular ion 266. c) MS molecular ion 424. d) MS molecular ion 328. e) MS molecular ion 321.

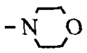
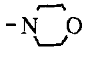
Reductive-furanization of unsaturated 1,4-diketones by phosphorus trichloride is a convenient method for synthesis of 3-alkoxy- and 3-aryloxyfurans, however, this approach provides 3-substituedaminofurans only in limited yields.

EXPERIMENTAL: 1-(4-tolyloxyl)-1,2-bis(4-bromobenzoyl)ethylene(4). To a solution of 1,2-dibromo-1,2-di(4-bromobenzoyl) ethane (11.1 g, 0.02 mole) in 35 ml of THF was added a suspension of sodium 4-methylphenoxide [prepared from 0.92 g (0.04

Table 2

3-Substituted-2,5-Diarylfurans.



Comp. No.	R	X	mp. (°C)	% yield	R'x time(hr)	δH_4[a]
8	OCH_3	H	112-113 (lit.[5] 115)[b]	64	2	6.55
9	OCH_3	Br	112-113 (lit.[6] 113)[c]	62	3	6.64
10	OC_6H_5	H	91-92 (lit.[6] 91)[d]	59	2	6.56
11	OC_6H_4 (*p*)CH_3	Br	97-98	56	4	6.47
12	OC_6H_4 (*p*)CO_2Et	Br	124-125	72	4	6.58
13		H	111-113 (lit.[9]113-114)[e]	33	6	6.75
14		Br	187-188	29	7	6.75

a) 1H NMR taken in $CDCl_3$ solution; see experimental section for detailed physical data on previously unreported compounds. b) MS molecular ion 250. c) MS molecular ion 408. d) MS molecular ion 312. e) MS molecular ion 542.

mole) sodium metal and 4.32 g(0.04 mole) 4-methylphenol in 30 ml THF by refluxing for 4-5 hr]. The yellow mixture was refluxed for 2-3 hr (monitored by TLC) after which the THF was removed under reduced pressure. The residue was treated with water, and the solid was filtered, washed with water, dried(Na_2SO_4), and dissolved in chloroform. The chloroform solution was passed through a silica column (elution with 2-5% ether in hexane). The result was an off white crystalline solid, 4.95 g (50%), mp 137-8°C. IR (KBr) 3087, 3035, 2868, 1687, 1646, 1587, 1572, 1557, 1502, 1399, 1364, 1194, 1068, 1009, 971, 876, 815, 772, 526. ^1H NMR ($CDCl_3$/35°C) 7.92 (d, 2H, J=8.8), 7.65 (d, 2H, J=8.8), 7.55 (d, 2H, J=8.8), 7.48 (d, 2H, J=8.8), 7.27 (d, 2H, J=8.3), 7.11 (d, 2H, J=8.3), 6.32 (s, 1H), 2.4 (s, 3H). ^{13}C NMR ($CDCl_3$/35°C) 189.4, 187.6, 168.4, 150.9, 136.6, 136.0, 133.4, 132.3, 131.8, 130.9, 130.3, 129.6, 129.2, 128.2, 120.6, 101.8, 20.95. Anal. Calcd. for: $C_{23}H_{16}Br_2O_3$: C, 55.23; H, 3.22. Found: C, 55.26, H, 3.19. MS: m/e 500 (M^+).

1-(4-Carboethyloxyphenoxy)-1,2-(4-bromobenzoyl)ethylene(5). The dibromoethane (11.08 g, 0.02 mole) in 75 ml dry THF was added dropwise to a suspension of sodium salt of ethyl-4-hydroxybenzoate (3.32 g, 0.04 mole, 0.92 g atom Na) in 100 ml dry THF (prepared by refluxing Na and the phenol in THF for 7-8 hr until all the sodium was consumed). The reaction mixture was heated gently with stirring for 1.5 h (TLC followed) and the solvent was distilled. The residue was treated with water, extracted with chloroform, washed with water, washed with brine and dried (Na_2SO_4). The solution was chromatographed over silica gel using (hexane: ether) (95:5 to 2:1). Recrystallization was from ether:hexane (1:2 to give an off white crystalline solid (7.8 g, 70% yield); mp 148-149°C. IR(KBr)2989,1715,1682,1656,1574,1401,1208,967,878, 752 cm^{-1}. ^1H NMR ($CDCl_3$) 8.17 (d, 2H, J=8.8), 7.91 (d, 2H, J=8.8), 7.65 (d, 2H, J=8.3), 7.54 (q, J=8.8), 7.3 (d, 2H, J=8.8) 6.4 (s, 1H), 4.41 (d, 2H, J=7.3), 1.42 (t, 3H, J=7.3). ^{13}C NMR ($CDCl_3$) 188.9, 187.3, 166.3, 165.4, 156.7, 135.8, 132.3, 132.1, 132.0, 129.7, 120.8, 103.6, 61.4, 14.3. . Anal. Calcd. for: $C_{25}H_{18}Br_2O_5$: C, 53.79; H, 3.25. Found: C, 53.76, H, 3.27. MS: m/e 558 (M^+).

