Mechanistic Studies of Tetraphenylstibonium Iodide-Catalyzed Cycloaddition of Oxiranes with Heterocumulenes

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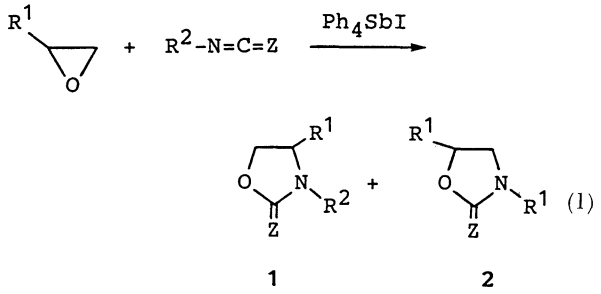
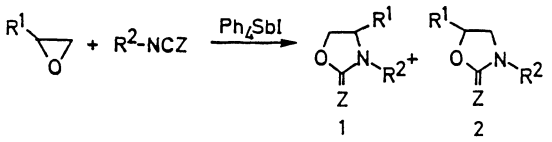
In the selective α-cleavage cycloaddition of oxiranes with heterocumulenes catalyzed by tetraphenylstibonium iodide, the direction of oxirane fission at first stage is not significant, while the difference of reaction behaviors of two antimony alkoxide intermediates ($Ph_4SbOCH_2CH(R^1)I$ and $Ph_4SbOCH(R^1)CH_2I$), insertion of heterocumulenes and cyclization to original oxiranes, is responsible for the unusual selectivity.

Recently, we reported the unusual cycloaddition promoted by tetraphenylstibonium iodide, where monosubstituted oxiranes added to isocyanates or carbodiimides via a selective cleavage at the substituted site (α-cleavage) of oxirane rings, producing 3,4-disubstituted oxazolidine derivatives (**1**) (Eq. 1).[1]



The results are summarized in Table 1.[1a,c] This type of cycloaddition has not been achieved by using conventional catalysts which predominantly gave 3,5-disubstituted derivatives **2** instead of **1**.[2] Some attempts to produce 3,4-disubstituted 2-oxazolidinones by using lithium bromide[3] or aluminium trichloride[4] resulted in failure, particularly even in the case of aluminium trichloride expected to cleave oxirane rings at the α-site effectively due to its high Lewis acidity. Thus it appears unreasonable why tetraphenylstibonium iodide plays as a peculiar and active catalyst under very mild conditions inspite of its low acidity and nonionic character.[5] We now wish to discuss the mechanistic investigations of this unique catalytic cycloaddition of oxiranes with heterocumulenes; isocyanates and carbodiimides.

Table 1. Cycloaddition of Oxiranes with Heterocumulenes Catalyzed by Tetraphenylstibonium Iodide



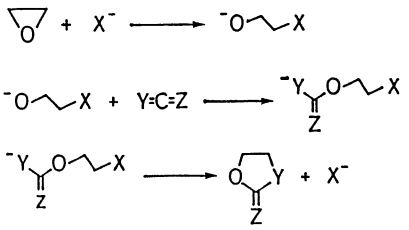
Entry	R^1	R^2	Z	Solv.	Yield %	Ratio 1 : 2
1	Me	Ph	O	CH_2Cl_2	100	80: 20
2	Me	*p*-ClC_6H_4	O	CH_2Cl_2	89	65: 35
3	Me	*p*-$MeOC_6H_4$	O	CH_2Cl_2	72	88: 12
4	Me	Bu	O	CH_2Cl_2	100	81: 19
5	Et	Ph	O	CH_2Cl_2	100	100: 0
6	Et	Ph	O	PhH	86	78: 22
7	Et	Ph	O	THF	85	79: 21
8[a]	Et	CH_2=$CHCH_2$-	O	CH_2Br_2	81	100: 0
9	Ph	Ph	O	PhH	86	99: 1
10[b]	$PhOCH_2$	Ph	O	CH_2Br_2	100	91: 9
11	Et	Ts[g]	O	CH_2Cl_2	100	0:100
12[c]	Et	Ph	O	CH_2Cl_2	0	—
13[d]	Me	Ph	N-Ph	PhH	97	100: 0
14[e]	Me	Ph	N-Ph	PhH	84[h]	41: 59[i]
15[f]	$MeOCH_2$	Ph	N-Ph	PhH	86	100: 0

Oxirane/heterocumulene/Ph_4SbI=20/10/1 mmol, 40 °C, solv. 5 mL, isocyanate was added dropwise for 1 h and carbodiimide was added at one portion. a) 80 °C. b) 90 °C. c) Catalyzed by Ph_4SbOTf. d) 15 h. e) Catalyzed by Ph_4SbBr, 110 h. f) 38 h. g) *p*-Toluenesulfonyl. h) Isolated yield. i) Determined by ^1H NMR.

