Oxyanionic Substituent Effect on the C–H Insertion of Carbenes. Reaction of Alkoxides with Dichlorocarbene and Chlorophenylcarbene

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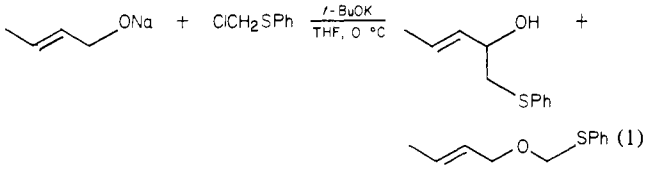
Abstract: The lithium alkoxides of benzylic, allylic, and simple alkyl alcohols were allowed to react with chloroform in the presence of *t*-BuOLi in THF–hexane to give, in 32–91% yields, dichloromethylcarbinols, which were produced by the insertion of dichlorocarbene into the α C–H bond of alkoxides but not by the Wittig rearrangement of carbanions of alkyl dichloromethyl ethers. The enhanced reactivity toward dichlorocarbene of the α C–H bond of alkoxides was clearly demonstrated by the high selectivity of the insertion. The potassium alkoxides of a series of analogous alcohols reacted analogously with benzal chloride in the presence of *t*-BuOK in THF to give the corresponding substituted oxiranes (16–79%); e.g., the reaction of potassium benzyl oxide gave 2,3-diphenyloxirane (79%) as a mixture of stereoisomers (trans:cis = 1.0). With 2-phenethoxide, *n*-octyl oxide, or 2-methoxyethoxide, the corresponding dialkyl acetals of benzaldehyde were also formed in 9, 6, and 6% yield, respectively, and their formation is explained in terms of nucleophilic attack of alkoxide on chlorophenylcarbene. With *trans*-crotyl oxide or 2-phenethoxide, 1,3-diphenylpropan-1-one (33%) and 1-phenylpent-3-en-1-one (6%) were produced, respectively, as byproducts through the isomerization of the primary product oxiranes. Oxiranes were produced by the insertion of chlorophenylcarbene into the α C–H bond of alkoxides followed by the cyclization of the intermediate 1-substituted 2-chloro-2-phenethyl alkoxide. These reactions provide us with new preparative methods of synthetically useful dichloromethyl carbinols and oxiranes.

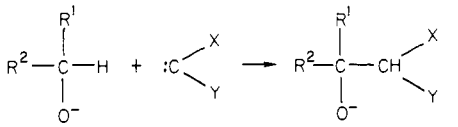
Among the carbon–carbon bond-forming reaction of carbenes, the C–H insertion reactions have generally been regarded as side reactions in carbene chemistry while cyclopropanation reactions are applicable in diverse ways. Nevertheless, it was expected that the insertion reaction would become an efficient and straightforward carbon–carbon bond-forming reaction provided that it would take place with high selectivities and in high yield.

We have recently disclosed a novel oxyanionic substituent effect that greatly facilitates the insertion of (phenylthio)carbene into the α C–H bond of alkoxide anions:[1,2] the reaction of sodium *trans*-crotyl oxide with chloromethyl phenyl sulfide in the presence of *t*-BuOK gave the corresponding C–H insertion product in 43% yield and the formal oxygen–metal insertion product in 38% yield (eq 1). It may well be deduced here that the reactivity of the



(1)

α C–H bond of alkoxides is generally enhanced toward a variety of carbenes, and studies on this subject will not only give valuable information on the mechanistic aspects of carbene chemistry but also reveal a novel method for the control of regioselectivity[3,4] in the C–H insertion of carbenes (eq 2). Herein we wist to report, as a proof of the versatile character of this reaction, our results



(2)

in which the enhanced reactivity of the α C–H bond of alkoxide anions toward dichlorocarbene (X, Y = Cl) and chlorophenylcarbene (X = Cl, Y = Ph) is clearly demonstrated. This study apparently reveals a synthetic significance of the carbene insertion reaction that has hitherto been disregarded for carbon–carbon bond formation.

Results and Discussion

Reaction of Alkoxides with Dichlorocarbene. While reactions of alcohols with dihalocarbenes have been studied extensively,[5] little is known about the reactivity of alkoxides toward dihalocarbenes. Hine and co-workers studied intensively the reaction behavior of haloforms in 2-propanol in the presence of potassium isopropoxide.[5b,c] However, they did not mention the formation of C–H insertion products, and it is still uncertain whether dihalocarbenes generated under these conditions react with the alkoxide or with the alcohol. To our knowledge, no work has been reported on the reaction of dihalocarbene with alkoxide in an aprotic solvent.

To a solution of lithium benzyloxide and *t*-BuOLi (3 equiv) in THF–hexane was added chloroform under nitrogen atmosphere at 0 °C, and the total reaction mixture was heated under reflux for 0.5 h. After aqueous workup followed by Kugelrohr distillation, 2,2-dichloro-1-phenylethanol (**1a**) was isolated in 87% yield (eq 3). The same product **1a** might have been produced via the

$$\mathrm{PhCH_2OLi} + \mathrm{CHCl_3} \xrightarrow[\text{THF–hexane}]{t\text{-BuOL}_i} \underset{\mathbf{1a}}{\mathrm{PhC(OH)HCHCl_2}} \quad (3)$$

$$\mathrm{PhCD_2OLi} + (p\text{-anisyl})\mathrm{CH_2OLi} \xrightarrow[t\text{-BuOLi}]{\mathrm{CHCl_3}} \underset{\mathbf{1a}\text{-}d_2}{\mathrm{PhCD(OH)CDCl_2}} + \underset{\mathbf{1b}}{(p\text{-anisyl})\mathrm{CH(OH)CHCl_2}} \quad (4)$$

(1) Harada, T.; Oku, A. *J. Am. Chem. Soc.* **1981**, *103*, 5965.

(2) For oxyanionic substituent effects see: (a) Evans, D. A.; Baillargeon, D. C. *Tetrahedron Lett.* **1978**, 3315, 3319 and references cited therein. (b) Steigerwald, M. L.; Goddard, W. A. III; Evans, D. A. *J. Am. Chem. Soc.* **1979**, *101*, 1994. For alkoxy-accelerated [3.3]- and [1,3]-sigmatropic rearrangements see: (c) Evans, D. A.; Golob, A. M. *J. Am. Chem. Soc.* **1975**, *97*, 4765. (d) Franzus, B.; Scheinbaum, M. L.; Waters, D. L.; Bowlin, H. B. *Ibid.* **1976**, *98*, 1241. (e) Wilson, S. R.; Mao, T.; Jernberg, K. M.; Ezmirly, S. T. *Tetrahedron Lett.* **1977**, 2559. (f) Thies, R. W.; Seitz, E. P. *J. Org. Chem.* **1978**, *43*, 1050. (g) Danheiser, R. L.; Martinez-Davila, C.; Auchus, R. J.; Kadonaga, J. T. *J. Am. Chem. Soc.* **1981**, *103*, 2443. (h) Danheiser, R. L.; Martinez-Davila, C.; Sard, H. *Tetrahedron* **1981**, *37*, 3943. (i) Boyle, W. J., Jr.; Bunnett, J. F. *J. Am. Chem. Soc.* **1974**, *96*, 1418.

(3) Kirmse, W. "Carbene Chemistry", 2nd ed.; Academic Press: New York, 1971.

