FORMATION OF DEOXYBENZOINS FROM 1,3-DIMETHYL-2-(α-BENZYLOXYBENZYL)BENZIMIDAZOLIUM IODIDES THROUGH REARRANGEMENT FOLLOWED BY EXPULSION OF AZOLIUM YLIDE

Akira MIYASHITA,* Yoshiyuki MATSUOKA, Ken-ichi IWAMOTO, and Takeo HIGASHINO

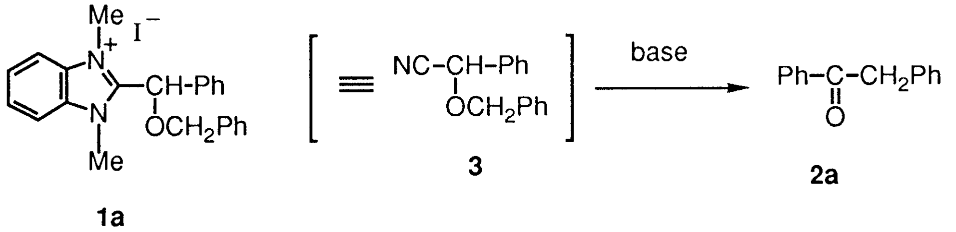
School of Pharmaceutical Sciences, University of Shizuoka, 52-1 Yada, Shizuoka 422, Japan

Treatment of several 1,3-dimethyl-2-(α-benzyloxybenzyl)benzimidazolium iodides **1** with K_2CO_3 gave deoxybenzoins **2** in moderate yields. Deoxybenzoins **2** were produced through rearrangement of benzyl groups followed by expulsion of 1,3-dimethylbenzimidazolium ylide (**4**). The reaction is classified as a Wittig rearrangement.

KEYWORDS 1,3-dimethyl-2-(α-benzyloxybenzyl)benzimidazolium iodide; rearrangement; elimination; 1,3-dimethylbenzimidazolium ylide; deoxybenzoin

During a series of catalytic actions of azolium salts, in benzoin condensation and related reactions, we have considered that the chemical behavior of azolium ylide was similar to that of cyanide ion.[1] But in comparison between azolium salts and potassium cyanide, several differences of their catalytic behavior were observed. In order to clarify the similarity of chemical behavior between cyanide ion and azolium ylide, the reaction promoted by cyanide ion or carbonitrile group was utilized for azolium ylide or azolium salt.

Wittig rearrangement [2] is well known as an anion rearrangement, like Stevens [3] and Sommelet-Hauser rearrangements,[3b,4] and a number of experimental results have been appeared in the literature. Cast *et al.* reported that the treatment of ethers with base yielded alcohols.[5] Among the ethers they used were a few examples of α-cyanobenzyl ethers, and on similar treatment, deoxybenzoins were given in low yield. They considered that deoxybenzoin was produced by rearrangement of benzyl group followed by expulsion of cyanide ion.

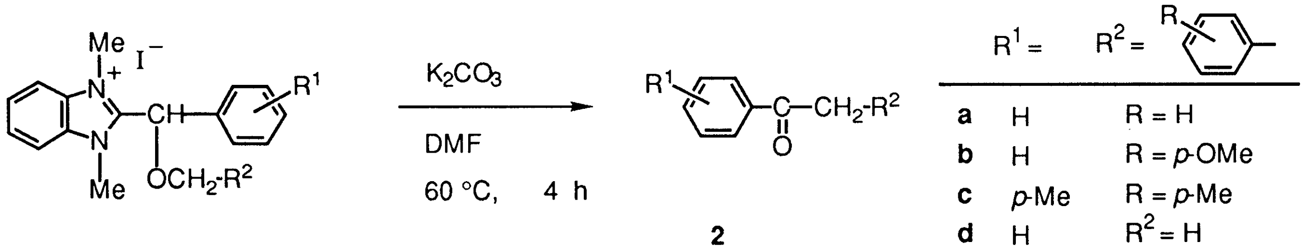


DMSO / KOH	35%
DMF / DBU	23%
DMF / K_2CO_3	56%
THF / K_2CO_3	53%
THF / NaH	57%

Chart 1

In consideration of the chemical similarity between carbonitrile group and azolium salt, it could be expected that treatment of 1,3-dimethyl-2-(α-benzyloxybenzyl)benzimidazolium iodide (**1a**) equivalent to benzyl α-cyanobenzyl ether (**3**) with base gave deoxybenzoin (**2a**) in a way similar to above reaction. When benzimidazolium salt **1a** was treated with NaH in THF, deoxybenzoin (**2a**) expected product was given in 57% yield. Several bases could be used for successful formation of deoxybenzoin **2a**. The rearrangement proceeded by K_2CO_3, which was considered a weak base, either in DMF or in THF. No difference of the yields for the solvent effect was observed.

In order to extend the reaction, several 1,3-dimethyl-2-(α-benzyloxybenzyl)benzimidazolium iodides **1** were prepared [6] and a similar treatment with K_2CO_3 in DMF was carried out. As shown in Chart 1, expected deoxybenzoins **2** [7] were given in moderate yields.



