

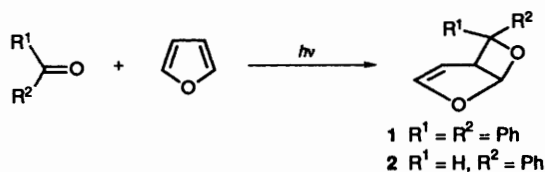
Highly Regioselective [2 + 2] Photocycloaddition of Aromatic Aldehydes to Acetylfurans

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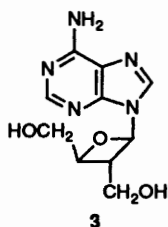
Stereospecific and highly regioselective oxetane formation occurs on irradiation of substituted aromatic aldehydes in the presence of 2-acetylfurans.

The [2 + 2] cycloaddition of carbonyl compounds to furan to yield bicyclic oxetanes (e.g. **1** in Scheme 1)¹ is an efficient photochemical process. This Paternò-Büchi reaction has been



Scheme 1

exploited in synthetic chemistry,^{2,3} with success particularly by Schreiber and his group.⁴ The bicyclic oxetanes which result from photocycloaddition can be transformed by ring opening at the strained acetal carbon.⁵ Alternatively, the dihydrofuran ring can be selectively manipulated, as in the recent photochemical synthesis of oxetanocin, **3**,⁶ a nucleoside with antiviral activity against HIV. The recent discovery of other oxetanes with significant anti-viral properties⁷ makes [2 + 2] photocycloaddition a route of potential importance.



The photocycloaddition of aldehydes to furans shows excellent stereoselectivity (>95%) in forming the *exo*-adduct (e.g. **2**),⁸ but does suffer from one disadvantage: in the attack on an unsymmetrically substituted furan, the reaction shows little regioselectivity. Attack of photoexcited benzaldehyde on 2-methylfuran, for example, gives the two adducts **4a** and **5a** in a 1.3:1 ratio^{4e} (Table 1). Although the adducts are difficult to separate, the greater reactivity of the bridgehead-substituted isomer **4a** can lead to its selective destruction on silica gel as a means of separation.⁶ Schreiber has attempted to overcome this problem by the use of a bulky trialkylsilyl or trialkylstannyl group at the 2-position of the furan ring, when improved regioselectivities of up to 20:1 can be obtained for attack at the *unsubstituted* double bond of the furan (Table 1, entries 2, 3),^{4e} yielding dominantly **5**. We now report that aromatic aldehydes undergo a remarkably selective photocycloaddition to 2-acetylfurans, with bicyclic oxetane formation occurring at the *more substituted* furan double bond, to give **4**.

Our initial investigations showed that the regioselectivity of photocycloaddition of aromatic aldehydes to alkylfurans and furfuryl alcohols or their derivatives was indeed low (Table 1, entries 4–7). For 3-substituted furans or unsymmetrical 2,5-

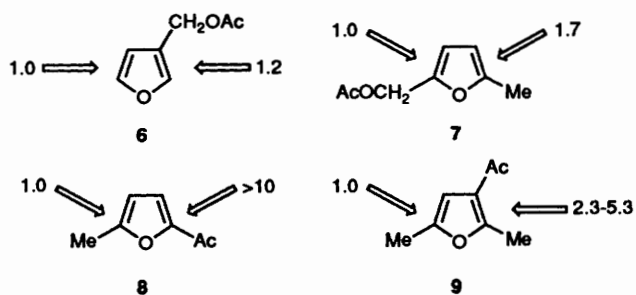
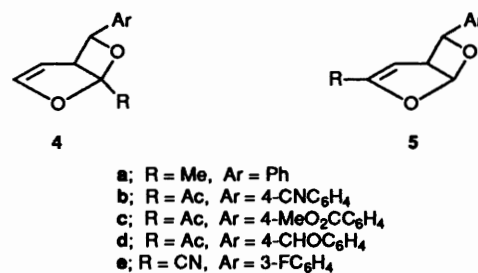