Results and Discussion

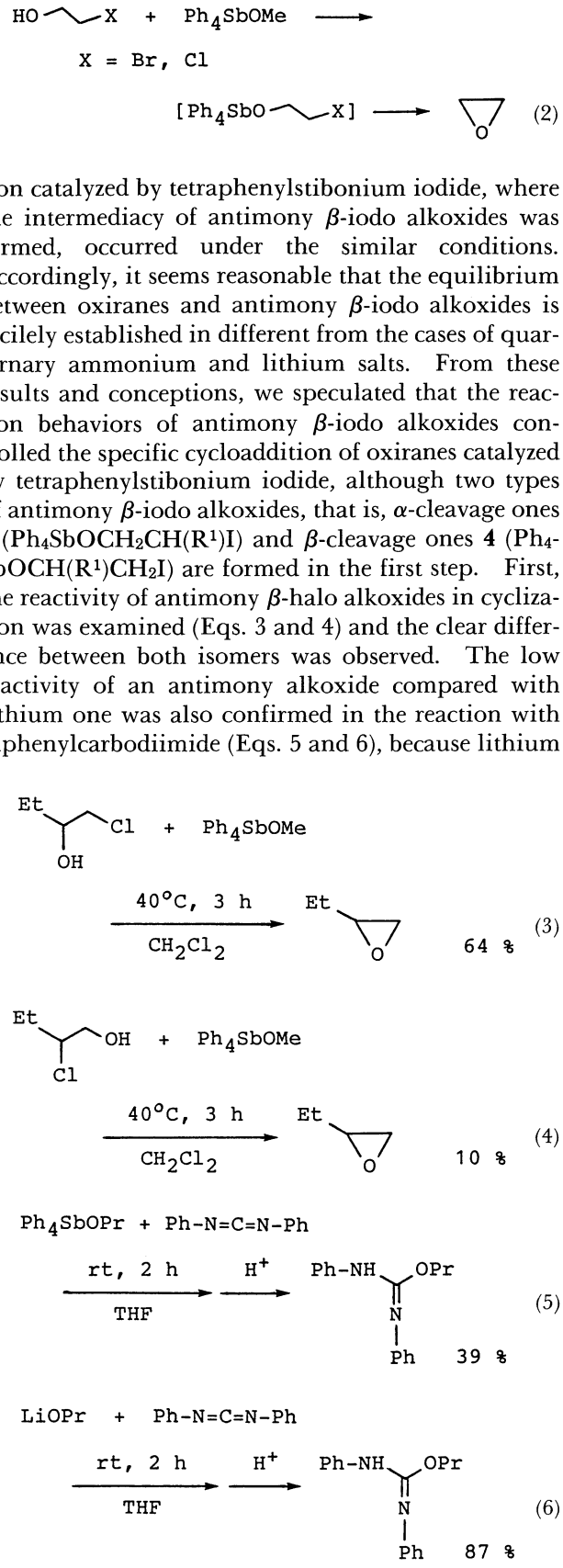
The ring cleavage reaction of oxiranes at the α-site is generally considered to take place under acidic conditions and to follow a "borderline S_N2" mechanism.[6] No reaction, however, was promoted by tetraphenylstibonium triflate[7] having an extremely lower nucleophilic anion species than tetraphenylstibonium iodide (Entry 12).[8] Generally, the selectivity order in α-cleavage of oxiranes with hydrogen halides (HX) as typical acid reagents is known to be X=Cl>Br>I.[6] On the contrary, the selective formation of **1** is inherent in tetraphenylstibonium iodide (Entries 13 and 14). Moreover, tetraphenylstibonium iodide isn't strong Lewis acid as mentioned above. These results indicated that this unusual cycloaddition of oxiranes can not be expained only by "borderline S_N2" mechanism.