(4) (a) Steinbeck, K. *Tetrahedron Lett.* **1978**, 1103; *Chem. Ber.* **1979**, *112*, 2407. (b) Steinbeck, K.; Klein, J. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 773.

(5) (a) Reference 3, p 429. (b) Hine, J. Tanabe, K. *J. Am. Chem. Soc.* **1957**, *79*, 2654; **1958**, *80*, 3002. (c) Hine, J.; Ketley, A. D.; Tanabe, K. *Ibid.* **1960**, *82*, 1398. (d) Seyferth, D.; Mui, J. Y.-P.; Todd, L. J. *Ibid.* **1964**, *86*, 2961. (e) Seyferth, D.; Mai, W. A.; Mui, J. Y.-P.; Darragh, K. Y. *J. Org. Chem.* **1966**, *31*, 4079. (f) Tabushi, I.; Yoshida, Z.; Takahashi, N. *J. Am. Chem. Soc.* **1971**, *93*, 1820.

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nucleophilic attack of dichloromethyl anion on benzaldehyde that could have been formed from benzyl oxide by hydride abstraction with dichlorocarbene. The following *d*-labeling experiments (eq 4) excludes this possibility: when a mixture of lithium α,α-dideuteriobenzyl oxide and lithium *p*-methoxybenzyl oxide was allowed to react under similar conditions, 1,2-dideuterio-2,2-dichloro alcohol **1a**-d_2 (70%) and 2,2-dichloro-1-(4-methoxyphenyl)ethanol (**1b**, 77%) were produced without deuterium exchange.[6,7]

There is another one to be considered as a possible pathway for the formation of **1a**, i.e., the Wittig rearrangement. The reaction of dichlorocarbene with alkoxides may compose a reversible equilibrium as shown in eq 5-1. To produce **1a**, the proton shift (eq 5-2) should take place followed by Wittig rearrangement (eq 5-3). However, eq 5–2 seems unlikely because it goes from

$$RCH_2\text{-}\underline{O}^- + :CCl_2 \rightleftarrows RCH_2\text{-}O\text{-}\bar{C}Cl_2 \qquad (5\text{-}1)$$

$$RCH_2\text{-}O\text{-}\bar{C}Cl_2 \rightleftarrows R\bar{C}H\text{-}O\text{-}CHCl_2 \qquad (5\text{-}2)$$

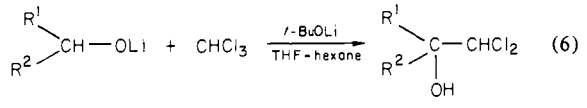
$$R\bar{C}H\text{-}O\text{-}CHCl_2 \xrightarrow{\text{Wittig}} RCH(CHCl_2)\text{-}O^- \qquad (5\text{-}3)$$

$$RCH_2\text{-}O\text{-}\bar{C}Cl_2 \xrightarrow{-Cl^-} RCH_2\text{-}O\text{-}\bar{C}\text{-}Cl \qquad (5\text{-}4)$$

the more stable to the less stable carbanion, and the rearrangement of the more stable carbanion, such being the usual case in reported literature,[8] was not observed in the present reactions. Moreover, the rearrangement path was clearly ruled out by the following experiment. When benzyl dichloromethyl ether was treated with a THF solution of *t*-BuOLi, benzyl chlroide (75%) was obtained as the sole product, but **1a** was not formed at all. Thus, alkoxychlorocarbanion, if formed, undergoes decomposition to generate alkoxycarbene (eq 5-4),[9] which liberates carbon monoxide to give the corresponding chloride, rather than isomerization (eq 5-2).

There are reports suggesting that α C–H bonds of alkoxides have smaller bonding energies than those of the corresponding alcohols.[2b,i] Our finding of the oxyanionic effect on the C–H insertion by carbenes is probably lying on the same line as those reported.

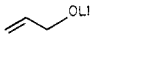
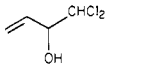
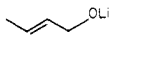
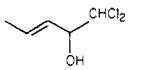
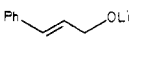
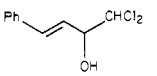
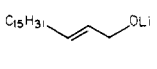
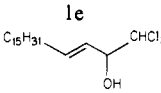
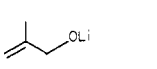
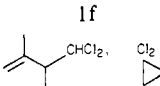
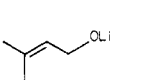
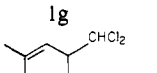
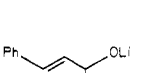
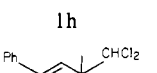
The present result forms a marked contrast to the reported reaction of benzyl alcohol with dichlorocarbene under phase-transfer conditions where the reaction is reported to proceed via O–H insertion followed by the decarbonylation of the intermediate to give benzyl chloride in high yield.[5f] It is also noteworthy from both synthetic and mechanistic points of view that the nucleophilic attack of oxyanion on dichlorocarbene does not take place appreciably, though a similar reaction takes place concurrently with the insertion reaction in the case of (phenylthio)carbene[1] (see eq 1), and the α C–H insertion products are formed in relatively high yields (vide infra). The results of the insertion of dichlorocarbene into the α C–H bond of various kinds of alkoxides (eq 6) are summarized in Table I.



(6)

The following observations clearly demonstrate the enhanced reactivity of α C–H bond of alkoxides. (1) The insertion reaction into the α C–H bond of alkoxides apparently predominates over the insertion into the α C–H bond of ether or benzylic C–H bond as shown in entries 2 and 10 (Table I). In both cases the formation of such insertion byproducts was not detected. (2) Moreover, when the reaction of lithium benzyl oxide with dichlorocarbene (1 equiv) was performed in the presence of benzyl methyl ether (5 equiv),

Table I. Reaction of Alkoxides with Dichlorocarbene[a]

entry	alkoxides	product(s)	yield,[b] % (ratio)[c]
1	$PhCH_2OLi$	$PhCH(OH)CHCl_2$[d] (1a)	87
2	(*p*-anisyl)CH_2OLi	(*p*-anisyl)$CH(OH)CHCl_2$ (1b)	81
3		 1c	55[e]
4		 1d	76[e]
5		 1e	83
6		 1f	91
7		 1g  2	78 (2.0:1)
8		 1h  3	74 (1:1.8)
9[g]		 1i	38
10[h]	$PhCH_2CH_2OLi$	$PhCH_2CH(OH)CHCl_2$ (1j)	32[e]

[a] Unless otherwise noted, lithium alkoxide (1 equiv) and *t*-BuOLi (3 equiv) were prepared in one pot from the corresponding alcohols with BuLi-hexane in THF and the mixture was allowed to react with $CHCl_3$ (3 equiv) under reflux for 0.5 h. [b] Yields refer to the isolated yield based on starting alcohols unless otherwise noted. [c] Ratios were determined by ^1H NMR. [d] Kobrich, G.; Grosser, J.; Werner, W. *Chem Ber.* 1973, *106*, 2610. [e] Yields were determined by VPC. [f] Reference 9b. [g] The reaction was performed at an ambient temperature for 10 h. [h] Six equivalents of *t*-BuOLi and $CHCl_3$ were used.

dichlorocarbene reacted exclusively with benzyl oxide to give **1a** (42%) without the formation of α C–H insertion product derived from benzyl methyl ether. (3) Seyferth and co-workers reported that dichlorocarbene generated from $PhHgCCl_2Br$ reacts with allyl ethyl ether to give mainly the addition product (82%) besides a minor amount of insertion product (14%).[10] Exclusive addition of dihalocarbene, under phase-transfer conditions, to allylic alcohols such as methallyl and prenyl alcohol was also reported.[11] In our study, however, in contrast to those reactions, the α C–H insertion reaction of allyl oxide or allylic alkoxides bearing a trans γ substituent proceeded in high yields without olefin addition. When the double bonds are activated by additional alkyl substitution or β substitution,[12] the addition reaction becomes comparable (entries 7 and 8, Table I). (4) Although THF, the solvent of the present reactions, is reported to be a reactive ether toward dichlorocarbene,[13] only a small amount of 2-(dichloromethyl)-tetrahydrofuran is produced. Thus the VPC yields of 2-(dichloromethyl)tetrahydrofuran based on chloroform were 4.3, 3.0,

(6) This result does not exclude the possibility of the hydride abstraction recombination which occurs within a solvent cage.

