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ENANTIOSELECTIVE ADDITION OF DICHLOROCARBENE TO OLEFINS BY USE OF CHIRAL TERTIARY AMINES

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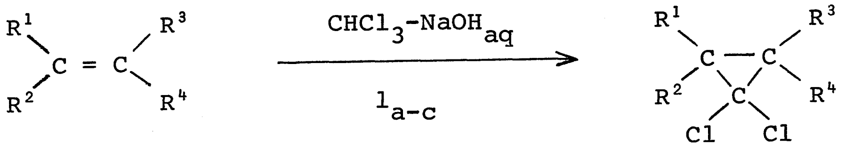
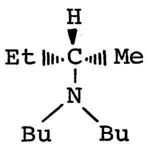
Dichlorocarbene generated from chloroform and aqueous sodium hydroxide using chiral tertiary amines as a catalyst adds enantioselectively to olefins to give chiral dichlorocyclopropane derivatives. Optical rotations of the products strongly depend on the structure of catalysts employed.

In a previous paper, we have shown that certain tertiary amines are an effective catalyst for the generation of dichlorocarbene from chloroform in two-phase system consisting of aqueous and organic solvents.(1) Some mechanistic investigations of this catalytic reaction implied that a nitrogen ylide, which is formed by the interation between dichlorocarbene and a tertiary amine, may participate as an intermediate of the reaction. Therefore, we studied the dichlorocarbene generation reaction in the presence of various olefins using chiral amines as a catalyst with the hope that the enantioselective addition of the carbene to the double bond of olefins may take place. The results are described in this communication.

In a typical experiment, a mixture of chloroform (5.5 ml, 68 mmol), styrene (2.2 g, 22 mmol), (S)-(+)-N,N-dibutyl-1-methylpropylamine [1a] (0.41 g, 2.2 mmol), and 50% aqueous NaOH solution (14 ml) was stirred at 30°C for 1 h. The reaction mixture was acidified with a dilute HCl and extracted with ether. The ether extract was washed succesively with a dilute HCl and water, and dried over Na_2SO_4. Ether was evaporated and residue was distilled to give (+)-1-phenyl-2,2-dichlorocyclopropane [(+)-2] in 30% yield; bp 65°C/ 3 mmHg (lit,(2) bp 105-106°C/ 12 mmHg), $[\alpha]_D^{27}+3.86$ (c 5.77, $CHCl_3$). The same optical active product [(+)-2] with somewhat lower optical rotation, $[\alpha]_D^{27}+0.28$ (c 14.5, $CHCl_3$), was obtained by use of (S)-(+)-N,N-dibutyl-1-phenylethylamine [1b] as a catalyst. In a similar manner, the dichlorocarbene

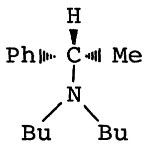


2: R^1=Ph, R^2=R^3=R^4=H
3: R^1=n-Pr, R^2=CH_3, R^3=R^4=H
5: R^1=Ph, R^2=R^3=H, R^4=CH_3



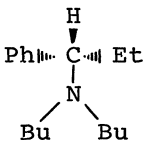
$[\alpha]_D^{27}$ +25.0
(c 2.8, $CHCl_3$)

[1a]



$[\alpha]_D^{27}$ +4.37
(c 1.3, $CHCl_3$)

[1b]



$[\alpha]_D^{27}$ −12.2
(c 2.03, $CHCl_3$)

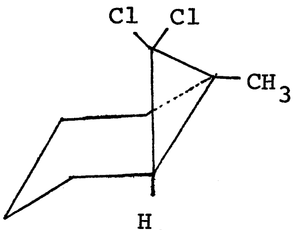
[1c]

addition to the double bond of other olefins was conducted using [1a], [1b], and (S)-(−)-N,N-dibutyl-1-phenylpropylamine [1c] as catalysts. The results are summarized in the Table.

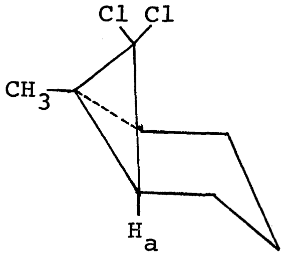
These results suggested that the catalytic reactions presented here have the following characteristics.

