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Stereoselectivity of Phenylcarbenoid of Zinc in Cycloaddition with Olefin

Jun NISHIMURA, Junji FURUKAWA,* Nariyoshi KAWABATA,** and Hiroaki KOYAMA
Department of Synthetic Chemistry, Kyoto University, Sakyo-ku, Kyoto

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The stereoselectivity of phenylcarbenoid of zinc generated from diethylzinc and benzal iodide was investigated in the cycloaddition reaction with olefin. The carbenoid showed larger *syn*-selectivity than phenylcarbenoid of lithium. Electron-donating substituent attached to the phenyl group of the phenylcarbenoid enhanced the *syn*-selectivity of the carbenoid. The *syn*-selectivity of the phenylcarbenoid was larger in ether than in *n*-pentane, contrary to the case of phenylcarbenoid of lithium.

The authors have reported briefly the formation of phenylcyclopropane by the reaction of diethylzinc and benzal iodide in the presence of olefin.[1] The generation of an phenylcarbenoid of zinc was assumed in the reaction.

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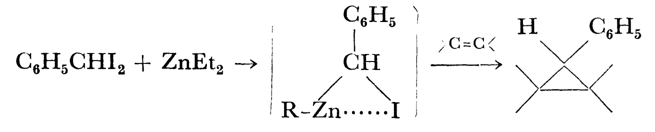
* To whom inquiries should be directed.

** Present address: Department of Chemistry, Kyoto Institute of Technology, Matsugasaki, Kyoto.

[1] J. Furukawa, N. Kawabata, and J. Nishimura, *Tetrahedron Lett.*, **1968**, 3495.

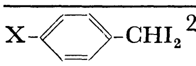
The present paper describes details of the stereochemistry of this reaction.



(1)

The reaction of diethylzinc and the substituted benzal iodide with 2-methylbut-2-ene and cyclohexene in moderate reaction conditions gave arylcyclopropanes in 18—69% yield. Results are given in Table 1.

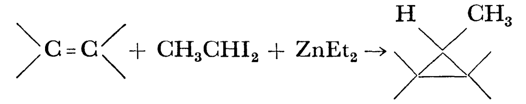
TABLE 1. FORMATION OF ARYLCYCLOPROPANES

 X	2-Methylbut-2-ene a) *syn*/*anti*	Yield (%) b)	Cyclohexene c) *syn*/*anti*	Yield (%) b)
p-CH_3	5.3	30	—	—
H	4.2	42	17.1	69 d)
p-Cl	2.0	18	—	—

a) Reactions were carried out at room temperature.
b) Based on the iodide.
c) Ref. 1.
d) Determined by vapor phase chromatography.

As was mentioned before,1) this phenylcarbenoid of zinc shows the *syn*-selectivity.

In the reaction of diethylzinc and ethylidene iodide with olefin, methylcyclopropanes were formed with the result that *syn* isomer generally predominated over *anti* isomer.2)



(2)

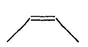
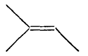
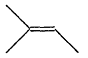
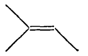
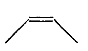
The electrostatic interaction between methyl group of the methylcarbenoid and substituents of olefin was proposed to explain the *syn*-selectivity of reaction (2).2)

In the reactions with cyclohexene, the phenylcarbenoid in reaction (1) showed higher *syn*-selective behavior (*syn*/*anti*=17.1)1) than the methylcarbenoid in reaction (2) (*syn*/*anti*=1.5).2) As can be seen in Table 1, the electron-donating substituent attached to the phenyl group of benzal iodide enhanced the *syn*-selectivity of reaction (1). The electrostatic interactions between substituents in carbenoid and olefin may be significant factors which determine the isomer ratio in reaction (1).

The stereoselectivity of phenylcarbenoid in reaction (1) is compared with those of other phenylcarbene and carbenoids (Table 2).

