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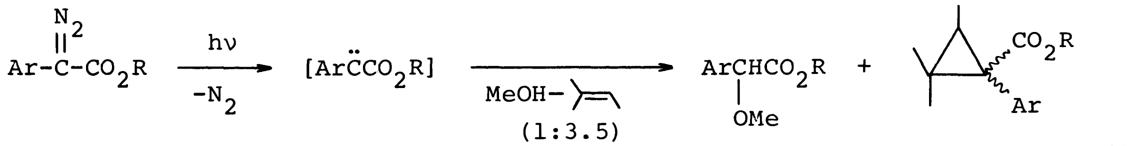
NEIGHBORING GROUP PARTICIPATION IN CARBENE CHEMISTRY. EFFECT OF NEIGHBORING CARBOXYLATE GROUP ON ARYLCARBENE REACTIVITY

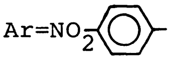
Hideo TOMIOKA,* Kazuo TABAYASHI, and Yasuji IZAWA
Department of Industrial Chemistry, Faculty of Engineering,
Mie University, Tsu, Mie 514

The carbene generated by photolysis of sodium α-diazoacetate in a binary mixture of methanol and 2-methyl-2-butene showed 3000 times enhanced reactivity toward methanol relative to the alkene compared to that derived from the corresponding ester or acid. The results are interpreted as indicating that the neighboring carboxylate group interacts with electron-deficient center of carbene.

Neighboring group participation, where internal nucleophiles become bonded (fully or partially) to the electron-deficient center for an interval of time during the reaction's progress, is well known to occur in many nucleophilic displacement (S_N) reactions.[1)] In a marked contrast, only a scant information is available on the neighboring group participation in carbene chemistry.[2)] This is rather surprising in view of the fact that most carbenes are classified as an electron-deficient species. In this paper we would like to report that neighboring carboxylate group, a well-known participating group in S_N reactions, dramatically alters the reactivity of carbenes but, nevertheless remains bonded to the atom to which it was originally attached.

Irradiation of methyl p-nitrophenyl-α-diazoacetate (**1a**) in a 1 : 3.5 binary mixture of methanol and 2-methyl-2-butene afforded α-methoxyacetate (**3**) and cyclopropanes (**4**, as a mixture of syn and anti isomers) in 7% and 71% yields, respectively. These products are apparently derived from photolytically generated carbene (**2**), which either underwent insertion into O-H bond of methanol or added to the alkene.[3)] Similar irradiation of the corresponding free diazoacid (**1b**)[4)] followed by CH_2N_2 treatment gave essentially the same product mixtures.[3)] When sodium salt[4)] of **1b** was irradiated under similar conditions, followed by

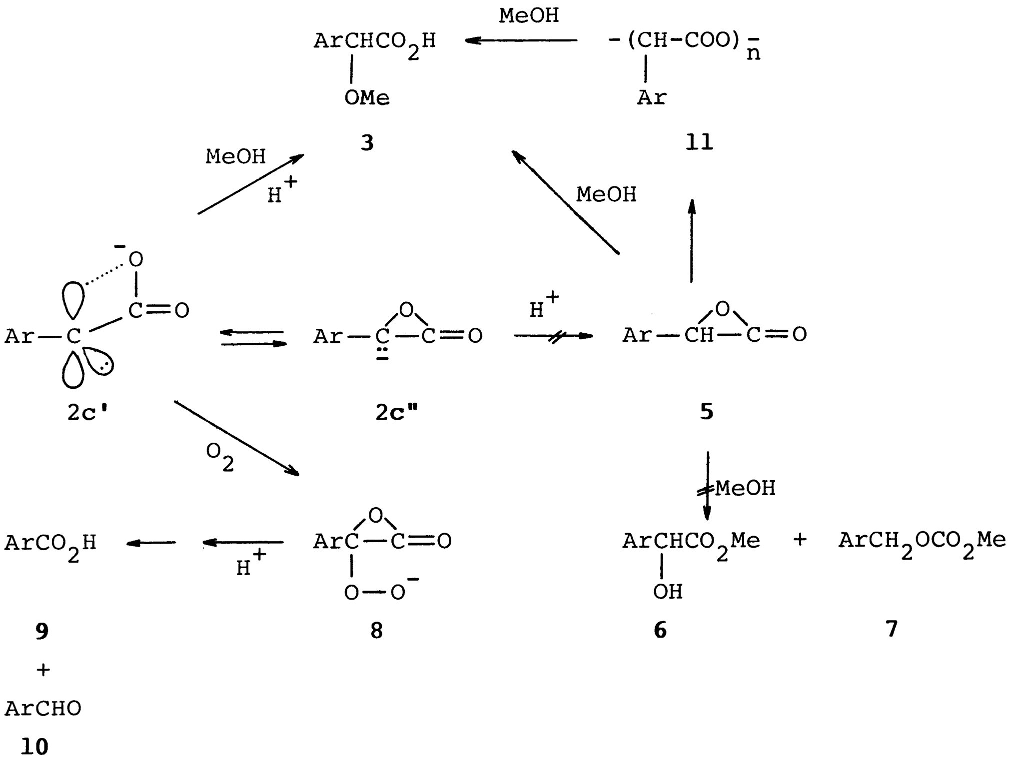


1	**2**	**3**	**4** (syn:anti)
a: R=Me		7.0%	70.8%(1:1)
b: R=H	Ar=	9.9%	71.0%(1:1.2)
c: $R=e^-$		>90%	<1% (1:0.8)

neutralization and esterification, however, the formation of the cyclopropane is almost completely eliminated and major product isolated was α-methoxyacetate (**3**).3) Similar irradiation of **1b** in the presence of 2 molar excess of triethylamine also resulted in the almost exclusive formation of the O-H insertion product.3)

Insertion-addition selectivities were calculated by means of the well-established equation of Doering and Henderson using the mole fraction of products and substrates and were listed in Table. Thus, the carbene derived from **1c** is shown to be some 3×10^3 times more reactive toward methanol relative to alkene than those from **1a** and **b**. Similar increase in the reactivity toward methanol caused by neighboring carboxylate group was also observed for the competition reaction using benzene. Moreover, similar dramatic effect of carboxylate group on the carbene reactivity was also observed when other nucleophiles, e.g., ethyl mercaptan or diethylamine was employed instead of methanol (Table).

