Novel Synthesis of Cyclopropylaminosulfoxonium Salts from (Dimethylamino)phenylsulfoxonium Methylide

Kentaro Okuma,* Yasunari Sato, Toshiro Ishii, and Hiroshi Ohta

Department of Chemistry, Faculty of Science, Fukuoka University, Jonan-ku, Fukuoka 814-01, Japan

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The reactions of (dimethylamino)phenylsulfoxonium methylide with aldehydes gave unusual cyclopropylaminosulfoxonium salts in good yields when 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) was used as a base. This ylide reacted with aldehydes to give the corresponding betaines, which resulted in the formation of vinylsulfoxonium salts. The additional ylide reacted with these salts to afford cyclopropylsulfoxonium salts.

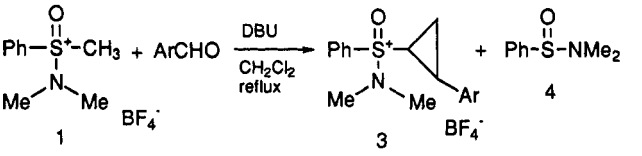
Cyclopropylsulfoxonium salts are important compounds for the synthesis of cyclobutanones and lactones.[1,2] Typical methods include the base-induced cyclization of (3-halopropyl)sulfonium or sulfoxonium salts.[2] For more than two decades, Johnson and co-workers studied the chemistry of aminosulfoximines and aminosulfoxonium salts 1.[3] We have shown that the reaction of (dimethylamino)phenylsulfoxonium methylide (2) with epoxides afforded the corresponding oxetanes and cyclopropyl sulfones.[4] However, there is no report on the direct synthesis of cyclopropylaminosulfoxonium salts (3) from these reagents. We now report a novel reaction of 1 leading to cyclopropylaminosulfoxonium salts and their mechanistic investigation.

Results and Discussion

Treatment of 1 with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) followed by the addition of aldehydes in refluxing dichloromethane resulted in the formation of cyclopropylaminosulfoxonium salts 3 and *N,N*-dimethylbenzenesulfinamide (4) in good yields (Scheme 1). Other reactions were carried out in a similar manner (Table 1).

Salts 3 were obtained as mixtures of *cis* and *trans* forms in a nearly 4:6 ratio. These results were quite different from those of Johnson and co-workers.[3,5] They found that the reaction of 2 with aldehydes in dimethyl sulfoxide gave the corresponding epoxides in good yields. When the present reaction was carried out at room temperature, starting salts 1 were recovered. When the reaction was

Scheme 1



carried out in sodium *tert*-butoxide in 2-methyl-2-propanol, the corresponding epoxides and sulfinamide 4 were obtained in moderate yields. Thus, refluxing dichloromethane and DBU as a base must be required for the preparation of salts 3.

Two mechanisms are reasonable to explain this reaction. First, ylide 2 reacts with aldehydes to afford the corresponding epoxides, which further react with additional 2 to give 3 (route A). Intermediacy of vinylsulfoxonium salts 5 is another pathway (route B). Ylide 2 reacts with aldehydes to afford the corresponding (2-hydroxyalkyl)-sulfoxonium salts, which are dehydrated to give the corresponding 5. Then, another ylide 2 reacts with 5 to afford salts 3 (Scheme 2).

To confirm which mechanism is operative, following reactions were carried out. The reaction of styrene oxide with 2 in refluxing dichloromethane afforded only the recovered styrene oxide and sulfinamide 4. Additionally, we have already communicated the reaction of 2 with epoxides.[4] When the reaction of 2 with styrene oxide was carried out by using sodium *tert*-butoxide as a base, the obtained products were 2-phenylcyclopropyl phenyl sulfone (6), 3-hydroxy-3-phenylpropyl phenyl sulfone (7), and 2-phenyloxetane (8) (Scheme 3). Thus, route A was excluded.