The *syn*-selectivity of phenylcarbenoid in reaction (1) is higher than that of phenylcarbenoid of lithium,3) but is much the same order of magnitude as that of other phenylcarbenoid of zinc.4)

TABLE 2. STEREOSELECTIVITY OF VARIOUS ARYLCARBENE AND CARBENOIDS

Reaction	Olefin	*syn*/*anti*	Yield %	Reference
$C_6H_5CHN_2$ + *hν*		1.1	—	3
$C_6H_5CHBr_2$ + MeLi		1.3	23	3
$C_6H_5CHI_2$ + Et_2Zn		4.2	42	This work
p-$CH_3C_6H_4CH_2$ + ZnI_2		2.6	—	4
$C_6H_5CHN_2$ + $ZnBr_2$		4.7	70	4

The *syn*/*anti* isomer ratio of 7-phenylnorcarane produced by reaction (1) depends largely upon the nature of solvents.

TABLE 3. SOLVENT EFFECT UPON *syn*/*anti* ISOMER RATIO IN REACTION (1) WITH CYCLOHEXENE a)

Solvent	Isomer ratio (*syn*/*anti*)	Yield b) (%)
n-Pentane	6.6	68
Benzene	6.2	67
Cyclohexanone	9.3	low
Acetonitrile	9.5	low
Diethyl ether	17.1	69
Di-*n*-butyl ether	16.0	68
t-Butyl methyl ether	14.0	67
Di-*iso*-propyl ether	12.0	71
Diethylene glycol dimethyl ether	9.6	low
Tetrahydrofuran	9.6	low

a) Reactions were carried out at 25°C.
b) Determined by vapor phase chromatography and based on the iodide.

The phenylcarbenoid shows much higher *syn*-selective behavior in ethers than in hydrocarbons. The *syn*/*anti*

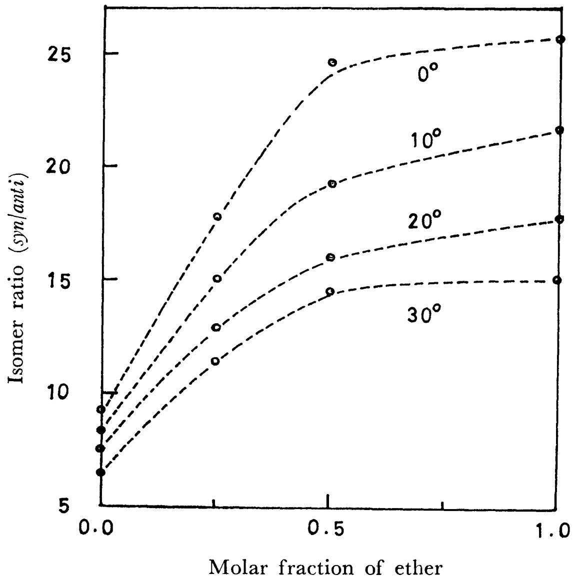


Fig. 1. Dependence of *syn*/*anti* isomer ratio on ether content in reaction (1) with cyclohexene in ether-pentane mixture.

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2) J. Nishimura, N. Kawabata, and J. Furukawa, *Tetrahedron*, **25**, 2647 (1969), and the literatures cited therein.

3) G. L. Closs and R. A. Moss, *J. Amer. Chem. Soc.*, **86**, 4042 (1964).

4) S. H. Goh, L. E. Closs, and G. L. Closs, *J. Org. Chem.*, **34**, 25 (1969).

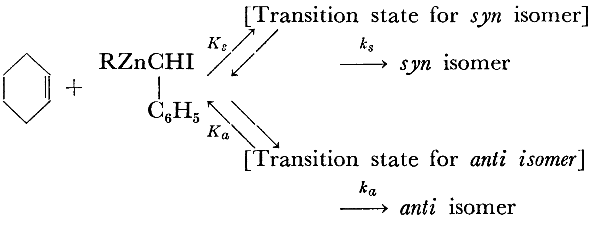
TABLE 4. TEMPERATURE DEPENDENCE OF *syn/anti* ISOMER RATIO IN REACTION (1) WITH CYCLOHEXENE IN ETHER-PENTANE MIXTURE