Fig. 1 Relative amounts of cycloaddition products formed by attack of photoexcited aromatic aldehydes on substituted furans: **6** and **7**, benzaldehyde; **8**, 2-chloro- or 4-cyano-benzaldehyde; **9**, 3-fluoro- (ratio 5.3), 4-methoxycarbonyl- (ratio 3.3) or 4-cyano-benzaldehyde (ratio 2.3)

disubstituted furans, this lack of selectivity was also evident. Fig. 1 shows the relative amounts of cycloaddition products which resulted from attack of benzaldehyde at each double bond of the substituted furans **6** and **7**. However, photolysis of a benzene solution of 4-cyanobenzaldehyde and 2-acetylfuran led to a single major adduct, **4b**, isolated by column chromatography in 70% yield. Proton NMR spectroscopy of the crude photolysate showed that the regioselectivity of the reaction was at least 20:1 in favour of attack at the acetyl-bearing double bond; we were unable to detect the alternative regioisomer **5b**. A similar selectivity of attack was found using 4-methoxycarbonylbenzaldehyde or terephthalaldehyde as the carbonyl components, which gave **4c** and **4d** in good yield (65–80%) (Table 1, entries 8–10).

High regioselectivity (>10:1) was also observed for photocycloaddition of 2-chlorobenzaldehyde or 4-cyanobenzaldehyde to 2-acetyl-5-methylfuran **8** (Fig. 1). Interestingly, 3-acetylfurans such as **9** also underwent photocycloaddition to aromatic aldehydes (3-fluoro-, 4-methoxycarbonyl- or 4-cyanobenzaldehyde), but with the reduced selectivity shown in Fig. 1. In these last mentioned examples, adducts corresponding to cycloaddition at the 2,3- and 4,5-double bonds of the furan were easily separated and identified by ¹H and ¹³C NMR spectroscopy. The notable regioselectivity for attack by excited aldehyde on the more substituted double bond of these furans having electron-withdrawing groups was also found for attack

Table 1 Regioisomeric oxetanes produced by photocycloaddition of 2-substituted furans to aromatic aldehydes

Entry	2-Substituted furan	Aldehyde ArCHO	Ratio 4:5	Ref.
1	R = Me	Ar = Ph	1.3:1	a
2	R = SiMe ₃	Ar = Ph	1:2.5	a
3	R = SiPr ^t ₃	Ar = Ph	1: >20	a
4	R = CH ₂ OH	Ar = Ph	1.5:1	b
5	R = CH ₂ OSiBu ^t Me ₂	Ar = Ph	1:1.1	b
6	R = Me	Ar = 2-Furyl	1:1	b
7	R = Me	Ar = 4-CNC ₆ H ₄	1:2	b
8	R = Ac	Ar = 4-CNC ₆ H ₄	>20:1	b
9	R = Ac	Ar = 4-MeO ₂ CC ₆ H ₄	>20:1	b
10	R = Ac	Ar = 4-CHOC ₆ H ₄	>20:1	b
11	R = CN	Ar = 3-FC ₆ H ₄	>10:1	b

^a Ref. 4e. ^b This work.

on 2-cyanofuran (Table 1, entry 11), but competitive polymerisation of the furan reduced the yield of oxetane **4e** to ca. 10% in this case.

Curiously, although the photocycloadditions were successful with electron-withdrawing substituted aromatic aldehydes or even 2-furaldehyde, they were very slow or not observed for electron-donating substituted examples (e.g. 4-methoxybenzaldehyde) or benzaldehyde itself. This may possibly be a consequence of triplet energy transfer from the latter (higher energy) triplet donors to the acetylfuran acceptors.⁹ However, a newly found method for metallation of the bicyclic oxetanes¹⁰ could extend the synthetic usefulness of these adducts.

