CONVERSION OF α-ARYLIDENE-γ-KETO ESTERS TO DIARYLFURAN CARBOXYLIC ACID ESTERS[†]

G. Sudhakar Reddy, Syed Salahuddin, Parvathi Neelakantan* and D.S. Iyengar

Organic Chemistry Division-II, Indian Institute of Chemical Technology, Hyderabad-500 007, India.

Abstract : Formation of unsymmetrical 2,5 diarylfuran-3-carboxylic acid methyl esters from α-arylidene-γ-oxo-benzenebutanoic acid methyl esters in presence of **N**-bromosuccinimide is described.

Introduction

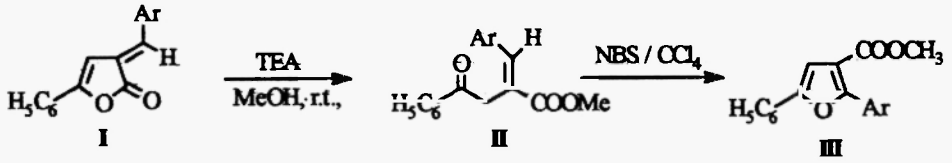
Polysubstituted furans have attracted considerable attention due to their presence as key structural units in many of the natural products,[1] important pharmaceuticals,[2] and also as good building blocks in synthetic chemistry. This has led to tremendous interest and demand for flexible synthetic strategies.

In general furans are synthesized by the ring closure of suitably substituted 1,4-diketones.[3] Alkynyloxiranes, alkynyl allyl alcohols and acetylenic ketones are other well-known synthons utilized for the synthesis of 2,3,5-trisubstituted furans.[4] Treatment of Grignard reaction product of 3-bromo 2,5-diphenyl furan with carbondioxide[5] and selenium initiated conversions of α-substituted β,γ-unsaturated ketones happen to be few of the known methods reported for the synthesis of 2,5-disubstituted derivatives of furan-3-carboxylic acid/ester.[6]

During the course of our study on the $\Delta^{\beta,\gamma}$-butenolides we came across a novel hitherto observation of forming furans from α-arylidene-γ-oxo-benzenebutanoic acid methyl ester

[†] IICT Communication No. 01/11/05

(II) on treatment with N-bromosuccinimide (NBS) as shown in scheme 1.



Scheme-1 : Formation of furan derivatives with NBS

Compound II, can be obtained in quantitative yield from the respective $\Delta^{\beta,\gamma}$-butenolides (I) by treatment with triethylamine in methyl alcohol at room temperature,[7] the reaction time being 1 to 4 h.

Results and Discussion

We envisaged the bromination of the active methylene of compound II with NBS, to extend it further for the synthesis of heterocycles, but instead resulted in the formation of 2-aryl 5-phenylfuran-3-carboxylic acid methyl esters (III)

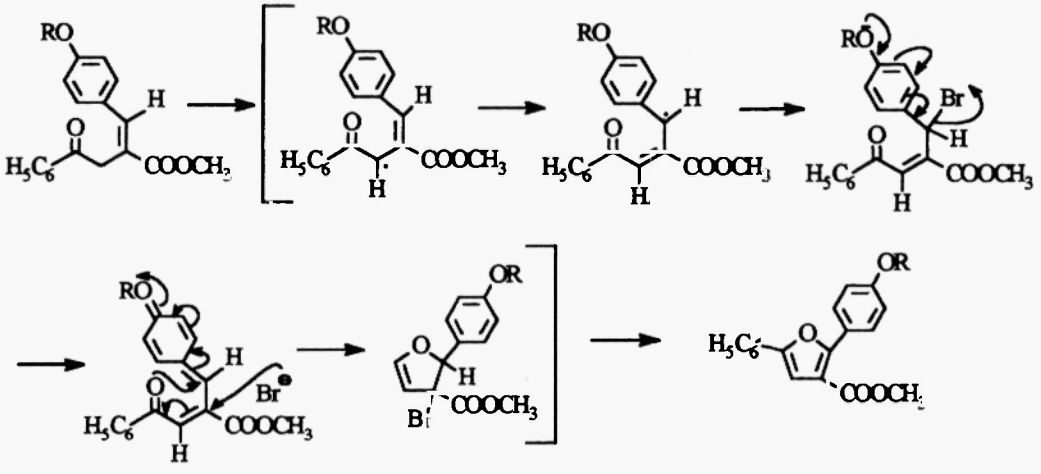
In a typical reaction α-arylidene-γ-oxo-benzenebutanoic acid methyl ester was treated with equimolar quantities of N-bromosuccinimide in refluxing carbon tetrachloride. Unsymmetrical diaryl substituted furan-3-carboxylic acid esters (III) were obtained in good yields.[8] All the products obtained were characterized on the basis of IR, NMR, Mass spectra and HRMS. The Table-1 depicts the results of the present investigation.

