Base-induced Reactions of *N*-Substituted Dibenzylamine *N*-Oxides and Related Compounds: A Novel Aziridine Forming Reaction

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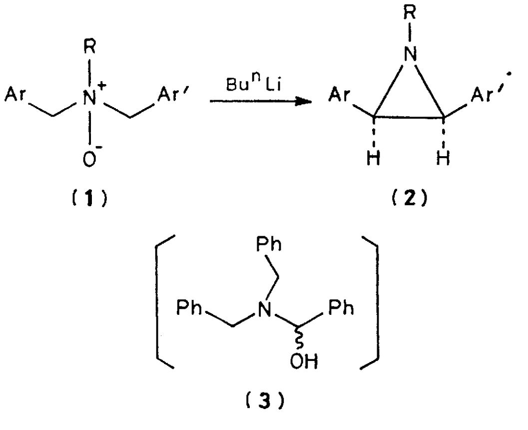
The reactions of the *N*-substituted dibenzylamine *N*-oxides (**1**) (R = benzyl, n-butyl, or cyclohexyl) with n-butyl-lithium in ether gave the corresponding *cis*-2,3-diphenylaziridines in moderate yields (20—42%); application of this reaction to other related compounds enabled a novel ring system, 10,11-dihydro-10,11,5-nitrilomethanodibenzocycloheptene to be synthesized.

It is well known that aziridines are useful intermediates in organic synthesis and some derivatives have interesting physiological activities. Several intramolecular aziridine forming reactions are known and are of great significance for synthetic and mechanistic organic chemistry.[1] Although there are known base-induced reactions of onium compounds and of aliphatic t-amine *N*-oxides (*e.g.* Meisenheimer rearrangement, Cope elimination, and Polonovski reaction) none of the base-induced reactions of aliphatic t-amine *N*-oxides has been applied to organic synthesis.† We report a novel aziridine forming reaction from t-amine *N*-oxides using strong bases.

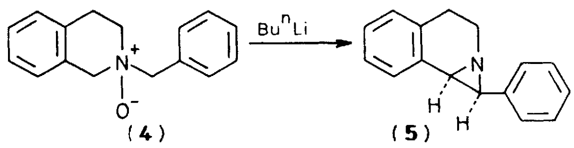
To a suspension of tribenzylamine *N*-oxide (**1a**) (mp. 133—134 °C, 1 mmol) in anhydrous ether was added $\mathrm{Bu^{n}Li}$ (1.2 mmol)‡ with ice-cooling under an argon atmosphere. After stirring for 3 h at room temp. [(**1a**) was completely consumed], the reaction mixture was poured into ice–water and extracted with dichloromethane followed by silica gel chromatography to give *cis*-1-benzyl-2,3-diphenylaziridine (**2a**) [42%; mass spectrum *m/e* 285(M^+); ^{1}H n.m.r. ($CDCl_3$) δ 3.03(2H,s) and 3.89(2H,s)], accompanied by *trans*-1-benzyl-2,3-diphenylaziridine [2—3%; *m/e* 285(M^+); ^{1}H n.m.r. ($CDCl_3$) δ 3.32(2H,br s), 3.38(1H,d,*J*14 Hz), and 3.66(1H,d,*J*14 Hz)], dibenzylamine [32%], and benzaldehyde [26%] (Scheme 1). The stereochemistries of the aziridines thus obtained were unequivocally determined by direct comparison of their n.m.r. spectra and g.l.c. retention times with those of authentic samples which were stereoselectively prepared.[2] The interconversion between two isomers under the reaction condition was not observed and the formation of benzaldehyde and dibenzylamine can be explained by the decomposition of the *gem*-aminoalcohol (**3**) during work-up. A series of similar aziridines (**2b**)—(**2e**) was also formed by the reactions of the corresponding *N*-oxides (**1b**)—(**1e**) with $\mathrm{Bu^{n}Li}$. The *cis*-stereochemistry of (**2b**)—(**2e**) was established on the basis of the coupling constants of the ring protons in their n.m.r. spectra in comparison with those of the analogous aziridines.[3] The results are summarized in Table 1.



