

The Reactivity of Benzyldimethylamine *N*-Oxide on Treatment with Strong Bases¹

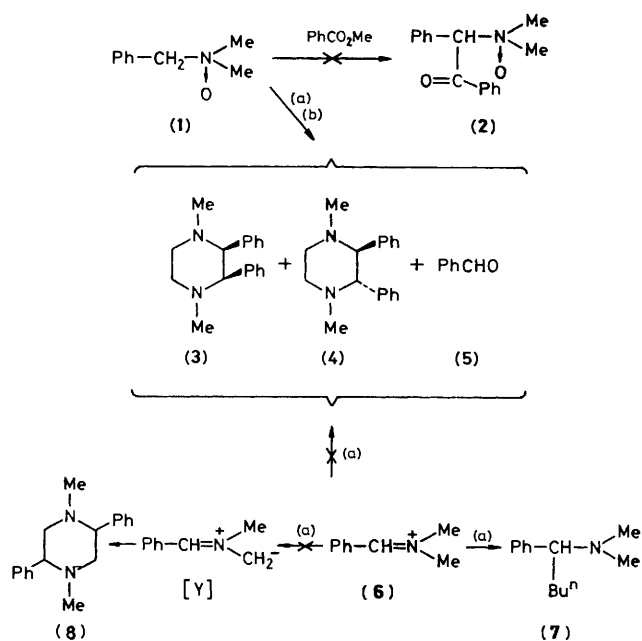
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Treatment of the title compound with lithium amide or *n*-butyl-lithium has revealed a hitherto unknown radical type reactivity for benzylic amine oxides.

The first example of polarity inversion for a tertiary amine (umpölung according to Seebach²) was reported to take place when quinuclidine *N*-oxide was treated with *n*-butyl-lithium.³ We have explored further the reactivity of amine oxides under these conditions and report here preliminary results for

benzyldimethylamine oxide (**1**). This compound, carefully dried, was treated at $-78\text{ }^{\circ}\text{C}$, with 2 mol. equiv. of either lithium amide in refluxing liquid ammonia or *n*-butyl-lithium in tetrahydrofuran (THF). In the presence of an electrophile (PhCO_2Me) it failed to give any adduct (**2**) of ionic origin (as



Scheme 1. (a) Bu^nLi (2 mol. equiv.), THF, -78°C ; (b) NH_3Li (2 mol. equiv.), NH_3 , -78°C .

was the case for quinuclidine *N*-oxide but gave the 2,3-diphenylpiperazines (3) (*cis*) and (4) (*trans*)† together with a very minor product, benzaldehyde (5). The results were identical without the electrophile (Scheme 1).

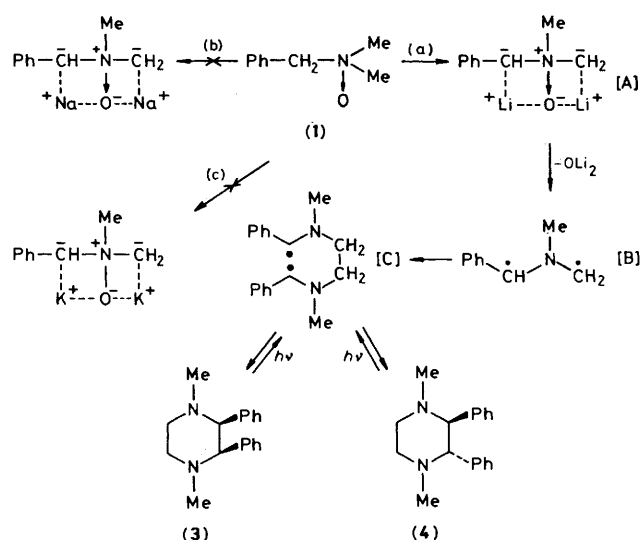
The formation of benzaldehyde from (1) suggests an iminium intermediate (as in the Polonovsky reaction) which in the presence of an excess of base could give rise to an azomethine ylide [Y], this species leading to its dimers: the piperazines (3) and (4). Examples of ylide precursors to dimerization^{4,5} are reported to give head-to-tail dimers (2,5-substituted piperazines) and not head-to-head products like (3) and (4). However, in line with our hypothesis, we decided to prepare (6)‡ and to treat it under our experimental conditions (a) which differ considerably from those reported. This experiment yielded (7) together with minute amounts of two other monomeric products,§ but no piperazines, either head-to-head [like (8)] or head-to-tail [like (3) and (4)].

We were thus led to postulate a radical intermediate [B], in the formation of (3) and (4), which is isoelectronic with the dianionic species [A] and stabilized by the capto-dative effect⁶ (Scheme 2). Experimental results, consistent with [A], [B], and [C] are as follows. (i) The benzyldimethylamine oxide (1), treated with a deficiency of *n*-butyl-lithium (1 mol. equiv.) yields the same mixture of products, (3), (4), and (5), in the same ratio (albeit in lower yield) as the reaction carried out with the base in excess. (ii) The reactivity of (1) treated with lithium amide in liquid ammonia at -33°C is similar to the reactivity of (1) exposed to *n*-butyl-lithium in THF at -78°C .

† (3) (m.p. 90°C) and (4) (m.p. 263°C) are identical (i.r.; mixed m.p.) to reference samples prepared according to T. Hayashi, *Sci. Pap. Inst. Phys. Chem. Res. (Jpn.)*, 1941, **38**, 466.

‡ (6) m.p. 89 – 90°C ; (i.r. 1670 cm^{-1} C=N) has data consistent with those of other iminium salts: perchlorate (m.p. 80 – 81°C) T. R. Keenan and N. J. Leonard, *J. Am. Chem. Soc.*, 1971, **93**, 6567; fluorosulphonate (m.p. 80 – 88.5°C), J. A. Deyrup and W. A. Szabo, *J. Org. Chem.*, 1975, **40**, 2048.

§ The structure of these two products is not yet established, owing to the small amount available.



Scheme 2. (a) NH_2Li , NH_3 , -33°C ; (b) NH_2Na , NH_3 , -33°C ; (c) NH_2K , NH_3 , -33°C .

However, sodium or potassium amide in liquid ammonia failed to react, and (1) was recovered unchanged. (iii) The addition of electron-trapping substances (nitrosobenzene, 0.5 mol. equiv. or *p*-dinitrobenzene, 1 mol. equiv.) significantly slowed the formation of the main products (3) and (4) (50% compared with the blank experiment). Observations (i) and (ii) support the existence of the dianion [A], stabilized by chelation of the oxygen atom of the amine oxide ($\text{N}^+ \rightarrow \text{O}^-$) by two small Li^+ cations (atomic radius 0.6 \AA) but not by larger cations such as Na^+ (0.95 \AA) and, *a fortiori*, K^+ (1.33 \AA). All our results, and especially the absence of (7) in the reaction undergone by (1) together with the absence of piperazines in the reaction from (6) strongly suggest that the piperazines (3) and (4) are not derived from an ionic species [Y] but rather from the radical species [B] formed from [A] by loss of OLi_2 .

The dimerization of [B] starting from the more reactive secondary radical site gives the biradical [C], which is indeed involved in the photochemical equilibration process (3) \rightleftharpoons (4).⁷ Additional studies on other benzylic amine oxides, with a view to improving the mass balance of the reaction (50%) and extending its scope, are now in progress. Depending upon the starting benzylic amine oxide, products of various structures including head-to-head piperazines were obtained, which can be derived from radical intermediates.

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