(7) We thank Professor H. Hart of Michigan State University for his suggestion of the deuterium-labeling experiment.

(8) For example: Hauser, C. K.; Kantor, S. W. *J. Am. Chem. Soc.* **1951**, *73*, 1437.

(9) Schollkopf, U.; Paust, J. *Chem. Ber.* **1965**, *98*, 2221.

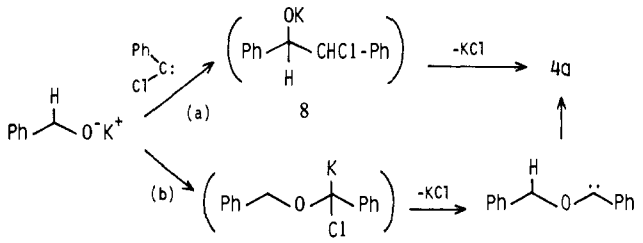
(10) Seyferth, D.; Burlitch, J. M.; Minasz, R. J.; Mui, J. Y.-P.; Simons, H. D., Jr.; Treibar, A. J. H.; Dowd, S. R. *J. Am. Chem. Soc.* **1965**, *87*, 4256.

(11) (a) Hiyama, T.; Tsukamoto, M.; Nozaki, H. *J. Am. Chem. Soc.* **1974**, *96*, 3713. (b) Kleveland, K.f Skatebøl, L.; Sydnes, L. K. *Acta Chem. Scand., Ser. B* **1977**, *B31*, 463.

(12) For relative reactivity of olefins see, for example: Moss, R. A. "Carbenes"; Moss, R. A., Jones, M., Jr.; Eds.; Wiley: New York, 1973; Vol I, Chapter 2.

(13) Seyferth, D.; Mai, V. A.; Gordon, M. E. *J. Org. Chem.* **1970**, *35*, 1993.

Scheme I

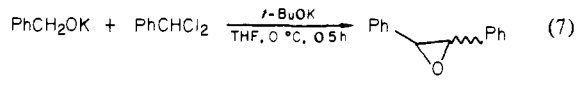


1.7, and 5.7%, respectively in entries 3, 4, 8, and 10 (Tables I). They were not determined for other entries.

In spite of structural limitations that are somewhat unfavorable for secondary (entry 9) and aliphatic alkoxides (entry 10), the present reaction will be applicable as a new method for preparing dichloromethylcarbinols[14] rated as synthetically useful intermediates.[15]

Reaction of Alkoxides with Chlorophenylcarbene. From the preceding section it is evident that dichlorocarbene, like (phenylthio)carbene, reacts with alkoxides regioselectivity to give α C–H insertion products in high yields. This implies that the oxyanionic effect thus observed in carbene insertion reactions is comprehensive and we were further prompted to examine the reaction of chlorophenylcarbene with which we could anticipate the formation of phenyl-substituted oxiranes as the α C–H insertion products from alkoxides.

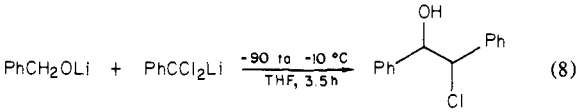
To a mixed suspension of potassium benzyl oxide (2.5 equiv) and *t*-BuOK (2.5 equiv) in THF was added a THF solution of benzal chloride, and the mixture was stirred at 0 °C under a nitrogen atmosphere for 0.5 h. After aqueous workup followed by column chromatography, 2,3-diphenyloxirane (**4a**) was isolated in 79% yield as a mixture of stereoisomers (*trans*:*cis* = ca. 1; eq 7). When the same reacfion was performed in the absence of



(7)

4a

t-BuOK, **4a** was obtained only in 11% yield, and 88% of benzyl alcohol and 78% of benzal chloride were recovered. The inefficient result in the absence of *t*-BuOK shows us that the nucleophilic displacement by the alkoxide anion to form an ether does not constitute the initial reaction stage but that the reaction of chlorophenylcarbene with benzyl oxide does. For the reaction of chlorophenylcarbene with benzyl oxide leading to the formation of oxirane **4a**, two routes (a and b) seem plausible: (a) the insertion of the carbene to the α C–H bond of alkoxide followed by C–O bond formation; (b) the initial formation of the C–O bond by the attack of oxyanion on the carbene (see Scheme I), The lack of stereoselectivity in the oxirene production supports route a. Additional evidence for a was provided by the isolation of 2-chloroethanol **12**, derived from the corresponding reaction intermediate 2-chloroalkoxide **8**, when lithium benzyl oxide was used. Thus, when a mixture of α,α-dichlorobenyllithium and lithium benzyl oxide in THF was allowed to warm from −90 to −10 °C, 2-chloro-1,2-diphenylethanol (**12**) was obtained in 28% yield (eq 8).



(8)

12

(14) These compounds were previously prepared through the reaction of thermally unstable dichloromethyllithium with aldehydes or ketones. Köbrich, G. *Angew. Chem., Int., Ed. Engl.* **1972**, *11*, 473 and references cited therein.

(15) (a) Blumbergs, P.; Lamontage, M. P. *J. Org. Chem.* **1972**, *37*, 1248. (b) Kbrich, G.; Grosser, J. *Tetrahedron Lett.* **1972**, 4117. (c) Taguchi, H.; Yamamoto, H.; Nozaki, H. *Ibid.* **1972**, *4461*. (d) Taguchi, H.; Tanaka, S.; Nozaki, H. *Ibid.* **1973**, *2465*. (e) Villieras, J.; Bacquet, C.; Normant, T. F. *J. Organomet. Chem.* **1972**, *40*, C-1.

