New Synthesis of Benzo[*b*]furans by $S_{RN}1$ Reaction of *ortho*-Iodoanisole[1]

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Summary Starting from *ortho*-iodoanisole, 2-substituted benzo[*b*]furans are obtained in high yield *via* aromatic nucleophilic radical substitution ($S_{RN}1$)

IT is well known that an aromatic radical formed by fragmentation of an aromatic anion radical in an $S_{RN}1$ reaction undergoes regiospecific nucleophilic attack [2] We now report a new synthesis of the benzo[*b*]furan skeleton based on this mechanism, starting from *ortho*-iodoanisole (**1**), *via* (**2**) [and (**3**), not isolated]

In a typical experiment, a solution of the appropriate potassium enolate (7 mmol) was prepared in a Pyrex three neck flask under nitrogen in 50 ml of liquid ammonia at $-33°$, using MeCOR (R = H, Me, Pr^i, Bu^t, Et) (7 mmol) and freshly sublimed potassium t-butoxide The anisole (**1**) (1 mmol) was added and after irradiation for a short time (5 to 15 min) with a high pressure 100 W Hanau Lamp the reaction was quenched with NH_4Cl and worked up

The crude products (**2a**—**e**) were purified by column chromatography and then treated with $ClSiMe_3$–INa according to Olah's procedure for deblocking a phenolic function [3] The hydroxyphenyl ketones (**3a**—**e**) thus obtained quantitatively from (**2a**—**e**) undergo spontaneously cyclodehydration to give the benzo[*b*]furan in quantitative yields [†] The reaction from (**2a**—**e**) to

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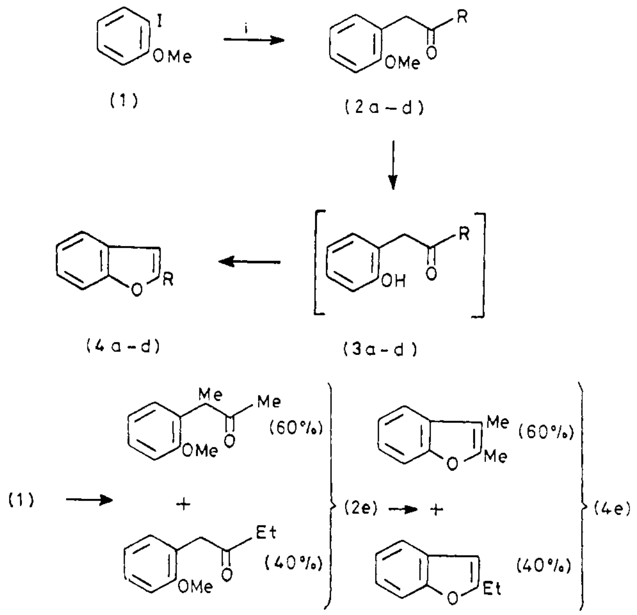
[†] An analogous reaction has been reported [L Christiaens and M Renson, *Bull Soc Chim Belg*, 1970, **79**, 235] Starting from (**2b**) (obtained after a four step synthesis) the authors used 48% HBr–AcOH for deblocking and cyclodehydration and obtained (**4b**) in 40% yield only, because of polymerisation undergone by the final product under these strongly acidic conditions



Reagents: i, *h*ν, $^-CH_2COR$. ii, hν, $MeCO\bar{C}HMe$ and $^-CH_2COEt$.

(**3a**—**e**) is extremely fast compared with a model reaction carried out on anisole, probably because of the anchimeric assistance provided by the side chain of (**2a**—**e**). This unexpected and favourable effect, coupled with the good yields of the substitution reaction (**1a**—**e**) to (**2a**—**e**) make the sequence (**1**) → (**2**) → (**3**) → (**4**) very easy to carry out in good overall yields giving access to the benzo[*b*]furan series.[4] The results are given in the Table.

TABLE. Reaction of *o*-IC_6H_4OMe with enolates to give the *o*-methoxyphenyl ketones (**2**)[a] and benzo[*b*]furans (**4**).[a]

	CH_2COR R	(**2**) % yield[b]	(**4**) % yield[b]
a	H	40	40
b	Me	67	67
c	Pr^i	66	66
d	Bu^t	100	100
e	Et	57	57[c]

[a] All products are liquids except (**4d**) (m.p. 125 °C) and spectral data (n.m.r., mass spectra) in agreement with the formulae (**2a**—**d**) and (**4a**—**d**) have been obtained. The furans (**4a**—**d**) are known [(**4a**) identical to a commercially available sample, (**4b**) L. Claisen, *Justus Liebig's Ann. Chem.*, 1919, **69**, 418; (**4c**) W. J. Davidson and J. A. Elix, *Aust. J. Chem.*, 1970, **23**, 2119 give n.m.r. data identical with ours; (**4d**) B. L. Lebedev, N. A. Karev, O. A. Korytina, and N. F. Shuikin, *Izv. Akad. Nauk SSSR Ser. Khim.*, 1969, 2601]. [b] Not optimized yields for isolated pure products. [c] Mixture [estimated by n.m.r. of 2,3-dimethylbenzofuran (60%) and 3-ethylbenzofuran (40%) (ref. 5b)].

This nucleophilic substitution requires photostimulation and is regiospecific, two features which are characteristic of an $S_{RN}1$ reaction. The extension of the $S_{RN}1$ reaction to an aromatic substrate bearing a nucleofugic group *ortho* to a functional group either blocked (OMe) or free (NH_2)[1] enlarges considerably the synthetic scope of this reaction, and other applications have already been realized[5] or are foreseen.

(*Received*, 18*th February* 1980; *Com.* 178.)

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[1] Previous report in this series: R. Beugelmans and G. Roussi, *J. Chem. Soc., Chem. Commun.*, 1979, 950.

[2] J. F. Bunnett, *Acc. Chem. Res.*, 1978, **11**, 413; J. F. Wolfe and D. R. Carver, *Org. Prep. Proc. Int.*, 1978, 227.

[3] G. A. Olah, S. C. Narang, B. G. Balaram Gupta, and R. Malhotra, *J. Org. Chem.*, 1979, **44**, 1247.

[4] (a) A. Hercouet and M. Le Corre, *Tetrahedron Lett.*, 1979, 2145; (b) P. Cagniant and D. Cagniant, *Adv. Heterocycl. Chem.*, 1975, **18**, 337.

[5] R. Beugelmans, B. Boudet, and L. Quintero, *Tetrahedron Lett.*, in the press.