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EFFICIENT NUCLEOPHILIC OXIRANE RING CLEAVAGE WITH DIBUTYLTIN DIAZIDE

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Abstract: Dibutyltin diazide has proven to be potential in nucleophilic ring opening of a variety of oxiranes to give 1,2-azido alcohols in less than four hours (DMF at 60 °C) in fair to excellent yields.

In the preceding paper, we have reported that tributyltin azide (TBT-N_3) can cleave oxirane ring without any promoter to give 1,2-azido alcohols in acceptable yields.[1] The reaction time, however, turned out to depend highly upon the structural difference of the oxiranes and varied, for instance, from 25 minutes in the case of cyclohexene oxide to 48 hours in the case of ethyl *trans*-2,3-epoxy-4-(*tert*-butyldimethylsilyloxy)butanoate for the completion of the reaction.[1] Our continuing interest in this chemistry, and the early publications[2] concerned with the Me_3SiN_3 ring cleavage of isolated oxiranes catalyzed by $Ti(O\text{-}i\text{-}Pr)_2(N_3)_2$ as well as the recent report[3] demonstrating the high reactivity of $Ti(O\text{-}i\text{-}Pr)_2(N_3)_2$ in the similar reactions of 2,3-epoxy alcohols motivated us to investigate on the related reaction with alternative organometallic diazides with still higher reactivity. We have now found that dibutyltin diazide (DBT-$(N_3)_2$)[4] requires no mediators and is about ten times as reactive as TBT-N_3 in oxirane ring cleavage. In addition, it has advantages where the reaction can be conducted under neutral conditions and the products are able to be separated easily from tin-based impurity on column chromatography which was sometimes troublesome in the case of TBT-N_3. Here, we deliver the first record of azide ring cleavage of oxiranes with DBT-$(N_3)_2$.

DBT-$(N_3)_2$ was prepared according to a one-pot, two stage protocol reported by J. Lorberth et al.[4a] which involves reaction between dibutyltin dichloride and lithium diethyl amide and subsequent reaction of stannylamine thus-obtained with hydrogen azide[5] as shown in Scheme I.

Scheme I

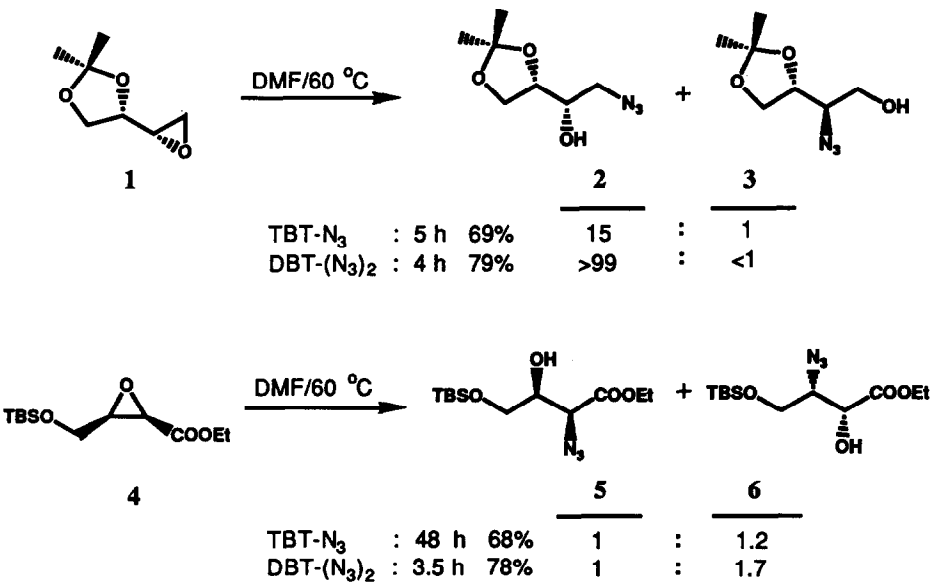
$$Bu_2SnCl_2 + 2LiNEt_2 \longrightarrow Bu_2Sn(NEt_2)_2 + 2LiCl$$

$$Bu_2Sn(NEt_2)_2 + 4HN_3 \longrightarrow Bu_2Sn(N_3)_2 + 2Et_2HNHN_3$$

DBT-$(N_3)_2$ was purified by fractional distillation under reduced pressure to separate from readily sublimable by-product, diethylammonium azide, and was obtained as moisture sensitive crystals: bp 175–180 °C/0.1 mmHg; mp 63–65 °C (lit.[2] bp 170–180 °C/0.1 mmHg; mp 63–65 °C). Thus, reactions between DBT-$(N_3)_2$ and oxiranes were carried out using well-dried glassware and under nitrogen atmosphere for every run. DMF turned out to be a good solvent for DBT-$(N_3)_2$ and satisfactory to effect the desired reaction.[6]

Typical features of DBT-$(N_3)_2$, compared to TBT-N_3, are worth noting, as exemplified in Scheme II. In the case of 1,2-*O*-isopropylidene-3,4-epoxy-1,2-butanediol (**1**), both TBT-N_3 and DBT-$(N_3)_2$ required nearly the same time for the completion of the reactions, whereas an overwhelming preference for terminal opening (**2**) was achieved for DBT-$(N_3)_2$. This is probably due to a higher azido nucleophilicity of the dialkyltin reagent with which the reaction proceeded cleanly in an S_N2 fashion. On the other hand, although no significant improvement in the ratio of regioisomers (**5** : **6**) was observed for the *cis*-2,3-epoxyester (**4**) even if DBT-$(N_3)_2$ was employed, the time needed for the completion of the reaction was extremely shortened. These findings suggest that both the reactivity and regioselectivity displayed in this reaction depend on a combination of nucleophilicity of DBT-$(N_3)_2$ and steric or electronic factors of oxirane.[7] Nevertheless, the high nucleophilicity of DBT-$(N_3)_2$ can ensure either higher regioselectivity or shorter reaction time for oxirane ring cleavage.