Table II. Reaction of Chlorophenylcarbene with Alkoxides[a]

4 5

entry	alkoxide R^1	alkoxide R^2	time, min	product[b] (yield, %)
1	C_6H_5	H	30	4a (79)[c]
2	*p*-ClC_6H_4	H	30	4b (76)[c]
3	CH_2=CH	H	20	4c (66)[d]
4	*trans*-CH_3CH=CH	H	60	4d (56),[d] 6 (6)[e]
5	CH_2=$C(CH_3)$	H	60	4e (69)
6	CH_2=CH	CH_3	30	4f (60)[f]
7	$C_6H_5CH_2$	H	30	4g (16),[g] 5g (9), 7 (33)
8	*n*-C_7H_{15}	H	60	4h (33),[g] 5h (6)
9	CH_3	CH_3	60	4i (28)[h]
10	CH_3OCH_2	H	60	4j (66), 5j (6)

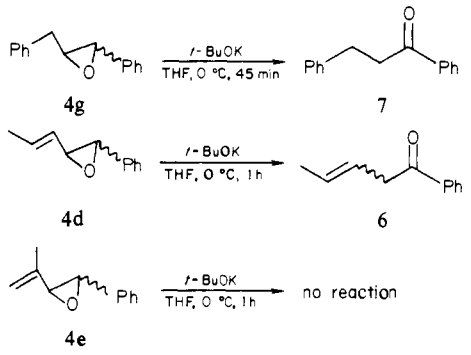
[a] Potassium alkoxides (2.5 equiv) prepared in situ from the corresponding alcohols with KH in THF were allowed to react with $PhCHCl_2$ (1 equiv) and *t*-BuOK (equivalent to alkoxide) at 0 °C for the period indicated. [b] Except entry 7, yields refer to the isolated one based on $PhCHCl_2$. For entry 7, see Experimental Section. [c] Reference 22. [d] Paladini, J.; Chuche, J. *Bull. Chim. Soc. Fr.* 1974, 192. [e] Manat, P.; Dieter, S. *Angew. Chem.* 1977, *89* (5), 333. [f] Mauzé, B. *J. Organomet. Chem.* 1979, *265*, 170. [g] Tamura, Y.; Bayomi, S. M. Sumoto, K.; Ikeda, M. *Synthesis* 1977, 693. [h] Hevesi, L.; Nagy, J. B.; Krief, A.; Derouane, E. G. *Org. Magn. Reson.* **1977**, *10*, 14.

The reaction of a series of potassium alkoxides with chlorophenylcarbene gave the corresponding phenyl-substituted oxiranes, and the results are summarized in Table II. Analogous to the discussion on the reaction of dichlorocarbene (vide supra), chlorophenylcarbene is predominantly inserted into the C–H bond of alkoxides that is activated by the α oxyanion substitution. β-Phenethoxide gave inserted product on the α C–H bond of oxyanion substituent but not on the benzylic C–H bond (Tables II, entry 7). In the reaction of 2-methoxyethoxide the ethereal α C–H bond did not undergo the insertion (entry 10). Additionally, none of the insertion products derived from the solvent THF were detected. Steinbeck and co-workers reported recently that chlorophenylcarbene generated from benzal chloride/*t*-BuOK/[18]-crown-6 was inserted into such relatively reactive substrates as 2-methyltetrahydrofuran or 2-phenyl-1,3-dioxolane derivatives[4b,16] but that the product yields were low (10–44%). It is thus apparent that the α C–H bond of alkoxides possesses a high reactivity toward insertion reactions of a variety of carbenes.

In the aforementioned reaction of dichlorocarbene with methallyl oxide an olefin adduct was formed besides the insertion product. Contrastingly, in the reaction of chlorophenylcarbene with methyl-substituted allylic alkoxides, the corresponding olefin adduct was not formed but only the oxirane product formed in relatively good yields (Table II, entries 4 and 5). The reaction of 3-methyl-2-buten-1-yl oxide gave none of the cyclopropanation nor C–H insertion product but a complex product mixture, probably due to the instability of the oxirane product (vide infra).

The formation of phenyl ketones in the reaction of phenethoxide or crotyl oxide (Table II, entries 7 and 4) shows the occurrence of an unique combination of base-catalyzed isomerization of oxiranes. Thus, the independent treatment of oxirane **4g** with *t*-BuOK in THF at 0 °C for 45 min yielded ketone **7** (90% based upon the consumed **4g**, conversion 89%; eq 9), and analogously **4g** gave crotyl ketone **6** (eq 10). However, oxirane **4e** survived under the same basic conditions and was recovered quantitatively (eq 11). Therefore, the production of ketones **7** and **6** in the carbene reaction can be explained in terms of the further isomerization of the primary product oxiranes although the presence

(16) Steinbeck and co-workers previously reported that the generation of free chlorophenylcarbene, under the presence of [18]-crown-6, was the requisite for the insertion reaction to occur.[4] In our experiments it should be noted that the insertion reaction proceeded effectively without adding a crown ether.



of active hydrogen on the substituent of oxiranes (at α position in case of **4g** and at γ position in case of **4d**) is essential. A possible mechanism for the transformation of oxiranes to phenyl ketones is shown in Scheme II where the allyl oxide intermediate underwent further base-catalyzed isomerization to enolate ion **9** by the action of a strong base.[17,18] In the reaction of *sec*-alkoxides with dichlorocarbene, the yield of insertion products was appreciably depressed, whereas with chlorophenylcarbene the insertion to the α C–H bond proceeded without lowering the product yield (entry 6).

The formation of benzaldehyde acetal derivatives **5** as byproducts (entries 7, 8, and 10) can be explained in terms of the nucleophilic attack of the oxyanion on chlorophenylcarbene as indicated in Scheme III. The acetal formation, however, is specific only for the reaction of simple alkyl alkoxides and was not observed with benzylic and allylic alkoxides. Thus, it is evident that the additive activation effect of phenyl as well as vinyl substituent on the reactivity of α C–H bond of alkoxides also plays an important role in suppressing the side reaction. For the fate of the initially formed α-alkoxychlorocarbanion **10** in producing acetal **5**, two routes are possible (path a and path b in Scheme III), but the criterion for distinguishing the preference between them is not clear yet.

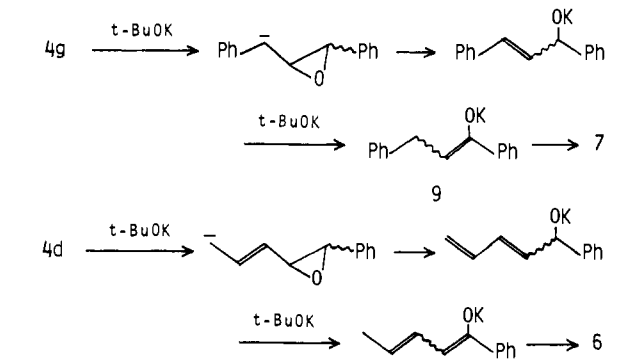
Conclusion

In the present study, so far as the reactions of not only (phenylthio)carbene but also dichlorocarbene and chlorophenylcarbene are concerned, the versatile character of the present novel oxyanionic effect on the carbene C–H insertion reactions has been unveiled. Among a variety of reaction substrates that have hitherto been reported to undergo the carbene insertion reactions, alkoxides seem to be the most reactive ones. In spite of structural limitations that are somewhat unfavorable for secondary and aliphatic alkoxides, these reactions can be adopted as a new synthetic method not only for synthetically useful dichloromethyl carbinols but also for other highly selective (regioselective and stereospecific) carbon–carbon bond formations on alcohols.