(1) Optical rotations of the products strongly depend on the structure of catalysts employed. For example, the reactions of 1-methylcyclohexene with dichlorocarbene in the presence of [1a] and [1b] gave *dextro-* and *levo-*rotatory 7,7-dichloro-1-methylbicyclo[4.1.0]heptanes ([(+)-4] and [(−)-4]), respectively (runs 6 and 7). Similar reactions of *trans*-propenylbenzene in the presence of [1a] and [1b] afforded *levo-* and *dextro-*rotatory 1,1-dichloro-2-methyl-3-phenylcyclopropanes ([(−)-5] and [(+)-5]), respectively (runs 9 and 10).

(2) The addition of dichlorocarbene to the double bond of olefins may be stereospecific in nature. The NMR spectra of [(+)-4] and [(−)-4] obtained by the reactions of runs 6 and 7 showed a doublet signal at $\delta(CCl_4)=1.10$ ppm (1H, J=10.5 Hz) assignable to an axial proton H_a of [4a] or [4b]; no products other than [(+)-4] and [(−)-4] were detected in the reactions of 1-methylcyclohexene. This structure indicates that the dichlorocarbene addition occurs from the *exo*-direction of the double bond of 1-methylcyclohexene.



[4a]



[4b]

(3) The optical yields of the products decrease with rise in reaction temperatures (runs 1 and 2). Furthermore, the products are not racemized by heating around ambient temperatures. Indeed, the optical rotation of [(+)-2] remained unchanged upon refluxing it in benzene overnight.

(4) The signs of optical rotations of the products may be correlated with the structure of the catalysts employed. The absolute configurations of pure [(+)-5] and [(−)-5] have been assigned to be (2R,3R) and (2S,3S), respectively.[3)] This result

Table. Reaction of Dichlorocarbene with Olefins in the Presence of Chiral Tertiary Amines

Run	Olefin	Catalyst[4)]	Reaction Conditions		Product		
			Time (h)	Temp (°C)	Compd	Isolated Yield(%)	$[\alpha]_D^{27}$ ($CHCl_3$)
1	Styrene	1a	1	30	2	30	+3.86(c 5.77)
2	"	1a	1	50	2	78	+0.99(c 8.10)
3	"	1b	1.5	30	2	24	+0.28(c 14.5)
4	2-Methyl-1-pentene	1a	1	40	3	53	+0.19(c 30.1)
5	"	1b	2	50	3	69	+0.06(c 40.0)
6	1-Methyl-1-cyclohexene	1a	2	50	4	68	+0.23(c 30.1)
7	"	1b	2	50	4	66	-0.09(c 30.0)
8	"	1c	18	58	4	5	-0.33(c 4.20)
9	*trans*-Propenyl benzene	1a	1	40	5	66	-1.10(c 11.8)
10	"	1b	53	50	5	1	+2.10(c 2.78)