No.	Molar fraction of ether	Isomer ratio (*syn/anti*) 0°C	10°C	20°C	30°C	$\Delta H_s^{\neq}-\Delta H_a^{\neq}$ (kcal/mol)	$\Delta S_s^{\neq}-\Delta S_a^{\neq}$ (e. u.)
1	1.00	25.6	21.7	17.9	15.1	−2.91	−4.18
2	0.50	24.6	19.3	16.1	14.6	−2.88	−4.23
3	0.25	17.7	15.0	12.9	11.4	−2.41	−3.14
4	0.00	9.2	8.3	7.5	7.3	−1.31	−0.42

isomer ratio in reaction (1) with cyclohexene was examined in the mixed solvent of ether and *n*-pentane. The *syn/anti* isomer ratio increased with the molar fraction of ether in the mixed solvent as is shown in Fig. 1. These facts show the special solvent effect of aliphatic ethers upon the stereoselectivity of reaction (1), which might include the coordination of ether to zinc atom of the carbenoid. In the case of the reaction of *n*-butyllithium and *p*-methylbenzal bromide with *cis*-but-2-ene in the mixed solvent of ether and *n*-pentane,[3] the *syn/anti* isomer ratio of 1-*p*-tolyl-*cis*-2,3-dimethylcyclopropane decreased with the increasing molar fraction of ether contrary to the case of reaction (1). Metal atom of carbenoid may play an important role in this solvent effect.

Temperature dependence of the *syn/anti* isomer ratio in reaction (1) with cyclohexene in the ether-pentane mixture is given in Table 4.

According to the theory of absolute reaction rate,[5] ln (k_s/k_a) is given by Eq. (3) if transmission coefficients κ_s is equal to κ_a:



$$\ln(k_s/k_a) \cong -\frac{\Delta H_s^{\neq}-\Delta H_a^{\neq}}{RT}+\frac{\Delta S_s^{\neq}-\Delta S_a^{\neq}}{R} \qquad (3)$$

where k_s and k_a are the rate constants for the formation of *syn* and *anti* isomer, respectively. If the reaction is kinetically controlled, k_s/k_a can be calculated from the *syn/anti* isomer ratio with Eq. (4).

$$[\textit{syn}\ \text{isomer}]/[\textit{anti}\ \text{isomer}] = k_s/k_a \qquad (4)$$

The isomerization between *syn*- and *anti*-7-phenylnorcaranes is not very significant under the conditions of reaction (1) and subsequent experimental procedures,[6] and consequently this reaction can be assumed to be kinetically controlled. The differences in activation enthalpy and entropy between *syn* and *anti* isomer formation in reaction (1) were calculated and given in Table 4.

The activation enthalpy and the activation entropy for the *syn* isomer formation are smaller than those for the *anti* isomer formation. This result means that the transition state for *syn* isomer formation is energetically more stable than that for *anti* isomer formation, but entropically the situation is reverse.

The difference in activation energy between *syn* and *anti* isomer formation is larger in ether than in *n*-pentane. The phenomenon might be attributed to the specific solvation of ether to zinc atom of the carbenoid. Further experiments are required to discuss this point.

Experimental

Elemental analyses were performed at the Elemental Analyses Center of Kyoto University. NMR spectra were obtained with a Varian associates A-60 NMR Spectrometer or a Japan Electron Optics Lab. Model C60H Spectrometer in carbon tetrachloride using tetramethylsilane as the internal standard. Vapor phase chromatographic analyses were made on a Shimadzu GC-2C gas chromatograph. Melting points were corrected, but boiling points were not.

Materials. *t*-Butyl methyl ether was prepared according to the procedure of Norris and Rigby.[7] Tosylhydrazones of arylaldehydes[3] and ring substituted benzal iodides[8] were prepared by conventional methods: $C_6H_5CHI_2$, mp 44—46°C; *p*-$CH_3C_6H_4CHI_2$, mp 36—38°C (lit,[8] 35—37°C); *p*-ClC_6H_4-CHI_2, mp 55—57°C.