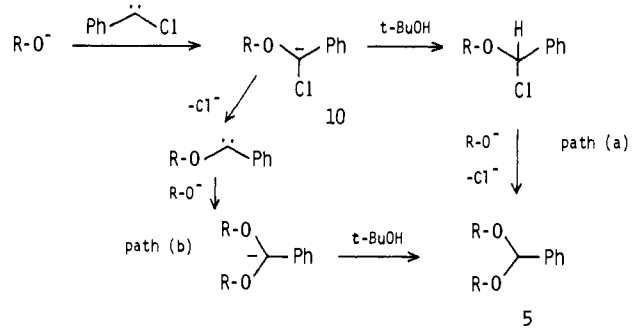
Although the activation effect of oxyanion on the reactivity of the α C–H bond of alkoxides toward carbenes is significant, the reaction behavior varies systematically with carbenes. With dichlorocarbene the insertion reaction proceeded most efficiently without any appreciable addition of alkoxide to the carbene carbon (formally the insertion reaction to an oxygen–metal bond) and with (phenylthio)carbene, a significant amount of phenylthio methyl ether (formal oxygen–metal insertion product) was formed besides the C–H insertion product (see eq 1). Chlorophenylcarbene, on the other hand, showed an intermediate behavior in which the formal oxygen–metal insertion reaction took place to a small extent only for simple alkoxides. Thus, the reactivity of carbenes in the C–H insertion reactions can be estimated to be in the decreasing order CCl_2 > Cl(Ph)C > PhSCH, which agrees with the order of their electrophilicity.

The oxyanionic substituent effect that facilitates the C–H insertion seems to result from (1) the decrease in the α C–H bond

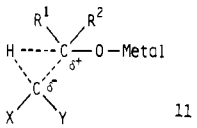
Scheme II



Scheme III



energy of alkoxides[2b] and (2) the stabilization of the polar transition state **11** by electron-donating substitution on the oxyanion.[19] Additionally but subsidiarily, the nature of the transition state illustrated in **11** suggests another way of promoting the C–H



insertion reaction: not only the substitution of such cation-stabilizing substituents as the phenyl or vinyl group on the α position of alkoxides but also the introduction of electron-withdrawing groups on the carbene center lower the energy of the transition state.

Experimental Section

Infrared spectra were measured on A JASCO IRA-1 grating spectrophotometer. ^{1}H NMR spectra were recorded on a Varian T-60A spectrometer in $CDCl_3$ taking Me_4Si as an internal standard. ^{2}H NMR spectra were measured at Kyoto University with a JEOL 90 Q spectrometer at 13.70 MHz with the field locked to an external ^{7}Li signal. Mass spectra were measured on a Hitachi RMU-7M mass spectrometer at Niigata College of Pharmacy or on a Hitachi Model RMU-6L. Microanalyses were preformed by Microanalysis center of Kyoto Unveristy and Institute for Chemical Research of Kyoto Unversity. Shimadzu GC-4APT gas chromatograph (glass column; 10% Apiezon L on Chromosorb unless otherwise noted) was employed for VPC analyses. Short-path (bulb-to-bulb) distillations were carried out with a Kugelrohr apparatus, and all boiling points correspond to the bath temperature. Silica gel (Wakogel C-200) was used as an absorbent in column chromatography. Starting alcohols, *t*-BuOH, and $PhCHCl_2$ were dried over CaH_2, distilled, and stored over 4-Å molecular sieves. THF was dried and distilled from benzophenone and sodium under nitrogen atmosphere prior to use. *t*-BuOK was purchased from Merck Chemical; BuLi (1.55 M, hexane solution) and KH (35% dispersion in mineral oil) were pur-

(17) Thummel, R. P.; Rickborn, B. *J. Org. Chem.* **1972**, *37*, 3919, 4250.
(18) (a) Crandall, J. K.; Lin, L. C. *J. Org. Chem.* **1968**, *33*, 2375. (b) Thummel, R. P.; Rickborn, B. *Ibid.* **1969**, *34*, 3583.

(19) The insertion may occur by attack either on the electrons of the C–H bond (**11**)[20] or on the hydrogen bond via the transition state with a linearly arranged $(X)(Y)C^{\delta-}\cdots H\cdots{}^{\delta+}C(O^-)(R^1)(R^2)$ conformation.
(20) (a) Doering, W. von E.; Prinzbach, H. *Tetrahedron*, **1959**, *6*, 24. (b) Skell, P. S.; Woodworth, R. C. *J. Am. Chem. Soc.* **1956**, *78*, 4496. (c) Reference 13. (d) Gutsche, C. D.; Bachman, G. L.; Udell, W.; Bauerlein, S. *Ibid.* **1971**, *93*, 5172.
(21) (a) Benzon S. W.; DeMore, W. B. *Adv. Photochem.* **1964**, 219. (b) Dobson, R. C.; Hayes, D. M.; Hoffman, R. *J. Am. Chem. Soc.* **1971**, *93*, 6188.

chased from Aldrich Chemical. α,α-Dideuteriobenzyl alcohol and *p*-methoxy-α,α-dideuteriobenzyl alcohol were prepared by the lithium aluminum deuteride (99%, Aldrich) reduction of methyl benzoate and methyl *p*-methoxybenzoate, respectively, and ^{1}H NMR spectrum of both compounds showed no proton incorporated at benzylic position.

General Procedure for the Reaction of Alkoxides with Dichlorocarbene. To a THF (10 mL) solution of the starting alcohol (3 mmol) and *t*-BuOH (9 mmol) was added BuLi (1.55 M hexane solution, 12 mmol) via a syringe under nitrogen atmosphere at 0 °C, and the mixture was stirred for 5 min at 0 °C. To this was added $CHCl_3$ (9 mmol) in one portion, and the total reaction mixture was heated under reflux for 0.5 h. Gradually the color of solution turned light or deep reddish brown. The mixture was cooled to room temperature, quenched by addition of aqueous NaCl, and extracted twice with ethyl acetate. After drying over Na_2SO_4 and subsequent evaporation of solvents, the corresponding C–H insertion product was isolated by Kugelrohr distillation. Analytically pure materials were obtained by purification with column chromatography (benzene–ethyl acetate gradient) followed by Kugelrohr distillation or preparative VPC. In Table I, the yields of entries 3, 4, and 10 were determined by VPC analysis employing durene as the internal standard. For entries 7 and 8, a mixture of the C–H insertion product and the olefin addition product was obtained after Kugelrohr distillation, and product ratios were determined by ^{1}H NMR spectroscopy. For entries 3, 4, 8, and 10, yields of 2-(dichloromethyl)tetrahydrofuran were determined by VPC analysis with durene internal standard. The physical and spectral data of new compounds in Table I are as follows.

2,2-Dichloro-1-(*p*-methoxyphenyl)ethanol (1b): bp 130 °C (0.05 mmHg); IR (liquid film) 3440 (br), 1615 (s), 1260 (s), 1040 (s), 840 (s), 795 (s) cm^{-1}; ^{1}H NMR δ 3.24 (1 H, br d, J = 4 Hz), 3.76 (3 H, s), 4,86 (1 H, br dd, J = 4 and 5.5 Hz), 5.74 (1 H, d, J = 5.6 Hz), 6.9 and 7.3 (4 H, AA′BB′); mass spectrum, m/e (relative intensity) 224, 222, 220 (M^+, 3.4), 137 (100), 121 (76). Anal. Calcd for $C_9H_{10}O_2Cl_2$: C, 48.90; H, 4.56. Found: C, 48.77; H, 4.48.

1,1-Dichloro-3-buten-2-ol (1c): bp 95–100 °C (17 mmHg); IR (liquid film) 3400 (br), 1050 (s), 990 (s), 945 (s), 895 (m), 790 (s) cm^{-1}; ^{1}H NMR δ 2.54 (br, 1 H), 4.46 (7, 1 H), 5.2–6.3 (m, 4 H, including 1 H of d, J = 4.3 Hz); mass spectrum, m/e (relative intensity) 57 (M^+ – $CHCl_2$, 100). Anal. Calcd for $C_4H_6OCl_2$: C, 34.07; H, 4.29. Found: C, 34.31; H, 4.34.