Then, we tried the synthesis of (dimethylamino)phenyl-(2-tolylethenyl)sulfoxonium tetrafluoroborate (5a) by the method described by Johnson and co-workers[6] to confirm intermediacy of vinylsulfoxonium salts. The reaction of salt 5a with ylide 2 gave 3b in 75% yield. Thus, the reaction proceeds through vinylsulfoxonium salts intermediates (route B).

The difference in the reactivity might be due to the difference in the solubility of solvents. Dichloromethane is insoluble in water and used as a solvent for azeotropic separation. In refluxing dichloromethane, dehydration might be faster than epoxide formation in the present reaction. Dehydration might be a key step for the synthesis of 3. Dichloromethane is much favorable than other

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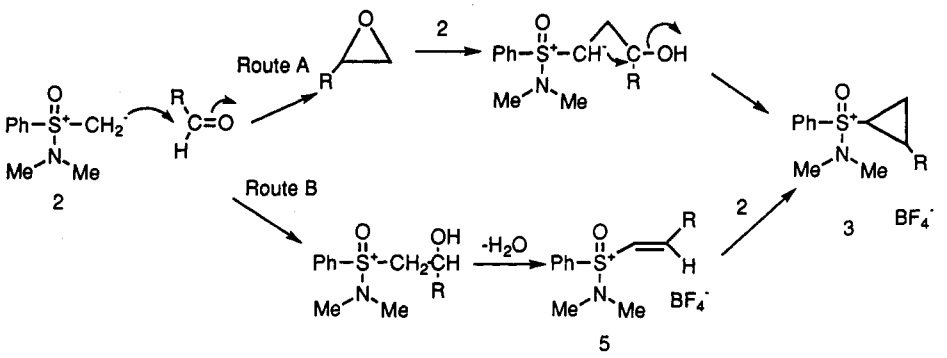
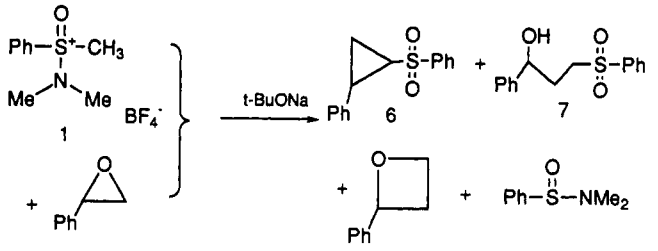
Table 1. Preparation of Cyclopropylaminosulfoxonium Salts 3

aldehyde (ArCHO)	conditions: solvent	Base	T/°C	time/h	product 3	(yield/%)
Ar = Ph	CH_2Cl_2	DBU	reflux	2	**3a**	80
Ph	CH_2Cl_2	DBU	rt	8	**3a**	0
Ph	*t*-BuOH	*t*-BuONa	50	8	**3a**	0
Ph	DMSO	CH_3SOCH_2Na	30	6	**3a**	0
4-Tol	CH_2Cl_2	DBU	reflux	2	**3b**	92
4-ClC_6H_4	CH_2Cl_2	DBU	reflux	2	**3c**	80
4-BrC_6H_4	CH_2Cl_2	DBU	reflux	2	**3d**	85
4-$NO_2C_6H_4$	CH_2Cl_2	DBU	reflux	2	**3e**	71