1,2-Bis(4-bromobenzoyl)-3-(N-morpholino)ethylene(7). Morpholine (1.74g, 0.02mole) in 10 ml dry acetone was added, with cooling (ca.5°C) and stirring to a solution of 2.77g(0.005mole)1,2-bis(4-bromobenzoyl)-1,2-dibromoethane in 40 ml of dry acetone over a 30 min period. The mixture was allowed to stir at 5°C for an additional 30 min and the reaction mixture was allowed to stir for two days at room temperature. Morpholine hydrobromide was remove by filtration and the acetone solution was concentrated *in vaccuo* to yield a solid which was recrystallized from $CHCl_3$:ether (1:4)to give a pale yellow solid(1.7g,72%); mp 184-185°C. IR(KBr) 2972,1677,1609,1560,1215,1075,785, cm^{-1}. ^1H NMR($CDCl_3$) 7.9(d,2H,J = 8.0), 7.71(d,2H, J = 8.0), 7.65(d, 2H, J = 8.0), 7.53(d,2H, J = 8.0), 6.09(s, 1H), 3.7 (br. m, 4H), 3.3-3.5(m, 4H). ^{13}C NMR($CDCl_3$) 192.8, 184.4, 161.3, 141.5, 137.9, 135.0,132.8, 131.9, 129.8, 129.7,129.2,127.0, 66.2 48.2. Anal. Calcd. for: $C_{20}H_{17}Br_2NO_3$: C, 50.12; H, 3.57; N,2.92. Found: C, 50.09, H, 3.61; N, 2.88. MS: m/e 479(M^+).

2,5-bis(4-Bromophenyl)-3-(p-tolyloxy)furan(11). A solution of 5.0 g (0.01 mole) 1-(4-tolyloxy)-1,2-bis-(4-bromobenzoyl)ethylene in 10 ml phosphorus trichloride was heated under reflux for 3-4 hr (monitored by TLC). The excess phosphorus trichloride was removed by distillation and the residue was triturated with ice/water (exothermic reaction). The solution was extracted with dichloromethane (75 ml) and the dichloromethane layer was washed with saturated sodium bicarbonate solution, water, and dried (Na_2SO_4). The solvent was removed under reduced pressure. The residual solid was chromatographed over silica gel using ether:hexane (2:8 to 1:1) as eluant. An off white crystalline solid was obtained, 2.78 g (56%), mp 92-3°C. IR (KBr) 2923, 2851, 1560, 1506, 1467, 1390, 1209, 1072, 1066, 945, 825, 707, 486. ^1H NMR ($CDCl_3$/35°C) 7.69 (d, 2H, J=8.8), 7.46-7.43 (m, 6H), 7.12 (d, 2H, J=8.3), 7.0 (d, 2H, J=8.3), 6.47 (s, 1H), 2.31 (s, 3H). ^{13}C NMR ($CDCl_3$/135°C) 150.8, 150.1, 142.8, 139.3, 133.0, 131.9, 131.7, 130.3, 129.1, 128.6, 125.1, 125.0, 121.8, 120.5, 117.1, 102.7, 20.6. . Anal. Calcd. for: $C_{23}H_{16}Br_2O_2$: C, 57.05; H, 3.33. Found: C, 56.91, H, 3.31. MS: m/e 484 (M^+).