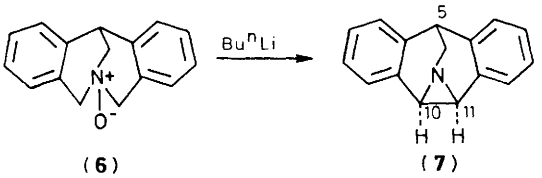
Scheme 1

We have also investigated the applicability of this reaction for the synthesis of some aziridine derivatives fused to alicyclics. Thus, 2-benzyl-3,4-dihydroisoquinoline *N*-oxide (**4**) (m.p. 177—178 °C) reacted with $\mathrm{Bu^{n}Li}$ in ether to afford the derivative (**5**) [23%, fairly unstable oil; *m/e* 221(M^+); ^{1}H n.m.r. ($CDCl_3$) δ 2.60—3.00 (4H,m) and 3.90(2H,s,*cis*-aziridine-H)] (Scheme 2) and similarly, when 6,12-methanodibenz[*c,f*]azocine *N*-oxide (**6**) (m.p. 231—232 °C) was allowed to react with $\mathrm{Bu^{n}Li}$ in dioxan, a novel ring system, 10,11-dihydro-10,11,5-nitrilomethanodibenzoheptene (**7**) (m.p. 144—146 °C), was isolated in 49% yield. The structure of (**7**) was confirmed by its spectroscopic data [*m/e* 219 (M^+); ^{1}H n.m.r. ($CDCl_3$) δ 2.82(2H,d,*J*2 Hz, H-13), 3.66(2H,s,H-10 and H-11), 4.02 (1H,t,*J*2 Hz,H-5); ^{13}C n.m.r. ($CDCl_3$) δ 39.8 (d,C-5), 40.0(d,C-10 and C-11), and 42.3 p.p.m. (t,C-13)] (Scheme 3).

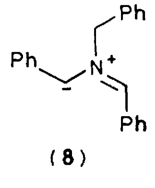
Finally, we have failed to isolate the corresponding pyrrolidine derivative from the reaction of the *N*-oxide (**1a**) with



Scheme 2



Scheme 3



(**8**)

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† Birch-type reduction of aliphatic t-amine *N*-oxides with Na–liq. NH_3 has been reported: J. P. Yardley, *Synthesis*, 1973, 543; K. Iwasa, P. Chinnasamy, and M. Shamma, *J. Org. Chem.*, 1981, **46**, 1378.

‡ In order to investigate the optimum reaction conditions affording (**2a**) preliminary experiments were carried out with the following results: base (mol. equiv.)–solvent, temp., yield of (**2a**) % (by g.l.c.); $\mathrm{Bu^{t}OK}$(1.2)–$\mathrm{Bu^{t}OH}$, reflux, 0 °C; lithium diisopropylamide(1.2)–tetrahydrofuran, room temp., 36; $\mathrm{Bu^{n}Li}$(1.2)–Et_2O, room temp., 48; $\mathrm{Bu^{n}Li}$(2.4)–Et_2O, room temp., 48; $(Me_3Si)_2NLi$(1.2)–Et_2O, room temp., 34.

Table 1

Compound[a]	Ar	Ar′	R	Isolated yield % of (**2**)	δ(*cis*-Ring-H, $CDCl_3$)
a	phenyl	phenyl	benzyl	42	3.03(2H,s)
b	phenyl	phenyl	n-butyl	25	2.78(2H,s)
c	phenyl	phenyl	cyclohexyl	35	2.89(2H,s)
d	p-ClC_6H_4	p-ClC_6H_4	cyclohexyl	20	2.84(2H,s)
e	phenyl	p-$MeOC_6H_4$	cyclohexyl	28	2.82(2H,s)

[a] Compounds (**1a**—**e**) and (**2a**—**e**) gave correct mass spectra.

Bu^nLi in the presence of an excess of dipolarophile to prove the azomethine ylide[5] (**8**) as a probable intermediate.[6]§

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§ When $PhCH_2N^+(CH_2Ph)=CHPh\ ClO^-_4$, prepared separately, was allowed to react with Bu^nLi in the presence of a dipolarophile such as dimethyl fumarate, a trace of the corresponding pyrrolidine derivative was detected.