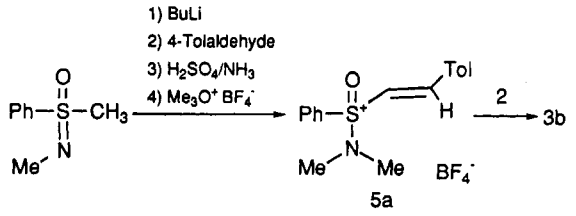
Scheme 2



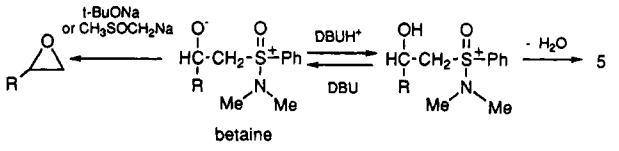
Scheme 3



Scheme 4



Scheme 5



solvents for dehydration. Another reason for the formation of cyclopropyl salts **3** might be the use of DBU as a base, which is a weak base compared with dimsylsodium or sodium *tert*-butoxide. As shown in Scheme 5, strong bases such as potassium *tert*-butoxide and butyllithium will afford epoxides, the normal reaction products. On the other hand, DBU:HBF_4 will afford a proton source of betaine intermediate, which resulted in the formation of (2-hydroxylalkyl)sulfoxonium salts. Dehydration of these salts produced vinylsulfoxonium salts **5**, which further reacted with additional ylides to give the salts **3**.

To confirm whether this reaction can be applied to other vinylsulfoxonium salts, the reaction of (2,2-diphenylethenyl)(dimethylamino)phenylsulfoxonium tetrafluoroborate (**5b**) with **2** was carried out. The corresponding cyclopropylsulfoxonium salt (**3f**) was obtained in 75% yield. Thus, this reaction might be applicable to vinylsulfoxonium salts.

In the past three decades, the chemistry of sulfoxonium ylides has been an area of substantial interest.[5] It is well known that sulfoxonium ylides are effective as nucleophilic methylene transfer reagents.[5] Cyclopropanation using ylide **2** was also reported by Johnson *et al.* starting from α,β-unsaturated ketones.[3,7] However, there is no report on the direct synthesis of cyclopropylaminosulfoxonium salts in one operation. This is the first example of direct synthesis of **3** from salts **1**.

We are now continuing the reaction and some synthetic application of salts **3**.

Experimental Section

Materials. Salt **1** was prepared by a method described in the literature.[8] Vinylsulfoxonium salts **5a** and **5b** were prepared by a method according to Johnson *et al.* (**5a**, mp 172–173 °C (lit.[6] mp 174–175 °C), **5b**, mp 139–140 °C (lit.[6] mp 140–141 °C)).

Reaction of 1 with Aromatic Aldehyde. To a solution of **1** (3.1 g, 11.3 mmol) in dichloromethane (30 mL) was added DBU (2.1 g, 13.5 mmol). After being stirred for 30 min, benzaldehyde (0.60 g, 5.6 mmol) was added to this solution and refluxed for 2 h. During this experiment, water was trapped on a condensor. The reaction mixture was washed with 1 N HCl (20 mL × 2) and water (20 mL × 2) and dried over $MgSO_4$. The suspension was filtered and evaporated to give brown crystals, which were roughly chromatographed over silica gel by elution with dichloromethane to give pale yellow crystals of salts **3a** as a mixture of *cis* and *trans* isomers (1.68 g, 4.5 mmol, 80%). Recrystallization from methanol afford a pure *trans*-**3a** (0.78 g, 2.1 mmol, 38%). *trans*-**3a**: (BPh_4) mp 172–173 °C. Other reactions were carried out in a similar manner.

trans-**3b**: (BPh_4) mp 167–168 °C.

trans-**3c**: (BPh_4) mp 206–207 °C.

trans-**3d**: (BPh_4) mp 199–200 °C.

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Reaction of 1 with Styrene Oxide. (a) By using DBU as a Base. To a solution of 1 (1.8 g, 6.6 mmol) in dichloromethane (20 mL) was added DBU (1.2 g, 8.0 mmol). After being refluxed for 30 min, a solution of styrene oxide (0.80 g, 6.6 mmol) in dichloromethane (5 mL) was added dropwise to this solution and refluxed for 2 h. The resulting solution was washed with water (10 mL × 3), dried over $MgSO_4$, and evaporated to give a brown oil, which was chromatographed over silica gel by elution with hexane and dichloromethane. The hexane fraction was evaporated to give styrene oxide (0.15 g, 1.25 mmol, 19%). The dichloromethane fraction was evaporated to give sulfinamide 4 (0.85 g, 5.0 mmol, 76%).