1,1-Dichloro-3-penten-2-ol (1d): bp 115–120 °C (22 mmHg); IR (liquid film) 3380 (br), 1035 (s), 970 (s), 935 (s), 785 (s) cm^{-1}; ^{1}H NMR δ 1.75 (3 H, br d, J = 5 Hz), 2.81 (1 H, br s), 4.28 (1 H, br dd, J = 5 and 4.0 Hz), 5.3–6.2 (3 H, m, including 1 H of d, J = 4 Hz); mass spectrum, m/e (relative intensity) 71 (M^+ – $CHCl_2$, 100). Anal. Calcd for $C_5H_8OCl_2$: C, 38.74; H, 5.20. Found: C, 38.10 (not satisfactorily agreed); H, 5.24.

1,1-Dichloro-4-phenyl-3-buten-2-ol (1e): IR (liquid film) 3360 (br), 1075 (s), 965 (s), 780 (s), 750 (s), 695 (s) cm^{-1}; ^{1}H NMR δ 2.75 (1 H, br d, J = 6 Hz), 4.52 (1 H, m), 5.68 (1 H, d, J = 4.5 Hz), 6.20 (1 H, dd, J = 5.5 and 16 Hz), 6.73 (1 H, d, J = 16 Hz), 7.27 (5 H, br s); mass spectrum, m/e (relative intensity) 220, 218, 216 (M^+, 5.6), 144 (83), 133 (72), 115 (100). Anal. Calcd for $C_{10}H_{10}OCl_2$: C, 55.33; H, 4.64. Found: C, 55.06; H, 4.62.

***trans*-1,1-Dichloro-3-nonadecen-2-ol (1f)**: bp 170 °C (0.01 mmHg); IR (liquid film) 3340 (br), 1035 (s), 965 (s), 785 (s), 725 (s) cm^{-1}; ^{1}H NMR δ 0.9 (3 H, m), 1.3 (26 H, m), 2.0 (2 H, m), 4.33 (1 H, m), 5.3–6.2 (3 H, including 1 H of d, J = 4.5 Hz); mass spectrum, m/e (relative intensity) 267 (M^+ –$CHCl_2$, 22), 265 (12), 57 (98), 43 (100). Anal. Calcd for $C_{19}H_{36}OCl_2$: C, 64.94; H, 10.33. Found: C, 64.89; H, 10.50.

1,1-Dichloro-3-methyl-3-buten-2-ol (1g): bp 110–125 °C (25 mmHg); IR (liquid film) 3420 (br, 1110 (s), 1055 (s), 920 (s), 890 (s), 870 (s), 715 (s) cm^{-1}; ^{1}H NMR δ 1.80 (3 H, br s), 2.68 (1 H, s), 4.33 (1 H, br d, J = 5.5 Hz), 5.15 (2 H, m), 5.77 (1 H, d, J = 6 Hz); mass spectrum, m/e (relative intensity) 120, 118 (M^+ – HCl, 4.3), 71 (100).

1,1-Dichloro-4-methyl-3-phen-2-ol (1h): bp 125 °C (8 mmHg); IR (liquid film) 3380 (br), 1040 (s), 840 (s), 790 (s), 750 (s), 705 (s) cm^{-1}; ^{1}H NMR δ 1.80 (6 H, m), 2.16 (1 H, br s), 4.62 (1 H, dd, J = 8.5 and 4 Hz), 5.30 (1 H, m), 5.68 (1 H, d, J = 4 Hz). Anal. Calcd for $C_6H_{10}OCl_2$: C, 42.63; H, 5.96. Found: C, 42.07; H, 6.18.

(2,2-Dichloro-3,3-dimethylcyclopropyl)methanol (3): bp 125 °C (8 mmHg); IR (liquid film) 3340 (br), 1040 (s), 1010 (m), 860 (s), 830 (s), 815 (s) cm^{-1}; ^{1}H NMR δ 1.29 (3 H, s), 1.4 (3 H, s), 1.52 (1 H, t, J = 7 Hz), 1.99 (1 H, s), 3.79 (2 H, d, J = 7 Hz); mass spectrum, m/e (relative intensity) 141, 139, 137 (M^+ – CH_2OH, 3), 85 (100). Anal. Calcd for $C_6H_{10}OCl_2$: C, 42.63; H, 5.96. Found: C, 42.47; H, 6.25.

1,1-Dichloro-3-phenyl-2-propanol (1j): bp 140 °C (1.5 mmHg); IR (liquid film) 3430 (br), 1085 (s), 1050 (s), 785 (s), 760 (s), 710 (s) cm^{-1}; ^{1}H NMR δ 2.47 (1 H, br), 2.97 (2 H, ABX, J_{AB} = 14.5 Hz), 4.10 (1 H, m), 5.60 (1 H, d, J = 4 Hz), 7.24 (5 H, br s); mass spectrum, m/e (relative intensity) 208, 206, 204 (M^+, 40), 121 (69), 91 (100); high-resolution mass spectrum, m/e 204.0094 (calcd for $C_9H_{10}O^{35}Cl_2$ 204.0107).

Deuterium-Labeling Experiment. To a mixed THF (10 mL) solution of lithium α,α-dideuteriobenzyl alcohol (1.5 mmol), *p*-methoxybenzyl alcohol (1.5 mmol), and *t*-BuOH (9 mmol) was added BuLi (1.55 M, hexane solution, 12 mmol) under a nitrogen atmosphere at 0 °C. To the resulting solution of the mixture of alkoxides was added $CHCl_3$ (9 mmol), and the mixture was heated under reflux for 0.5 h. After aqueous workup as described above followed by the purification by means of column chromatography (benzene–ethyl acetate gradient), 2,2-dichloro-1,2-dideuterio-1-phenylethanol (**1a**-d_2) (202 mg, 70%) and 2,2-dichloro-1-(*p*-methoxyphenyl)ethanol (**1b**) (254 mg, 76%) were obtained. ^{1}H NMR spectrum of **1a**-d_2 contained no signals for protons attached to C(1) (δ 5.82) and C(2) (δ 4.92).[22] ^{2}H NMR spectrum of **1b** contained no signals for the deuterium attached to C(1) and C(2). 2,2-Dichloro-1,2-dideuterio-1-(*p*-methoxyphenyl)ethanol (**1b**-d_2) was prepared by the reaction of lithium α,α-dideuterio-*p*-methoxybenzyl alkoxide with dichlorocarbene in 60% yield. ^{2}H NMR spectrum (13.70–MHz) of **1b**-d_2 in $CHCl_3$ contained two signals (–1.53 and –2.42 ppm with respect to $CDCl_3$), and the spectrum of **1a**-d_2 in $CHCl_3$ contained two signals (–1.50 and –2.35 ppm with respect to $CDCl_3$).

Reaction of Lithium Benzyl Oxide with Dichlorocarbene in the Presence of Benzyl Methyl Ether. To a mixed solution of lithium benzyl alkoxide (5 mmol), benzyl methyl ether (15 mmol), and *t*-BuOLi (5 mmol) in THF–hexane was added 5 mmol of $CHCl_3$, and the mixture was heated under reflux for 0.5 h. 2,2-Dichloro-1-phenethyl methyl ether[23] could not be detected by VPC analyses (10% Apiezon L and 10% PEG) of the reaction mixture. Purification with column chromatography (benzene–ethyl acetate gradient) provided 403 mg (42% yield) of **1a**.

