Novel Catalytic System consisting of a 3,3′-Tetramethylene-bridged 4-Methylthiazolium Salt Leading to the Partial Reduction of Nitrobenzene with Benzaldehyde to a Nitrone

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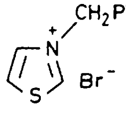
A 3,3′-tetramethylene-bridged 4-methylthiazolium salt catalyses the reduction of nitrobenzene with benzaldehyde and triethylamine in methanol–water to give a nitrone.

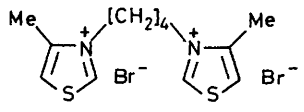
The application of biological systems to organic reactions is important in developing new types of catalyst and reagent. We reported previously that 3-benzylthiazolium bromide (**1**), a model compound for thiamine pyrophosphate, catalyses the reduction of various organic substances with aldehydes in methanol containing triethylamine.[1] We now report the novel catalytic function of the 3,3′-tetramethylene-bridged 4-methylthiazolium salt (**2**) in giving the nitrone (**6**) in the reduction of nitrobenzene with benzaldehyde and triethylamine in methanol–water [reaction (1)].

$$3PhCHO + PhNO_2 + 2MeOH \xrightarrow[MeOH\text{–}H_2O]{(2),\ Et_3N} \underset{(6)}{PhCH{=}N(O)Ph} + 2PhCO_2Me + 2H_2O \qquad (1)$$

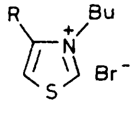
The reactions were carried out as follows, using procedures similar to those described previously.[1] Triethylamine was added under argon to a frozen solution of a mixture of the thiazolium salt (**1**)–(**5**), benzaldehyde, and nitrobenzene in degassed methanol or methanol–water. The mixture, after melting, was stirred under argon at 40 °C for 20 h. The reactions were stopped by adding dilute hydrochloric acid. The products were analysed by g.l.c. and the results are summarized in Table 1. The amount of methyl benzoate produced corresponded almost exactly to the stoicheiometric amount based on the reduction products, thus indicating that an activated aldehyde, derived from benzaldehyde and the thiazolium salt in the presence of triethylamine, is a reducing species, as shown in our previous paper.[1]



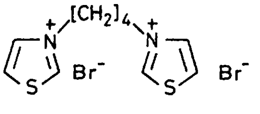
(**1**)



(**2**)

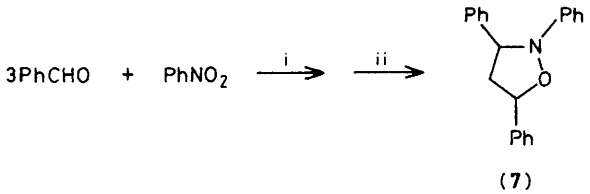


(**3**) R = Me
(**4**) R = H



(**5**)

In methanol solvent, the PhCHO–(**1**)–Et_3N system gave aniline together with *N*-benzoyl-*N*-phenylhydroxylamine, while the system with (**2**) gave aniline and the nitrone (**6**) with a decrease in the yield of *N*-benzoyl-*N*-phenylhydroxylamine. In methanol–water, the system with (**1**) gave only aniline, in a much lower yield than in methanol. Thus, the presence of water in the reaction system retards the reduction of nitrobenzene. In the case of (**2**), the nitrone (**6**) is produced catalytically as a major product. The formation of benzoin was also depressed considerably. Furthermore, the lowering of the reduction yields caused by the presence of water was found to be smaller than in the case of (**1**).



(**7**)

Reagents: i, (**2**), Et_3N, MeOH–H_2O; ii, PhCH=CH_2.

Table 1. The thiazolium salt-catalysed reduction of nitrobenzene with benzaldehyde and triethylamine in MeOH–H_2O and MeOH.[a]

Thiazolium salt	Vol./ml		Yield, %[b]			Mol[c] of $PhCO_2Me$[c] (per theor. mol)	Molar ratio benzoin/ester
	MeOH	H_2O	$PhNH_2$	PhN(OH)COPh	PhCH=N(O)Ph		
(**1**)	7	0	40	27	0	1.07	0.16
	6	1	18	0	0	0.88	0.07
(**2**)	7	0	34	7	36	1.02	0.05
	6	1	8	1	40	0.90	0.02
	7	0.4[d]	5	9	33	0.96	0.03
(**3**)	7	0	37	14	20	1.15	0.06
	6	1	13	3	26	1.09	0.03
(**4**)	7	0	45	26	6	1.02	0.26
	6	1	20	2	2	0.91	0.11
(**5**)	7	0	35	9	15	1.12	0.31
	6	1	17	Trace	3	0.95	0.15

[a] Thiazolium salt: 0.25 mmol in MeOH–H_2O or MeOH (7 ml) under Ar, 40 °C, 20 h. PhCHO : Et_3N : $PhNO_2$: thiazolium unit = 12 : 10 : 4 : 1. [b] Based on nitrobenzene. The remainder is unchanged nitrobenzene. [c] Calculated as $PhCO_2Me$(mmol)/[3×$PhNH_2$(mmol) + PhN(OH)COPh(mmol) + 2×PhCH=N(O)Ph(mmol)]. [d] (**2**): 0.1 mmol. PhCHO : Et_3N : $PhNO_2$: thiazolium unit = 30 : 10 : 10 : 1. 40 °C, 20 h.

This reaction system was also applied to the 1,3-dipolar addition of the nitrone (**6**) to styrene. Nitrobenzene (2 mmol) was treated with benzaldehyde (6 mmol) in the presence of (**2**) (0.25 mmol) and triethylamine (5 mmol) in methanol–water (6:1; 7 ml) at 40 °C for 20 h; styrene (10 mmol) was then added under argon, and the solution was heated at 50 °C for 40 h. 2,3,5-Triphenylisoxazolidine (**7**)[2] (0.63 mmol) was obtained together with the nitrone (**6**) (0.19 mmol).

The results in Table 1 allow the function of (**2**) to be compared with that of the thiazolium salts (**3**)—(**5**). In the case of (**3**), the yield of the nitrone (**6**) was lower than that with (**2**). The salts (**4**) and (**5**) functioned similarly to (**1**). Thus, the methyl group in the 4-position, the hydrophobic group in the 3-position, and bridging of the two thiazolium rings are responsible for the formation of nitrone (**6**), showing that the reducing behaviour of the activated aldehyde is governed significantly by the environment.

The above results thus provide evidence that the bridged thiazolium salt (**2**) favours the formation of the nitrone (**6**) from nitrobenzene and benzaldehyde in the presence of triethylamine by retarding the reduction to aniline and *N*-benzoyl-*N*-phenylhydroxylamine.

Received, 29th October 1984; Com. 1533

References

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