Since styrene oxide was recovered only 19%, the following GLC analysis was carried out. After the reaction mixture was poured into water, the dichloromethane layer was subjected to GLC analysis by using nitrobenzene as an internal standard. Styrene oxide was recovered in 72% yield.

(b) By Using Sodium *tert*-butoxide as a Base. To a solution of salt 1 (5.42 g, 20 mmol) in 2-methyl-2-propanol (40 mL) was added dropwise a solution of *t*-BuONa (2.40 g, 25 mmol) in 2-methyl-2-propanol (25 mL) at 65 °C. After being stirred for 2 h, a solution of styrene oxide (2.40 g, 20 mmol) in 2-methyl-2-propanol (10 mL) was added dropwise to this solution and refluxed for 2 days. Water (15 mL) was added to this solution and evaporated to a give brown oil, which was extracted with hexane (15 mL × 3) and dichloromethane (15 mL × 3). The hexane layer was dried over $MgSO_4$, filtered, and evaporated to give a pale brown oil, which was chromatographed over silica gel by elution with dichloromethane-hexane to give cyclopropyl sulfone 6 (0.98 g, 3.8 mmol, 19%), sulfinamide 4 (0.51 g, 3.0 mmol, 15%), and 2-phenyloxetane (8)[9] (0.14 g, 1.0 mmol, 5%).

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Cyclopropyl sulfone 6: mp 98–99 °C. Anal. Calcd for $C_{15}H_{14}O_2S$. C, 65.18; H, 5.85. Found: C, 65.19; H, 5.95.

The dichloromethane eluant was dried over $MgSO_4$, filtered, and evaporated to give a pale brown oil, which was chromatographed over silica gel by elution with dichloromethane to afford (3-hydroxy-3-phenylpropyl)phenylsulfone (7, 0.52 g, 2.0 mmol, 10%). colorless crystals, mp 114–115 °C. Anal. Calcd for $C_{15}H_{16}O_3S$. C, 69.74; H, 5.47. Found: C, 69.44; H, 5.43.

Reaction of 5a with Ylide 2. To a solution of salt 1 (0.43 g, 1.57 mmol) in dichloromethane (20 mL) was added DBU (0.29 g, 1.88 mmol) and refluxed for 30 min. A solution of **5a** (0.59 g, 1.57 mmol) in dichloromethane (5 mL) was added to this solution and refluxed for 2 h. The resulting solution was washed with 1 N HCl (10 mL × 2) and water (10 mL × 2), dried over $MgSO_4$, and evaporated to give pale orange crystals. Recrystallization from methanol afforded the corresponding salt **3b** (0.46 g, 1.18 mmol) in 75% yield. mp 167–168 °C.

Reaction of 5b with Ylide 2. To a solution of salt 1 (0.19 g, 0.71 mmol) in dichloromethane (20 mL) was added DBU (0.13 g, 0.86 mmol) and refluxed for 30 min. A solution of **5b** (0.31 g, 0.71 mmol) in dichloromethane (5 mL) was added to this solution and refluxed for 2 h. The resulting solution was washed with 1 N HCl (10 mL × 2) and water (10 mL × 2), dried over $MgSO_4$, and evaporated to give pale orange crystals. Recrystallization from methanol afforded the corresponding salt **3f** (0.11 g, 0.24 mmol, 34%). **3f**; mp 204–205 °C. Anal. Calcd for $C_{23}H_{24}BF_4NOS$: C, 60.67; H, 5.76; N, 3.20. Found: C, 60.54; H, 5.44; N, 2.81.

Supplementary Material Available: ^1H NMR and ^{13}C NMR data of compounds **3**, **6**, and **7** (2 pages). This material is contained in libraries of microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.