General Procedure for the Reaction of Chlorophenylcarbene with Alkoxides (Table II). To a mixed suspension of *t*-BuOK (5 mmol) and KH (35% in oil, 6 mmol) in 8 mL of THF was slowly added the starting alcohol via syringe under nitrogen atmosphere. To the resulting suspension of mixed alkoxide was added slowly a solution of $PhCHCl_2$ (322 mg, 2 mmol) in 4 mL of THF at 0 °C. After being stirred for the period indicated in Table II, the reaction was quenched by the addition of aqueous NaCl and extracted twice with ethyl acetate. After drying over Na_2SO_4 and evaporation of solvents, a mixture of trans and cis isomers (approximately equal amounts) of the corresponding oxirane and in some cases byproduct(s) indicated in Table II were obtained by means of column chromatography. In entry 7 a mixture of *trans*- and *cis*-2-benzyl-3-phenyloxirane (**4g**), 3-phenyl-propiophenone (**7**), and benzaldehyde di-β-phenethyl acetal (**5g**) was obtained, but they could not thoroughly be separated by means of column chromatography. Yields were calculated from ^{1}H NMR spectra of the mixture. Authentic samples of *trans*- and *cis*-**4g** were prepared by the epoxidation of 1,3-diphenylpropene (E/Z = ca. 1) with MCPBA in CH_2Cl_2. The authentic sample of acetal **7** was prepared by the reaction of benzaldehyde with an excess amount of β-phenethyl alcohol in the presence of *p*-toluenesulfonic acid and grounded 4-Å molecular sieves in refluxing toluene for 13 h.

The physical and spectral data of the new compounds in Table II are as follows.

2-Phenyl-3-vinyloxirane (4c): bp 90 °C (2.5 mmHg); IR (liquid film) 995 (s), 935 (s), 880 (s), 750 (s), 705 (s) cm^{-1}; ^{1}H NMR δ 3.32 (1 H, dd, J = 2 and 6 Hz, trans), 3.58 (1 H, m, cis), 3.61 (1 H, d, J = 6 Hz, trans), 4.18 (1 H, d, J = 5 Hz, cis), 5.1–6.0 (3 H, m), 7.3 (5 H, br s); mass spectrum, m/e (relative intensity) 146 (M^+, 90), 117 (100), 115 (84), 91 (72). Anal. Calcd for $C_{10}H_{10}O$: C, 82.16; H, 6.89. Found: C, 82.39; H, 7.00.

2-Phenyl-3-propen-2-yloxirane (4e): bp 95 °C (1.1 mmHg); IR (liquid film) 1655 (m), 910 (s), 880 (m), 750 (s), 705 (s) cm^{-1}; ^{1}H NMR δ 1.46, 1.73 (3 H, br s), 3.34 (1 H, d, J = 2 Hz, trans), 3.61 (1 H, br d, J = 4.4 Hz, cis), 3.77 (1 H, d, J = 2 Hz, trans), 4.14 (1 H, d, J = 4.5 Hz, cis), 4.8–5.2 (2 H, m), 7.25, 7.30 (5 H, br s); mass spectrum, m/e (relative intensity) 160 (M^+, 100), 145 (32), 131 (56), 117 (75), 91 (96). Anal. Calcd for $C_{11}H_{12}O$: C, 82.46; H, 7.55. Found: C, 82.74; H, 7.69.

Benzaldehyde di-β-phenethyl acetal (5g): bp 165 °C (0.015 mmHg); IR (liquid film) 1350 (m), 1110 (s), 1075 (s), 1035 (s), 750 (s), 700 (m) cm^{-1}; ^{1}H NMR δ 2.84 (4 H, t, J = 7 Hz), 3.62 (4 H, t J = 7 Hz), 5.50 (1 H, s), 7.2–7.3 (15 H, m); mass spectrum, m/e (relative intensity) 211 (M^+ – $PhCH_2CH_2$, 14), 105 (100), 91 (54). Anal. Calcd for $C_{23}H_{24}O_2$:

(22) **1a**: ^{1}H NMR δ 3.54 (1 H, br s), 4.92 (1 H, d, J = 5.4 Hz), 5.82 (1 H, d, J = 5.4 Hz), 7.36 (5 H, br s).

(23) Authentic sample of 2,2-dichloro-1-phenethyl methyl ether[13] was prepared by the reaction of benzyl methyl ether with dichlorocarbene generated under phase-transfer conditions.

C, 83.10; H, 7.28. Found: C, 83.12; H, 7.13.

Benzaldehyde dioctyl acetal (5h): bp 155 °C (0.015 mmHg); IR (liquid film) 1360 (m), 1115 (s), 1040 (s), 760 (m), 710 (s) cm^{-1}; ^1H NMR δ 0.8–1.8 (30 H, m), 3.5 (4 H, br t, J = 6 Hz), 5.5 (1 H, s), 7.3 (5 H, m); mass spectrum, m/e (relative intensity) 219 ($M^+ - C_8H_{17}O$, trace), 106 (45), 105 (50), 57 (97), 56 (99), 43 (97), 41 (100). Anal. Calcd for $C_{23}H_{40}O_2$: C, 79.25; H, 11.57. Found: C, 79.35; H, 11.70.

2-Methoxymethyl-3-phenyloxirane (4j): bp 130 °C (2.5 mmHg); IR (liquid film) 1460 (s), 1115 (s), 880 (s), 750 (s), 700 (s) cm^{-1}; ^1H NMR δ 3.1–3.9 (6 H, m, including s at 3.23 and 3.43 and d at 3.77, J = 2 Hz, trans), 4.10 (1 H, d, J = 4 Hz, cis), 7.30, 7.33 (5 H, br s); mass spectrum, m/e (relative intensity) 164 (M^+, 16), 132 (46), 104 (56), 103 (100). Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.14; H, 7.37. Found: C, 73.07; H, 7.45.

Benzaldehyde di-2-methoxyethyl acetal (5j): bp 86 °C (0.02 mmHg); IR (liquid film) 1370 (m), 1140 (s), 1105 (s), 1070 (s), 760 (s), 705 (s) cm^{-1}; ^1H NMR δ 3.39 (6 H, s), 3.64 (8 H, m), 5.69 (1 H, s), 7.4 (5 H, m); mass spectrum, m/e (relative intensity) 165 ($M^+ - CH_3OCH_2CH_2$, 33), 105 (10), 59 (100). Anal. Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 65.18; H, 8.50.

1-Phenyl-3-penten-1-one (6): bp 115 °C (2.5 mmHg); IR (liquid film) 1690 (s), 1210 (s), 970 (s), 740 (s), 700 (s) cm^{-1}; ^1H NMR δ 1.70 (3 H, br d, J = ca. 4 Hz), 3.7 (2 H, m), 5.65 (2 H, m), 7.3 (3 H, m), 7.85 (2 H, m); mass spectrum, m/e (relative intensity) 160 (M^+, 11), 120 (17), 105 (100), 78 (70).