Table-1 : Effect of substitution in product formation

Entry	Ar	Product Yield (%)	Melting Point (°C)
1.	4-$OCH_3C_6H_4$	95	78
2.	4-$CH_3C_6H_4$	80	101
3.	4-OHC_6H_4	50	124
4.	4-OH-3-$OCH_3C_6H_3$	80	72
5.	C_6H_5	No reaction	
6.	4-$NO_2C_6H_4$	No reaction	
7.	2,6-$Cl_2C_6H_3$	No reaction	
8.	3-$OPhC_6H_4$	No reaction	

The presence of an electron releasing group at the para position of the arylidene phenyl group in II leads to the formation of the furan derivatives while an electron withdrawing group do not facilitate the furan formation. In view of the observation made for entry 5 where no furan formation is observed it may be concluded that a para activation is required for the furan formation.

The probable mechanism of formation of furan-3-carboxylic acid methyl ester is represented in Scheme-2.



Scheme-2 : Probable mechanism for the formation of furan derivatives

In case of entry 2, the corresponding furan is obtained in 80% yield which may be attributed to the hyperconjugative activation of the methyl group.

Alternatively initial bromination by NBS can also occur at the α-position of the carbonyl group resulting in the elimination of the bromide at the instance of the para activating group at the arylidene ring thereafter following the same sequence as represented in scheme-2 leading to the formation of furans (**III**).

In conclusion, the present study provides a new approach for the preparation of unsymmetrical 2,5-diarylfuran-3-carboxylic acid esters in an elegant way from suitably substituted γ-keto esters derived from butenolides.

References and notes:

1. B.H. Lipshutz, *Chem. Rev.*, **86**, 795 (1986).
2. H.L. Hou, H.Y. Cheung, T.Y. Hon, P.L. Kwan, T.H. Lo, S.Y. Tong and Henry N.C. Wong, *Tetrahedron*, **54**, 1955 (1998).
3. A. Miyashita, Y. Matsuoka, A. Numata and T. Higashino, *Chem. Pharm. Bull.*, **44**, 448 (1996).
4. a) J.A. Marshall and W.J. Du Bay, *J. Org. Chem.*, **56**, 1685 (1991). b) J.A. Marshall and W.J. Du Bay, *J. Am. Chem. Soc.*, **114**, 1450 (1992). c) B. Seiller, C. Bruneau and P.H. Dixneuf, *Tetrahedron*, **51**, 13089 (1995). d) Y. Fukuda, H. Shiragami, K. Utimoto and H. Nozaki, *J. Org. Chem.*, **56**, 5816 (1991).
5. R.E. Lutz and R.J. Rowlett Jr., *J. Am. Chem. Soc.*, **70**, 1359 (1948).
6. M. Tiecco, L. Testaferri, M. Tingoli and F. Marini, *Synlett.*, 373, (1994).
7. G. Sudhakar Reddy, Parvathi Neelakantan and D.S. Iyenger, *Indian. J. Chem;* **39b**, 894 (2000).
8. General method for the preparation of 2-aryl-5-phenylfuran-3-carboxylic acid methyl ester: Synthesis of 2-(p-methoxyphenyl)-5-phenylfuran-3-carboxylic acid methyl ester is representative. N-Bromosuccinimide (0.348 g, 2 mmol) was added to a solution of α-[(4-methoxyphenyl) methylene]-γ-oxo-benzenebutanoic acid methyl ester (**II**, 0.620 g, 2 mmol) in 20 mL of carbon tetrachloride and the contents were refluxed for about 3 h. After the completion of the reaction (by tic) solvent was removed under reduced pressure, the residue was extracted with ethyl acetate (25 mL) and the organic layer was successively washed with water (2 x 25 mL). The organic layer was dried over sodium sulphate, concentrated and the product was purified by column chromatography over silica gel using ethyl acetate-hexane (2 : 98) as eluent and isolated in 90% yield (0.55 g) m.p. 78°C. IR (KBr) : 1720, 1500, 1240 & 1100 cm^{-1}. ^1H NMR ($CDCl_3$) : δ 3.9 (s, 6H), 6.9 (d, J = 10.0 Hz, 2H), 7.0 (s, 1H), 7.3-7.45 (m, 3H), 7.7 (d, J = 10.0 Hz, 2H), 8.1 (d, J = 10.0 Hz, 2H). ^{13}C NMR ($CDCl_3$) : δ 163.98 (C=O), 160.45, 156.94, 151.62 (aromatic carbons bound to oxygen), 126.2 (C), 122.35 (C), 114.04 (C), 129.90 (CH), 128.67 (CH), 127.78 (CH), 123.79 (CH), 122.35 (CH), 51.44 (OCH_3) and 55.2 (OCH_3). ES-Mass (70 eV) m/e : 308 (M^+). HRMS for $C_{19}H_{16}O_4$: Found : 308.103, Calcd. 308.104.

Received on February 25, 2002