Experimental

Synthesis of exo-1-Acetyl-6-(4'-cyanophenyl)-2,7-dioxabicyclo[3.2.0]hept-3-ene 4b.—A solution of 4-cyanobenzaldehyde (1.0 g, 7.6 mmol) and 2-acetylfuran (2.66 g, 24 mmol) in benzene (85 cm³) in the presence of sodium carbonate (0.1 g) under nitrogen was irradiated for 4 h, using a 450 W Hanovia medium-pressure mercury arc and Pyrex glassware. Evaporation and chromatography of the residue on silica gel, eluting with 10% acetone–90% light petroleum (b.p. 40–60 °C)–0.03% triethylamine, gave the adduct **4b** (70%); δ_{H} (270 MHz; CDCl₃) 7.68 (2 H, d, *J* 8.6, 3'-H and 5'-H), 7.47 (2 H, d, *J* 8.6, 2'-H and 6'-H), 6.72 (1 H, dd, *J* 2.7 and 1.2, 3-H), 5.64 (1 H, d, *J* 3.5, 6-H), 5.53 (1 H, t, *J* ca. 3, 4-H), 3.92 (1 H, dt, *J* 1.2, ca. 3 and ca. 3, 5-H) and 2.33 (3 H, s, CH₃CO); δ_{C} (67.9 MHz; CDCl₃) 198.5 (CO), 149.0 (C-3), 144.4 (C-1'), 132.6 (C-2' and C-6'), 126.1 (C-3' and C-5'), 118.5 (CN), 113.7 (C-1), 112.3 (C-4'), 104.6 (C-4), 89.8 (C-6), 51.4 (C-5) and 23.7 (CH₃).

References

- G. O. Schenck, W. Hartmann and R. Steinmetz, *Chem. Ber.*, 1963, **96**, 498.
- G. Jones, II, *Org. Photochem.*, 1981, **5**, 1.
- H. A. J. Carless, in *Synthetic Organic Photochemistry*, ed. W. M. Horspool, Plenum Press, New York, 1984, p. 425.
- (a) S. L. Schreiber, *Science*, 1985, **227**, 857; (b) *threo* aldols: S. L. Schreiber, A. H. Hoveyda and H.-J. Wu, *J. Am. Chem. Soc.*, 1983, **105**, 660; (c) (\pm)-asteltoxin: S. L. Schreiber and K. Satake, *J. Am. Chem. Soc.*, 1984, **106**, 4186; (d) (\pm)-avenaciolide: S. L. Schreiber and A. H. Hoveyda, *J. Am. Chem. Soc.*, 1984, **106**, 7200; (e) kadsurenone-ginkgolide hybrid: S. L. Schreiber, D. Desmaele and J. A. Porco, Jr., *Tetrahedron Lett.*, 1988, **29**, 6689.
- A. Zamojski and T. Koźluk, *J. Org. Chem.*, 1977, **42**, 1089; S. Jarosz and A. Zamojski, *J. Org. Chem.*, 1979, **44**, 3720.
- R. Hambalek and G. Just, *Tetrahedron Lett.*, 1990, **31**, 5445; for other examples of dihydrofuran functionalisation, see R. Hambalek and G. Just, *Tetrahedron Lett.*, 1990, **31**, 4693.
- Y. Wang, G. W. J. Fleet, R. Storer, P. L. Myers, C. J. Wallis, O. Doherty, D. J. Watkin, K. Vogt, D. R. Witty, F. X. Wilson and J. M. Peach, *Tetrahedron: Asymmetry*, 1990, **1**, 527; C. O-Yang, W. Kurz, E. M. Eugui, M. J. McRoberts, J. P. H. Verheyden, L. J. Kurz and K. A. M. Walker, *Tetrahedron Lett.*, 1992, **33**, 41.
- A. G. Griesbeck and S. Stadtmüller, *Chem. Ber.*, 1990, **123**, 357; A. G. Griesbeck, H. Mauder, K. Peters, E.-M. Peters and H. G. von Schnering, *Chem. Ber.*, 1991, **124**, 407.
- D. R. Arnold, *Adv. Photochem.*, 1968, **6**, 301.
- S. L. Schreiber and J. A. Porco, Jr., *J. Org. Chem.*, 1989, **54**, 4721.

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