On the other hand, the reaction mechanism of the cycloaddition of oxiranes with heterocumulenes by free-anion catalysts such as quarternary ammonium salts and lithium salts is thought as follows (Scheme 1)[9] and 3,5-disubstituted 2-oxazolidinones are formed

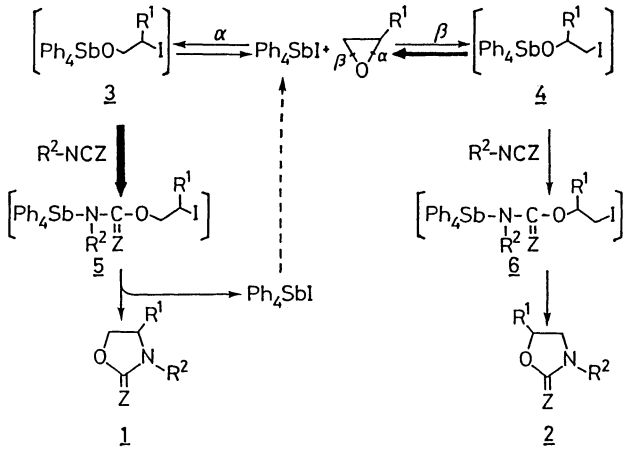


Scheme 1.

selectively. First step, where a β-halo alkoxide is obtained from an oxirane and a free halide ion, is known to be slow. This difficulty of oxirane cleavage requires drastic conditions in the case of conventional catalyst systems. Although no counter cation is not taken into consideration at all in this free-anion mechanism, the role of tetraphenylstibonium moiety must be important because both the antimony-iodine[5] and antimony-oxygen bonds[10] are highly covalent not to be dissociated into ions in organic solvents especially. Indeed, the high reactivity of tetraphenylstibonium iodide as a catalyst indicated the facile formation of antimony β-halo alkoxide, which was unaccountable by a simple nucleophilic attack of the iodide ion without the participation of tetraphenylstibonium moiety. Consequently, it seems that this cycloaddition proceeds in three steps like as free-anion mechanism, that is, oxirane cleavage, insertion of heterocumulenes and ring closure to cycloadducts. On the other hand, our current report revealed that antimony β-halo alkoxides were readily transformed into the corresponding oxiranes (Eq. 2).[11] Both cyclic ether formation and the cycloaddition catalyzed by tetraphenylstibonium iodide, where the intermediacy of antimony β-iodo alkoxides was formed, occurred under the similar conditions. Accordingly, it seems reasonable that the equilibrium between oxiranes and antimony β-iodo alkoxides is facilely established in different from the cases of quarternary ammonium and lithium salts. From these results and conceptions, we speculated that the reaction behaviors of antimony β-iodo alkoxides controlled the specific cycloaddition of oxiranes catalyzed by tetraphenylstibonium iodide, although two types of antimony β-iodo alkoxides, that is, α-cleavage ones **3** ($Ph_4SbOCH_2CH(R^1)I$) and β-cleavage ones **4** ($Ph_4SbOCH(R^1)CH_2I$) are formed in the first step. First, the reactivity of antimony β-halo alkoxides in cyclization was examined (Eqs. 3 and 4) and the clear difference between both isomers was observed. The low reactivity of an antimony alkoxide compared with lithium one was also confirmed in the reaction with diphenylcarbodiimide (Eqs. 5 and 6), because lithium



β-halo alkoxides are thought to be formed in the cycloaddition using lithium halides as a conventional catalyst.[9] This result proved that the insertion of