1

2

2b; 54%, **2c**; 53%, **2d**; —, **2g**; 50%

	R¹ =	R² =
a	H	R = H
b	H	R = *p*-OMe
c	*p*-Me	R = *p*-Me
d	H	R^2 = H
e	*p*-Me	R = H
f	H	R = *p*-Me
g	*m*-OMe	R = H

Chart 2

An attempt at production of acetophenone from 1,3-dimethyl-2-(α-methoxybenzyl)benzimidazolium iodide (**1d**) by the above rearrangement failed to proceed in a manner similar to the carbonitrile group.[4]

In general, Wittig rearrangement requires strong bases, such as *n*-butyllithium and potassium butoxide, because of the low acidity of hydrogen of the benzyl group. In contrast, the rearrangement applied to benzimidazolium salts **1** proceeded by K_2CO_3, because the acidity of the hydrogen of benzyl group is higher than that of ordinary benzyl ether owing to the attachment effect of 1,3-dimethylbenzimidazolium salt. It could be considered that a driving force of the rearrangement is formation of the carbanion and expulsion of azolium ylide. In fact, the rearrangement of 1-methyl-2-(α-benzyloxybenzyl)benzimidazole (**6a**) failed to proceed under similar conditions.

In order to determine the reaction pathway, cross-reaction was carried out. Namely, when the mixture of 1,3-dimethyl-2-(α-benzyloxybenzyl)benzimidazolium iodide (**1a**) and 1,3-dimethyl-2-[α-(4-methylbenzyloxy)-4-methylbenzyl)benzimidazolium iodide (**1c**) was treated with K_2CO_3 in THF, the expected products of deoxybenzoin (**2a**) and 4,4'-dimethyldeoxybenzoin (**2c**) were given together with the unexpected products of 1-(4-methylphenyl)-2-phenylethanone (**2e**) and 1-phenyl-2-(4-methylphenyl)-ethanone (**2f**).[8] The structures of the deoxybenzoins were determined on the basis of each retention time compared with authentic samples in GC. Furthermore, when **1a** was treated with K_2CO_3 in MeOH, only methyl benzoate (5) was obtained (46%). These results suggested that the rearrangement of benzyl group proceeds through intermediate b and the reaction process is intermolecular. But the detailed reaction pathway is not clear yet. As shown in Chart 3, it is considered that the reaction pathway for the formation of deoxybenzoins **2** from azolium salts **1** is similar to that of benzyl α-cyanobenzyl ether **3**.

As deoxybenzoins were generally prepared by Friedel-Crafts reaction of arene with areneacetyl halide, the deoxybenzoins substituted with *ortho-para* directing group at *meta*-position were difficult to synthesize. However, with this procedure, 1-(3-methoxyphenyl)-2-phenylethanone (**2g**) could be synthesized in 50% yield.

An attempt at benzylation of 1,3-dimethyl-2-(α-hydroxybenzyl)benzimidazolium iodide (**7a**, active aldehyde) with benzyl bromide was unsuccessful in producing deoxybenzoin.[9] The result confirmed that the rearrangement proceeds through 1,2-carbanion shift. The reaction pathway is similar to that of Wittig rearrangement, whose process was investigated in detail by Lansbury *et al.*[10] The reaction newly found by us is an example proving a similarity between carbonitrile group and azolium salts.

We found a new rearrangement, which was promoted by expulsion of azolium ylide. The rearrrangement proceeds through formation of the carbanion with subsequent benzyl migration in a similar way to Wittig rearrangement. Finally, elimination of 1,3-dimethylbenzimidazolium ylide gave deoxybenzoin. The rearrangement proceeds under mild conditions because of the electron-accepting effect of azolium salt. In addition, several deoxybenzoins are produced by the reaction .