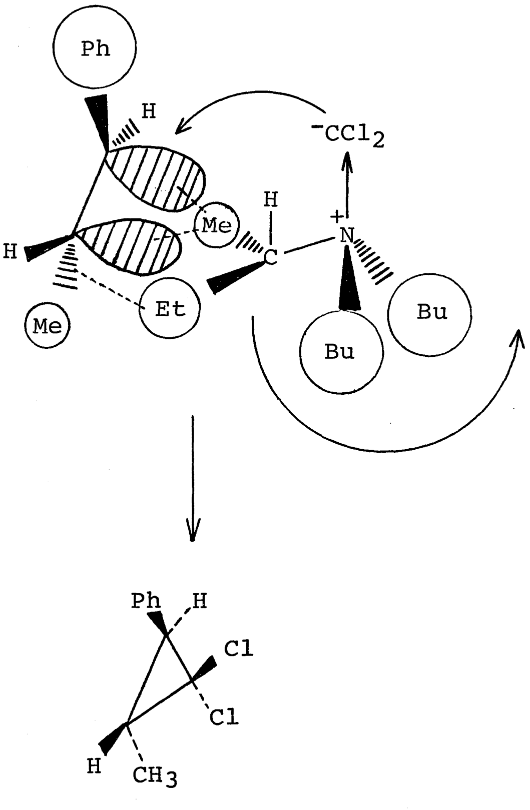


Fig. 1a

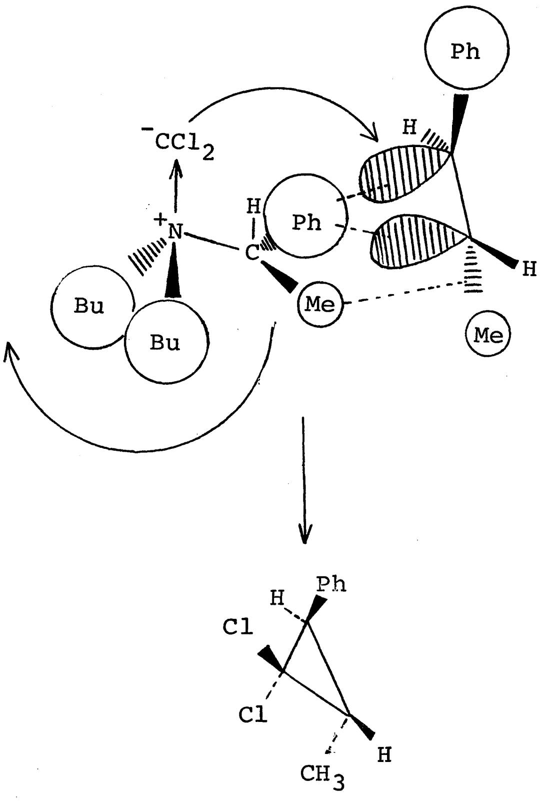


Fig. 1b

implies that the reactions leading to [(+)-5] and [(-)-5] proceed through the transition states as depicted in Figs. 1a and 1b. The methyl group of [1a] interacts with the π-bond of the olefin, and the ethyl group with the σ-bond linking between CH_3- and C=C group.[5] These specific interations are associated with the fact that the methyl group has a larger π-character by its hyperconjugative ability compared with that of ethyl group. Similarly, in [1b] the phenyl group with a larger π-character interacts with the olefinic π-bond and the methyl group with the σ-bond as indicated above.

Straightforward extension of this consideration leads to the prediction that [(+)-4] and [(-)-4] would have the absolute configurations of [4b] and [4a], respectively. This consideration was partly supported by the experiment that the optical yield of [(-)-4] was improved by use of [1c] as a catalyst (run 8). For [1c], rather distinctive π-π and σ-σ interactions between the catalyst and the olefin are expected compared with those of [1a] and [1b], since the ethyl group has little hyperconjugative π-character.

The above characteristics suggest that the reactions proceed through weakly stabilized ylide intermediates such as those illustrated in Figs. 1a and 1b. Detailed mechanism and synthetic applications of these catalytic reactions will be reported in subsequent papers.

References and Notes

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4) The chiral amines [1a] and [1b] were prepared respectively by treating (S)-(+)-2-methylpropylamine, $[\alpha]_D^{27}$+8.0(c 2.8,H_2O) (lit,[6] $[\alpha]_D^{15}$+7.8(c 2.8,H_2O)) and (S)-(-)-1-phenylethylamine, $[\alpha]_D^{27}$-32.7(c 3.1,$CHCl_3$) (lit,[7] $[\alpha]_D^{29}$-39.4(neat)), with butyl bromide: optical active primary amines were obtained by the resolution of the corresponding commercial racemic amines with tartaric acid. The chiral amine [1c] was prepared by the following sequence of reactions: 1-phenylpropylamine oxime $\longrightarrow$ (±)-1-phenylpropylamine $\longrightarrow$ (S)-(-)-1-phenylpropylamine($[\alpha]_D^{27}$-2.56(c 1.87,$CHCl_3$)) (lit,[8] $[\alpha]_D^{17}$-19.85) $\longrightarrow$ [1c].
5) Other types of the transition states are also possible in which the attack of dichlorocarbene occurs from the opposite side of the olefinic double bonds, and would lead to the products enantiomeric to those obtained by experiments. However, examination of the molecular models for the transition states shows that these transition states are energetically unfavorable compared to those depicted in Figs. 1a and 1b by the steric interaction between the bulky phenyl group of the substrate and the dichlorocarbene moieties, if the maximal interation between the substrate and the catalysts is kept until the carbene addition takes place.
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