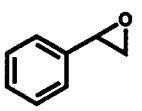
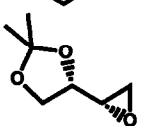
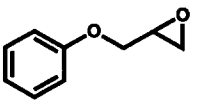
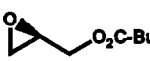
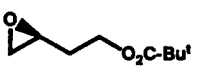
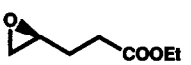
Scheme II



Another factor which may be responsible for the enhanced reactivity of DBT-$(N_3)_2$ as compared with TBT-N_3 should be a larger Lewis acidity of DBT-$(N_3)_2$ than that of TBT-N_3, judging from a general principle that Lewis acidity of organometallic compounds increases with the number of electronegative groups attached to the metal.

The reaction of various oxiranes with DBT-$(N_3)_2$ have been examined in DMF at 60 °C. The general procedure is as follows. A solution of oxirane (1.4 mmol) in DMF (1 ml) was heated at 60 °C under stirring. To this was added DBT-$(N_3)_2$ (2.8 mmol) in one-portion and the mixture was stirred at that temperature until a disappearance of the oxirane on TLC diagnosis. The mixture was cooled to room temperature and distributed

Table I. Oxirane-ring opening with DBT-$(N_3)_2$ in DMF at 60 °C[a]

Entry	Oxiranes[c]	Time/h	Product[b] Yield/%	prim-N_3		sec-N_3
1		0.2	94	1	:	13
2		4.0	79	>99	:	<1
3		1.5	96	31	:	1
4		0.5	85	50	:	1
5		0.5	83	>99	:	<1
6		0.4	59	14[d]	:	1
7		4.0	45 (76)[e]	4 (α)	:	1 (β)
8		3.5	78	1 (α)	:	1.7 (β)

a) Oxirane = 1.4 mmol, DBT-$(N_3)_2$ = 2.8 mmol, DMF = 1 ml; the yields determined for pure products after column chromatographical purification (SiO_2); b) The structures and the ratio of regioisomers determined for the product itself or corresponding acetate (Ac_2O/4-(dimethylamino)-pyridine/CH_2Cl_2) by ^1H NMR (200 or 500 MHz, if necessary, $CDCl_3$) and/or capillary GLC: ^{13}C NMR and IR spectra left no problem at all; optical purity of the products for Entries 2, 4 - 8 not determined; c) Oxiranes available from commercial product for Entries 1 and 3 and synthesized for others; optically pure oxiranes employed for Entries 2, 4 - 8; d) Obtained almost quantitatively as the corresponding γ-butyrolactone; e) Based on consumed epoxyester (recovered unchanged ester: 31%).

between ether (30 ml) and water (15 ml), the ether solution being dried ($MgSO_4$) and concentrated to give an oil. Column chromatography on silica gel (hexane : EtOAc = 10 : 1) of this oil afforded the pure products. Regiochemical outcomes were determined by ^1H NMR spectroscopy (200 or 500 MHz, if necessary, $CDCl_3$)[8] for the azido alcohols itself or corresponding acetates (Ac_2O/4-(dimethylamino)pyridine/CH_2Cl_2). The results are summarized in Table I.

Every entry required 4 hours or less for the completion of the reaction except for Entry 7 where unchanged epoxyester was recovered (31%). Prolonged reaction for Entry 7 did not have the intended effect and rather increased an amount of impurity. The regioselectivity turned out to be very high except for Entries 7 and 8.[9] Thus, a remedy for both the product yield from *trans*-epoxyester and the regioselectivity from the cis-isomer was left to future challenge. Nevertheless, workup as well as the reaction can be carried out under essentially neutral conditions in a conventional way which makes the present method applicable to the oxiranes bearing even acid or base sensitive functional groups such as silyl and acetonide protective groups, or ester group (Entries 2, 7 and 8).[10] Thus, DBT-$(N_3)_2$ is of benefit to organic synthesis.

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4) a) J. Lorberth, J.; Krapf, H.; Noth, H. *Chem. Ber.* **1967**, *100*, 3511. b) Thayer, J. S. *Organometal. Chem. Rev.* **1966**, *1*, 157.

5) ***Caution! Hydrogen azide is extremely explosive and toxic. All the reactions employing this should be carried out in a well-ventilated hood and handled never as a neat liquid but as a solution in ether or water. We have prepared a solution of HN_3 in ether several times without no accident. For human toxicity, see The Merck Index, 9th Ed. ; 1976, p 631***

6) DBT-$(N_3)_2$ can readily dissolve in CH_2Cl_2, THF, and benzene, which, however, have not been examined as a reaction medium in the present study. This is virtually insoluble in ether, which, therefore, is recommended as a solvent for extraction of the products free from an excessive DBT-$(N_3)_2$.

7) The regioselectivity for the reaction between Ti(O-i-Pr)$_2(N_3)_2$ and 2,3-epoxy alcohol depends on a delicate balance of steric and electronic factors: see reference (3).

8) Two-dimensional relayed COSY experiments gave expeditious solutions to the structures.

9) Regioselectivity observed for azide ring cleavage of several *cis*-2,3-epoxy alcohols with Ti(O-i-Pr)$_2(N_3)_2$ in benzene has been reported to be 1:1 ~ 1:1.5: see reference (3).

10) For instance, sulfuric acid promoted hydrolysis of an excessive titanium diazide was executed in the workup following the Ti(O-i-Pr)$_2(N_3)_2$ ring cleavage of oxiranes: see reference (3).

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