Solvents were purified by the usual methods.[9] Other reagents were purified as described in the previous paper.[10]

Aryl-2,2,3-trimethylcyclopropanes. The reaction procedure was the same as have been described in a previous paper.[2] The reaction was carried out at room temperature. Stereochemical structures of products were determined by NMR chemical shift of methyl protons as shown in Table 5.[3] Physical properties and analytical data of the compounds were given in Table 6.

Temperature and Solvent Dependence of endo/exo *Isomer Ratio in Reaction (1) with Cyclohexene.* Cyclohexene (0.10 mol, 10.2 m*l*), benzal iodide (0.01 mol, 3.44 g) and solvent (20 m*l*) were placed in a 50 m*l* three necked flask equipped with a magnetic stirrer, a reflux condenser, a dropping funnel, and a gas-inlet with three-way cock under an atmosphere of nitrogen. The mixture was heated or chilled to prescribed temperature, and diethylzinc (0.02 mol, 2 m*l*) was added slowly from dropping funnel. After stirred for 5 hr, tetralin (0.005 mol) was added as internal standard for vapor phase chromatographic analysis. The reaction mixture was treated with aqueous ammonium chloride and analysed by vapor phase chromatography.

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5) S. Glasstone, K. J. Laidler, and H. Eyring, "The Theory of Rate Processes," McGraw-Hill, New York & London (1941).

6) See experimental section.

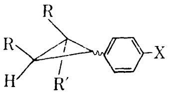
7) J. F. Norris and G. W. Rigby, *J. Amer. Chem. Soc.*, **54**, 2088 (1932).

8) R. A. Moss, *J. Org. Chem.*, **30**, 3261 (1965).

9) A. Weisserberger, E. P. Proskauer, J. A. Riddick, and E. E. Toops, Jr., "Organic Solvents," Interscience, New York (1957).

10) J. Furukawa, N. Kawabata, and J. Nishimura, *Tetrahedron*, **24**, 53 (1968).

TABLE 5. CHEMICAL SHIFT (τ) OF METHYL PROTONS OF ARYL-2,2,3-TRIMETHYLCYCLOPROPANE



($R=R'=CH_3$)

X	Obsd (Reported)[a]			
	syn Isomer		*anti* Isomer	
	R	R′	R	R′
p-CH_3	9.10 (9.12)	8.79 (8.82)	—	—
H	9.14 (9.10)	8.82 (8.78)	8.81 (8.83)	9.24 (9.23)
p-Cl	9.12 (9.12)	8.79 (8.78)	8.80 (8.82)	9.21 (9.22)

a) Ref. 3.

TABLE 6. ARYL-2,2,3-TRIMETHYLCYCLOPROPANES PREPARED BY REACTION (1) WITH 2-METHYLBUT-2-ENE

$XC_6H_4CH—CHCH_3$ \ / $C(CH_3)_2$	Bp (lit)[a] (°C/mmHg)	Elemental analysis Calcd (Found)		
		C	H	Cl
p-CH_3	81—88/9 (43/0.8)	89.59 (89.62)	10.41 (10.29)	
H	91—92/19 (61/3.5)	89.94 (90.15)	10.06 (10.01)	
p-Cl	55—57/5 (70/0.2)	74.03 (74.22)	7.77 (7.97)	18.21 (18.43)

a) Ref. 3.

The reaction of diethylzinc, methylene iodide, and cyclohexene was carried out under a similar reaction condition for 5 hr at room temperature in the presence of an isomer mixture (*syn*/*anti*= 19.4) of 7-phenylnorcarane. The reaction mixture was treated in a similar manner as mentioned above. Vapor phase chromatographic analysis of the reaction mixture indicated that the *syn*/*anti* isomer ratio of the recovered 7-phenylnorcarane was 18.4. Thus, the isomerization between *syn*- and *anti*-7-phenylnorcarane during reaction (1) and subsequent experimental procedures is not so significant.