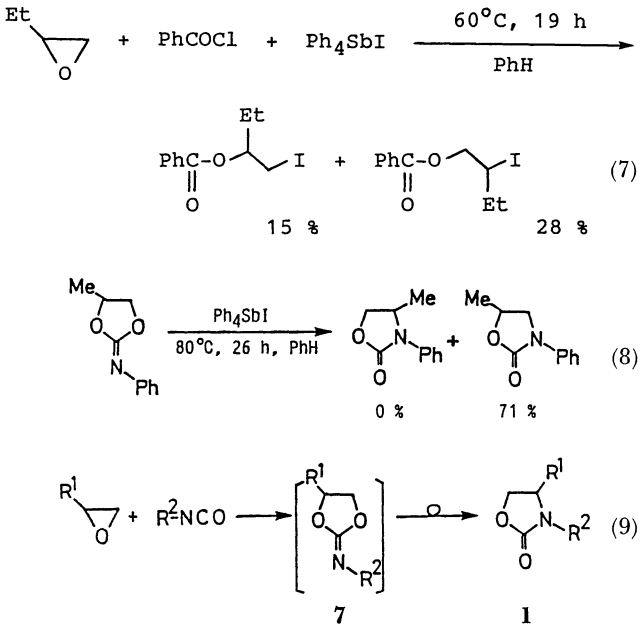


Scheme 2.

heterocumulenes to antimony alkoxide isn't facile in contrast with the cycloaddition by conventional catalysts.[9] Moreover, it is plausible that reactivity of antimony alkoxides **3** to insertion of heterocumulenes is higher than that of antimony alkoxides **4**, perhaps because a primary alkoxide is more active than the secondary one. From these informations, we propose the reaction mechanism of the cycloaddition of oxiranes with heterocumulenes catalyzed by tetraphenylstibonium iodide as shown in scheme 2.

In the first step, non selective cleavage of oxiranes occurs and two types of antimony alkoxides **3** (α-cleavage) and **4** (β-cleavage) are produced. Both higher reproducible ability to original oxiranes and lower nucleophilicity of **4** would be responsible for little formation of antimony carbamates **6**. On the other hand, antimony alkoxides **3**, which would be hardly transformed into oxiranes, would readily react with heterocumulenes to afford antimony carbamates **5**, producing 3,4-disubstituted oxazolidine derivatives. Consequently, even though the fission of oxirane rings by tetraphenylstibonium iodide at the first stage might be β-cleavage preferential,[12] 3,4-disubstituted cycloadducts **1** via α-cleavage were obtained selectively. The most significant factor of the formation of **1** is not the direction of oxirane cleavage but the difference in reaction behaviors of two antimony alkoxides **3** and **4**, and the former react with heterocumulenes and the latter reproduce starting oxiranes. Specifically higher selectivity in the reaction with carbodiimides can be explained by the idea that the difference of two antimony alkoxides in reaction behaviors would be exactly distinguished by moderate electrophilicity of carbodiimides. As the high electrophilicity of acid chloride, however, led to unclear distinction of two antimony alkoxides, a β-cleavage product was obtained in a considerable selectivity (Eq. 7).

Dichloromethane was the most suitable solvent for the selective formations both of 3,4-disubstituted 2-oxazolidinones[1c] and of the oxirane formation from



β-halo alkoxides as previously reported.[11] We rationalized this result as promoting the oxirane reproduction from antimony β-iodo alkoxides by this solvent. The worse selectivity of **1** in the reaction using tetraphenylstibonium bromide as a catalyst (Entry 14) is due to lower ability of antimony β-bromo alkoxides to reproduce oxiranes, permitting the reaction of **4** with heterocumulenes.

The reaction with isocyanates has another problem in the cyclization step. 2-Oxazolidinones have been reported to be formed via the rearrangement of 1,3-dioxolan-2-imines (**7**) as well, the formation of which is irrespective of the direction of oxirane cleavge.[2a] However, as shown in Eq. 8, the resulting selective-isomerization of 4-substituted 1,3-dioxolan-2-imines to 3,5-disubstituted 2-oxazolidinones excluded this possibility of producing **1** from **7** (Eq. 9). Therefore, it was suggested that 3,4-disubstitued ones **1** are obtained by direct cyclization of **5**, which the possibility of the formation of 3,5-disubstituted ones **2** from **5** can be also proposed. A little contamination of **2** in the reaction of isocyanates is partly due to this rearrangement from 1,3-dioxolane-2-imines in addition to the higher electrophilicity of isocyanates than carbodiimides. In the case of electron-withdrawing substitutent isocyanates, especially *p*-toluenesulfonyl isocyanate, the lower nucleophilic attack of nitrogen atom leads to the intramolecular *O*-alkylation in **5** gives a 1,3-dioxolan-2-imine selectviely (Entry 11), while the path via **6** is still important. However, in the case of carbodiimides, the lack of the rearrangement also makes it possible to form 3,4-disubstituted 2-oxazolidinimines exclusively.