2,5-Bis(4-bromophenyl)-3-(4-carboethoxyphenoxy)furan(12). A mixture of the phenoxyethylene (5.6 g, 0.01 mole in phosphorus trichloride (10 ml) was heated under reflux for 4-5 hr (TLC monitored). The excess phosphorus trichloride was distilled and the residue was treated with ice and water (exothermic, external cooling required). The resultant gummy mass was extracted with chloroform and washed with brine and dried (Na_2SO_4). The resultant gummy mass was chromatographed over silica gel; elution was with hexane:ether (90:10 to 10:90). The solid was an off white crystalline; 3.9 g (72%); mp 124-5°C. IR (KBr) 2970, 1706, 1596, 1503, 1388, 1159, 1008, 820, cm^{-1}. ^1H NMR ($CDCl_3$) 8.04 (d, 2H, J=8.8), 7.65 (d, 2H, J=8.8), 7.5 (brs, 4H), 7.48 (d, 2H, J=8.8), 7.13 (d, 2H, J=8.8), 6.58 (s, 1H), 4.36 (q, 2H, J=7.3), 1.38 (t, 3H, J=7.3). ^{13}C NMR ($CDCl_3$) 165.9, 160.6, 150.6, 140.3, 132.0, 131.9, 128.9, 128.1, 126.3, 125.7, 125.3, 122.2, 121.1, 116.2, 103.0, 60.9, 14.3. . Anal. Calcd. for: $C_{25}H_{18}Br_2O_4$: C, 55.37; H, 3.34. Found: C, 55.32, H, 3.40. MS: m/e 542 (M^+).

2,5-Bis(4-bromophenyl)-3-(N-morpholino)furan(14). The procedure outlined above was followed using 1.5g(0.03mole) of **7** and 20ml of phosphorus trichloride and a 7 hr reflux time was required. The crude product was isolated as above and the compound was purified using a silica gel column. Elution was with benzene, 1:2 ether:benzene , to yield an off white crystalline solid (0.42 g, 29%); mp 187-188°C. IR(KBr) 2953, 1610, 1480, 1393, 1111, 1001, 800, 715 cm^{-1}. ^1H NMR ($CDCl_3$) 7.82 (d, 2H, J=8.8), 7.52-7.49 (m, 6H), 6.72 (s, 1H), 3.84 (m, 4H), 2.92 (m, 4H). ^{13}C NMR ($CDCl_3$) 150.7, 140.9, 138.8, 131.6, 129.8, 129.3, 125.6, 125.1, 121.4, 120.2, 102, 3, 67.1, 52.3. Anal. Calcd. for: $C_{20}H_{17}Br_2NO_2$: C, 51.86; H, 3.69; N, 3.02. Found: C, 51.91, H, 3.63; N, 2.96. MS: m/e 463 (M^+).

ACKNOWLEDGMENT

This work was supported by NIH Grants NIAID AI-27196 and AI-33363. An award by the Chemical Instrumental Program of NSF (CHE 8409599) provided partial support for acquisition of the Varian VXR400 spectrometer.

REFERENCES

1. Bossard, P. and Eugster, C.H., Adv. Het. Chem., **1966**, 7, 460.
2. Dean, F.M., Adv. Het. Chem., **1982**, 31, 250.

3. Farina, F., Martin, M.V., Martin-Aranda, R.M. and de Guerenu, A.M., Synth. Commun. **1993**, 23, 459.

4. Lythgoe, D.J., McClenaghan, I. and Ramsden, C.A., J. Heterocycl. Chem., **1993**, 30, 113.

5. Conant, J.B. and Lutz, R.E., J. Am. Chem. Soc., **1925**, 47, 881.

6. Lutz, R.E., J. Am. Chem. Soc., **1929**, 51, 3008.

7. Bailey, P.S. and Lutz, R.E., J. Am. Chem. Soc., **1949**, 69, 498.

8. Bailey, P.S. and Kelly, J.T., J. Am. Chem. Soc., **1948**, 70, 3442.

9. Lutz, R.E., Bailey, P.S. and Shearer, N.H., J. Am. Chem. Soc., **1946**, 68, 2224.

10. Lutz, R.E. and Welstead, W.J., J. Am. Chem. Soc., **1963**, 85, 755.

11. Lutz, R.E., Hankins, W.M., Hankins, M.G., Welstead, W.J. and Dickenson, C.L., J. Heterocycl. Chem., **1970**, 7, 569.

12. Lutz, R. E., J. Am. Chem. Soc. **1926**, 48, 2905.

13. Lutz, R. E. and Smithy, W. R., J. Org. Chem., **1951**, 16, 51.

(Received in the USA 01 December 1994)