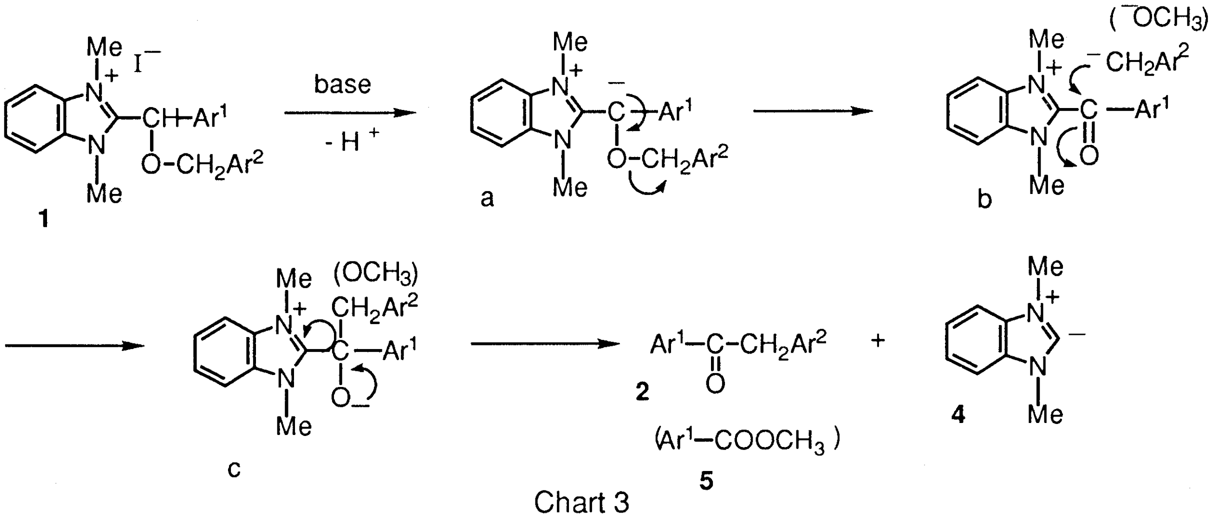


Chart 3

REFERENCES AND NOTES

1) *a*) T. Ugai, R. Tanaka, S. Dokawa, *Yakugaku Zasshi*, **63**, 296 (1943); *b*) W. S. Ide, J. S. Buck, *Org. React.*, **4**, 269 (1948); *c*) J. Castells, F. Pujol, H. Llitjos, M. M. Manas, *Tetrahedron*, **38**, 337 (1982); *d*) A. Miyashita, H. Matsuda, C. Iijima, T. Higashino, *Chem. Pharm. Bull.*, **38**, 1147 (1990); *e*) A. Miyashita, H. Matsuda, T. Higashino, *Chem. Pharm. Bull.*, **40**, 2627 (1992).

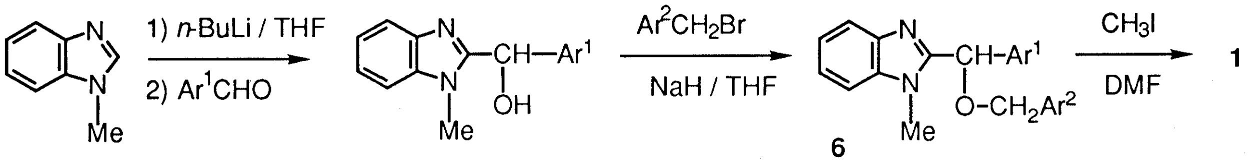
2) *a*) G. Wittig, E. Stahnecker, *Ann.*, **605**, 69 (1957); b) U. Schollkopf, *Angew. Chem.*, **82**, 795 (1970).

3) *a*) T. S. Stevens, E. M. Creighton, A. B. Gordon, M. MacNicol, *J. Chem. Soc.*, **1928**, 3193; *b*) S. H. Pine, *Org. React.*, **18**, 403 (1970).

4) *a*) M. Sommelet, *C. R.*, **205**, 56 (1937); *b*) C. R. Hauser, S. W. Kantor, *J. Am. Chem. Soc.*, **73**, 1437 (1951).

5) J. Cast, T. S. Stevens, J. Holmes, *J. Chem. Soc.*, **1960**, 3521.

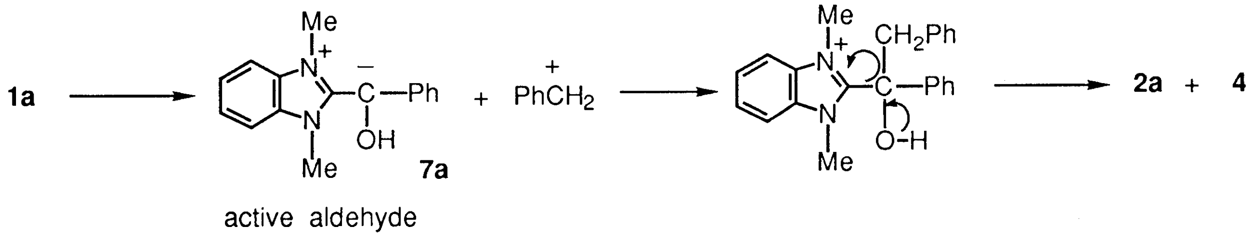
6) The starting azolium salts **1** were prepared through three steps, as shown below.



7) The structures were confirmed by spectral data and comparison of melting points with authentic samples.

8) The formation ratio of deoxybenzoins were given in **2a** : **2c** : **2e** : **2f** = 5 : 5 : 1 : 1. The ratio was determined on the basis of the integration of each hydrogen of benzyl groups in ^{1}H-NMR spectrum.

9) If the rearrangement proceeded through the formation of benzyl cation as shown below, the deoxybenzoin might be given by benzylation of 1,3-dimethyl-2-(α-hydroxybenzyl)benzimidazolium iodide (**7a**, active aldehyde) in the presence of base.



10) P. T. Lansbury, V. A. Pattison, *J. Am. Chem. Soc.*, **84**, 4295 (1962).

(Received July 4, 1994; accepted August 10, 1994)