In conclusion, tetraphenylstibonium iodide-catalyzed cycloaddition of oxiranes with heterocumulenes consists of three steps, that is, ring opening of oxiranes, insertion of heterocumulenes and cycliza-

tion of antimony carbamates. The difference in the reaction behaviors between antimony alkoxides **3** (α-cleavage) and **4** (β-cleavage) is the most decisive factor and the selectivity of ring cleavage direction of oxiranes is not so significant as to be thought. The preferential reaction of **3** with heterocumulenes more than **4** leads to the specific α-cleavage cycloaddition. Although the detailed investigation is necessary, as tetraphenylstibonium part was confirmed to play an effective role in oxirane ring cleavage,[12] the mildness of reaction conditions was due to "pull and push" effect of tetraphenylstibonium moiety and anionic iodide.

Experimental

Melting points were obtained by using a Yanaco Micro-melting point apparatus and are uncorrected. The IR spectra were recorded on a Hitachi 260-30 spectrometer using potassium bromide pellets or KRS-5 cells. Mass spectra were obtained on a JEOL JMS-DX303 mass spectrometer. The ^{1}H NMR and ^{13}C NMR spectra were performed on Hitachi R-90H. Analytical GLC was performed on a Shimadzu GC-8A with FID. Elemental analyses were performed by the section on elemental analysis in our department.

All oxiranes were freshly distilled from calcium hydride. Isocyanates were commercial ones and used without further purification. All carbodiimides, tetraphenylstibonium iodide, tetraphenylstibonium bromide,[1c] tetraphenylstibonium triflate[7] and tetraphenylstibonium propoxide[14] were produced according to described methods.

General procedures for the preparation of 3,4-disubstituted 2-oxazolidinones and 3,4-disubstitued 2-oxazolidinimines are refered to our previous report.[1c]

The Reaction of Tetraphenylstibonium Propoxide and Lithium One with Diphenylcarbodiimide. To a solution of tetraphenylstibonium propoxide (0.49 g, 1 mmol) in 5 mL of dry THF was added diphenylcarbodiimide (0.20 g, 1 mmol) successfully at ambient temperature under nitrogen. The reaction mixture was stirred at room temperature for 2 h. The solution was chromatographed over silica gel by using benzene as an eluent to give the product, *N,N'*-diphenyl-*O*-propylisourea (0.10 g, 39%). The reaction of lithium propoxide prepared from 1-propanol and butyllithium was performed in a similar manner and the yield was 87% (0.22 g).

The Formation of Ethyloxirane from 2-Chloro-1-butanol and 1-Chloro-2-butanol. The reaction and determination were carried out by the described procedure.[11] 2-Chloro-1-butanol was obtained from the reduction of 2-chlorobutanal by lithium aluminium hydride. 1-Chloro-2-butanol was prepared from the reaction of ethyloxirane and trimethylsilyl chloride,[15] followed by desilylation.

The Reaction of Ethyloxirane with Benzoyl Chloride in the Presence of Tetraphenylstibonium Iodide. To a solution of ethyl oxirane (0.43 g, 6 mmol) and tetraphenylstibonium iodide (1.02 g, 2 mmol) in 5 mL of dry benzene was added benzoyl chloride (0.28 g, 2 mmol) at room temperature under nitrogen. The mixture was stirred at 60 °C for 19 h. After the removal of volatiles under reduced pressure, the residue was subjected to silica-gel column chromatography and nearly pure products were obtained (eluted by benzene). Yields were determined by GLC.

The Isomerization of 4-methyl-1,3-dioxolan-2-imine. To a solution of 4-methyl-1,3-dioxolan-2-imine (0.27 g, 1.5 mmol) prepared by the described method[16] in 3 mL of dry benzene was added tetraphenylstibonium iodide (0.084 g, 0.15 mmol) at room temperature under nitrogen atmosphere. The resulting mixture was stirred at 80 °C for 26 h. After the removal of volatiles, the residue was subjected to active alumina column chromatograph (eluted by benzene). Identification was achieved by ^{1}H NMR and the yield was determined by GLC.