Reaction of Potassium Benzyl Oxide with $PhCHCl_2$ in the Absence of *t*-BuOk. A reaction of potassium benzyl oxide (5 mmol) with $PhCHCl_2$ (2 mmol) was performed by a procedure similar to that described above in the absence of *t*-BuOK at 0 °C for 1 h. VPC analysis showed 78% recovery of $PhCHCl_2$, and 42.4 mg (11%) of diphenyloxirane (**4a**) and 476 mg (88%) of benzyl alcohol were obtained after column chromatography (benzene–ethyl acetate gradient).

2-Chloro-1,2-diphenylethanol (12).[24] To a THF (5 mL) solution of $PhCHCl_2$ (2 mmol) was added slowly 2.2 mol of BuLi (1.55 M hexane solution) at −90 °C under nitrogen atmosphere, and the reaction mixture was stirred for 0.5 h at the same temperature. To this was added a THF (5 mL) solution of lithium benzyl oxide (5 mmol, prepared from benzyl alcohol and BuLi) at −90 °C, and the mixture was slowly warmed up to −10∼10 °C within 3.5 h. After the addition of brine followed by extractive workup and column chromatography (cyclohexane–benzene gradient) 129 mg (28%) of **12** (mixture of isomers) was obtained: bp 106 °C (0.015 mmHg); IR (liquid Film) 3420 (br), 1060 (s), 760 (m), 730 (s), 705 (s) cm^{-1}; ^1H NMR δ 2.60, 3.15 (1 H, br), 4.9 (2 H, m), 7.2 (10 H, m); mass spectrum, m/e (relative intensity) 196 (M^+ − HCl, 6), 194 (6), 167 (100), 165 (40), 105 (63). Anal. Calcd for $C_{14}H_{13}OCl$: C, 72.26; H, 5.63. Found: C, 72.54; H, 5.63. 2-Chloro-1,2-diphenylethanol (**12**) (67.6 mg, 0.29 mmol) thus obtained was treated with *t*-BuOK (0.35 mmol) in THF at 0 °C for 0.5 h to give 53.3 mg (94%) of **4a** (trans:cis = ca. 1).

Isomerization of 2-Benzyl-3-phenyloxirane (4g) to 3-Phenylproplophenone (7). To a THF (8 mL) solution of 120 mg (1.07 mmol) of *t*-BuOK was added a solution of 150 mg (0.71 mmol) of **4g** (trans:cis = ca. 1) at 0 °C under nitrogen atmosphere, and the mixture was stirred for 0.75 h. After the usual workup followed by column chromatography (cyclohexane–benzene gradient), 137 mg of the mixture of **4g** and **7** was obtained. Yield of **7** based on the consumed **4g** was 90% (determined by ^1H NMR spectroscopy, conversion of **4g** was 89%).

Isomerization of 2-Phenyl-3-(1-propenyl)oxirane (4d) to 1-Phenyl-3-penten-1-one (6). Starting with 150 mg (0.94 mmol) of **4d** (trans:cis = ca. 1) by the similar procedure as described above, 19.3 mg of **6** (40% yield based on the consumed **4d**) was obtained besides the recovery of **4d** (102 mg, conversion 32%) afte florisil column chromatography (cyclohexane–benzene gradient).

Treatment of Benzyl Dichloromethyl Ether with *t*-BuOLi. Benzyl dichloromethyl ether[25] (9 mmol) that was dissolved in 3 mL of THF was added to a solution of *t*-BuOLi (9 mmol in 7 mL of THF–hexane) at 0 °C under a nitrogen atmosphere. After being stirred at 70–80 °C for 30 min, the reaction was quenched by adding water. After workup, the product mixture was analyzed by VPC using reference compounds (benzyl chloride, **1a**, and starting ether). Benzyl chloride was the major product (74%) besides small amounts of benzyl alcohol and some high-boiling products in which **1a** was not detected at all.

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Registry No. 1a, 2612-36-4; **1b**, 58622-56-3; **1c**, 84987-59-7; **1d**, 84987-60-0; **1e**, 84987-61-1; **1f**, 84987-62-2; **1g**, 84987-63-3; **1h**, 62836-22-0; **1i**, 84987-64-4; **1j**, 84987-65-5; **2**, 64670-26-4; **3**, 52815-11-9; *cis*-**4a**, 1689-71-0; *trans*-**4a**, 1439-07-2; *cis*-**4b**, 70332-50-2; *trans*-**4b**, 28291-10-3; *cis*-**4c**, 21699-63-8; *trans*-**4c**, 21699-64-9; *cis*-**4d**, 53274-96-7; *trans*-**4d**, 53274-97-8; *cis*-**4e**, 81411-53-2; *trans*-**4e**, 81411-56-5; *cis*-**4f**, 53226-69-0; *trans*-**4f**, 53226-68-9; *cis*-**4g**, 65095-04-7; *trans*-**4g**, 65095-03-6; *cis*-**4h**, 65094-94-2; *trans*-**4h**, 65094-93-1; **4i**, 10152-58-6; *cis*-**4j**, 84987-66-6; *trans*-**4j**, 84987-67-7; **5g**, 84987-68-8; **5h**, 84987-69-9; **5j**, 71412-83-4; **6**, 73481-93-3; **7**, 1083-30-3; **12**, 54060-36-5; $PhCH_2OLi$, 15082-42-5; (*p*-anisyl)CH_2OLi, 57965-13-6; $H_2C{=}CHCH_2OLi$, 52203-12-0; (*E*)-$H_3CCH{=}CHCH_2OLi$, 84987-70-2; (*E*)-$PhCH{=}CHCH_2OLi$, 84987-71-3; (*E*)-$C_{15}H_{31}CH{=}CHCH_2OLi$, 84987-72-4; $H_2C{=}C(CH_3)CH_2OLi$, 84987-73-5; $(CH_3)_2C{=}CHCH_2OLi$, 84987-74-6; (*E*)-$PhCH{=}CHCH(CH_3)OLi$, 84987-75-7; $PhCH_2CH_2OLi$, 15082-43-6; $PhCH_2OK$, 22379-62-0; *p*-$ClC_6H_4CH_2OK$, 73447-13-9; $H_2C{=}CHCH_2OK$, 33374-41-3; *trans*-$CH_3CH{=}CHCH_2OK$, 79695-50-4; $H_2C{=}C(CH_3)CH_3OK$, 84987-76-8; $H_2C{=}CHCH(CH_3)OK$, 79695-48-0; $PhCH_2CH_2OK$, 2245-69-4; *n*-$C_7H_{15}CH_2OK$, 56281-85-7; $(CH_3)_2CHOK$, 6831-82-9; $CH_3OCH_2CH_2OK$, 20246-66-6; dichlorocarbene, 1605-72-7; chlorophenylcarbene, 19807-41-1.

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Interdependence of Carbon–Nitrogen and Carbon–Oxygen Bond Lengths in Urea Structures and in Ureido Ring Structures

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Abstract: Crystallographic data on the C–N and C–O bond lengths in the N–C(O)–N group in 114 urea and ureido ring structures are analyzed and interpreted in terms of classical valence-bond chemical structures. Substituent effects, the effect of ureido ring closure, and hydrogen-bonding effects are discernible. The structural data have implications for interpretation of the chemical mechanism of the coenzyme biotin.

In connection with studies of the structural biochemistry of biotin (**1**), we have surveyed the crystallographic literature on urea and ureido ring structures. We find that the C–N and C–O bond lengths in these structures clearly illustrate certain basic chemical

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