What is the origin for the observed dramatic change in reactivity caused by neighboring carboxylate group? It is well documented in S_N reactions that the carboxylate group functions as a neighboring group participating the reaction while the carboxyl and ester groups lose a great deal of the effectiveness as a participant.1) Thus, it is quite tempting to assume that the neighboring carboxylate group can also interact with the vacant p orbital of singlet carbene, as depicted in **2c'**, and consequently alters its electronic nature. Such interaction should greatly reduce the electrophilicity of the carbene toward external reagents by suppressing freeness of its vacant p orbital. Simple alkene such as 2-butene and benzene are efficient trapping agents for many electrophilic carbenes, but not always reactive toward nucleophilic carbene.6) On the other

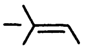
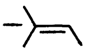
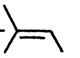


Scheme 1.

hand, methanol is shown to be equally reactive to both electrophilic and nucleophilic carbenes, since the former carbene can attack on the lone pair electron of oxygen while the latter undergoes protonation.[7)] Thus, carbenes derived from **1a** and **b** have ordinary electrophilic nature and therefore react with usual trapping agents for electrophilic carbene. Once carboxylate group is introduced, however, nonbonding interaction between the carboxylate and electron-deficient center on carbenic orbital results in suppression of freeness of its vacant p orbital and a carbene trends to behave as a nucleophile via the carbenic lone pair.

Alternative explanation is that carbene can be covalently bonded to the internal carboxylate group leading to anion (**2c"**) which undergoes protonation to give α-lactone (**5**). Subsequent nucleophilic cleavage of **5** by nucleophiles (X-H), e.g., MeOH, affords the formal X-H insertion product. It is quite interesting to note here in this connection that phosphonyl-carbene generated from α-diazophosphonate dianions in methanol actually undergoes intramolecular cyclization leading to oxaphosphirane intermediate.[8)] Subsequent nucleophilic attack on phosphorus by methanol is followed either by phosphorus-oxygen bond cleavage to give α-hydroxyphosphonate or by phosphorus-carbon cleavage leading to phosphate. No trace of α-hydroxyacetate (**6**) and carbonate (**7**), which were expected to be formed according to the above mechanism, were however detected in the present reaction mixture. This is not surprising since α-lactones generally undergo[9)] nucleophilic attack on the carbon adjacent to C=O group to give α-substituted acetate, e.g., **3**.

Table 1. Effect of Neighboring Carboxylate Group on the Reactivity of Arylcarbene

Diazo compd	Substrate A B	Relative reactivity k_A/k_B
1a	MeOH–	0.34
1a[a)]		0.35
1b		0.48
1c[b)]		>100
1c[c)]		>100
1a	MeOH-PhH[d)]	13
1c[c)]		>1000
1a	EtSH–	5.1
1c[c)]		>100
1a	$HNEt_2$–	5.6
1c[c)]		>100
1a	$HNEt_2$-PhH[d)]	60
1c[c)]		>1000

a) Methyl diazoacetate (**1a**) was irradiated in the presence of triethylamine.

b) Sodium p-nitrophenyl-α-diazoacetate. c) Diazoacetic acid (**1b**) + NEt_3.

d) Norcaradiene was formed.

Two control experiments were done in order to get more information about the exact nature of the intermediate. In the first, irradiation of **1c** was conducted in such electron-deficient alkenes as acrylonitrile or dimethyl fumarate. Analysis of the reaction mixture showed that no cyclopropanes which would be expected to be formed in the reaction of these alkenes with nucleophilic carbene (i.e., **2c'**) were formed. In the second experiments, **1c** was irradiated in non-degassed anhydrous benzene, followed by refluxing in methanol. Attempts to detect **3** in the reaction mixture were unsuccessful, although most α-lactones have been reported to polymerize in the absence of efficient trapping agents to give polyester (e.g., **11**) which undergoes methanolysis to yield α-methoxyacid (e.g., **3**). Instead, oxidative cleavage products, i.e., benzoic acid (**9**, 5.9%) and benzaldehyde (**10**, 4.2%) were detected. Since the intermediates generated by irradiation of neutral diazo compound (**1a** and **b**) were much less susceptible to the oxidation under similar conditions, the formation of these oxidative products can be interpreted as indicating the anionic nature of the intermediate involved in the photolysis of **1c**.

Thus, the present results clearly indicate that neighboring carboxylate group plays an important role as a participant also in carbene reaction and hence dramatically changes the reactivity of carbene. Although the exact nature of the intermediate is still not clear at present, the presently available data suggest that the intermediate would not be either "free" carbene (**2c**) or α-lactone (**5**). Presumable possibility is that the intermediate would be perturbed carbene (**2c'**) or lactone anion (**2c"**).

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2) See for recent review, K. G. Taylor, Tetrahedron, 38, 2751 (1982).
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