3-(*p*-Tolylsulfonyl)-5-ethyl-1,3-oxazolidin-2-one. Mp 105—107 °C (benzene-hexane); IR (KBr) 1760 cm^{-1} (C=O); MS *m/z* 269 (M^+). ^{1}H NMR ($CDCl_3$) δ=0.97 (t, 3H, *J*=7.0 Hz), 1.03—1.95 (m, 2H), 2.48 (s, 3H), 3.63 (dd, 1H, *J*=7.5 and 8.6 Hz), 4.14 (t, 1H, *J*=7.5 Hz), 4.25—4.65 (m, 1H), 7.20—7.50 (m, 2H), 7.75—8.10 (m, 2H); ^{13}C NMR ($CDCl_3$) δ=8.34 (q), 21.51 (q), 27.12 (t), 49.10 (t), 75.60 (d), 127.86 (d), 129.66 (d), 133.80 (s), 145.48 (s), 151.51 (s); Found: C, 53.48; H, 5.51; N, 5.13%. Calcd for $C_{12}H_{15}O_4NS$: C, 53.52; H, 5.61; N, 5.20%.

***N,N'*-Diphenyl-*O*-propylisourea.** Bp 157 °C (0.01 mmHg) (Kügelrohr); IR (neat) 1660 cm^{-1} (C=N); ^{1}H NMR ($CDCl_3$) δ=1.05 (t, 3H, *J*=7.5 Hz), 1.60—2.05 (m, 2H), 4.36 (t, 2H, *J*=6.3 Hz), 5.65—6.10 (m, 1H), 6.75—7.50 (m, 10H); ^{13}C NMR ($CDCl_3$) δ=10.75 (q), 22.15 (t), 68.49 (t), 120.45 (d), 122.83 (d), 129.08 (d), 138.53 (s), 147.83 (s), 149.96 (s).

2-Chloro-1-butanol. Bp 68 °C (36 mmHg); IR (neat) 3330 cm^{-1} (O-H); ^{1}H NMR ($CDCl_3$) δ=1.07 (t, 3H, *J*=6.8 Hz), 1.65—2.40 (m, 3H), 3.60—4.85 (m, 3H).

1-Chloro-2-butanol. Bp 57 °C (30 mmHg); IR (neat) 3320 cm^{-1} (O-H); ^{1}H NMR ($CDCl_3$) δ=1.00 (t, 3H, *J*=7.5 Hz), 1.35—1.90 (m, 2H), 2.19 (d, 1H, *J*=4.8 Hz), 3.30—4.20 (m, 3H).

1-(Iodomethyl)propyl Benzoate. Oil; IR (neat) 1720 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) δ=1.00 (t, 3H, *J*=7.8 Hz), 1.60—2.20 (m, 2H), 3.45 (d, 2H, *J*=5.5 Hz), 4.65—5.15 (m, 1H), 7.10—7.80 (m, 3H), 7.80—8.3 (m, 2H); ^{13}C NMR ($CDCl_3$) δ=7.97 (t), 9.37 (q), 27.21 (t), 73.68 (d), 127.43 (s), 128.16 (d), 129.47 (d), 132.83 (d), 165.30 (s).

2-Iodobutyl Benzoate. Oil; IR (neat) 1720 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) δ=1.06 (t, 3H, *J*=7.8 Hz), 1.60—2.20 (m, 2H), 4.10—4.50 (m, 1H), 4.50—4.7 (m, 2H), 7.10—7.80 (m, 3H), 7.80—8.35 (m, 2H); ^{13}C NMR ($CDCl_3$) δ=13.76 (q), 29.74 (t), 32.91 (d), 68.95 (t), 127.43 (s), 128.16 (d), 129.47 (d), 132.83 (d), 165.30 (s).

4-Methyl-1,3-dioxolan-2-imine. Bp 120 °C (0.01 mmHg); IR (neat) 1710 cm^{-1} (C=N); ^{1}H NMR ($CDCl_3$) δ=1.35—1.6 (m, 3H), 4.00 (t, 1H, *J*=7.0 Hz), 4.35—5.05 (m, 2H), 6.70—7.70 (m, 5H).

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