Mechanism of the Reaction of Methoxycarbonylcarbene as Revealed by CIDNP. V. Thermal Reaction of Methyl Diazoacetate with Benzyl Ethers

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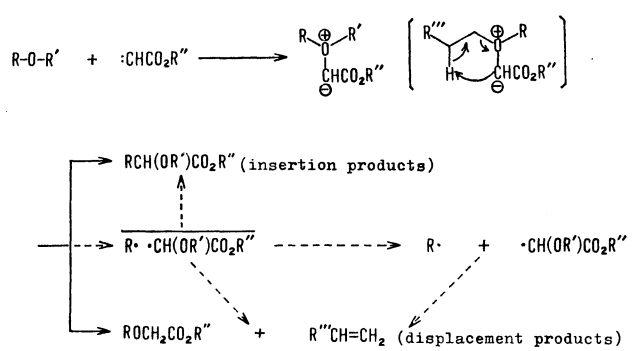
When methyl diazoacetate is allowed to react thermally with dibenzyl, benzyl phenyl and benzyl ethyl ethers, insertion into the benzylic carbon-oxygen bonds takes place *inter alia* to give $PhCH_2CH(OR)CO_2CH_3$(**3**, R=$PhCH_2$, Ph, and CH_3CH_2, respectively). Strongly polarized signals due to the insertion products **3** were observed in the ^1H and ^{13}C NMR spectra of the reacting mixture. Application of Kaptein's rules to the CIDNP signals demonstrates the formation of **3** by the cage recombination of radical pairs $\overline{PhCH_2\cdot\cdot CH(OR)CO_2CH_3}$ (**2**). Product analyses by VPC have also been performed and escape products toluene and $ROCH_2CO_2CH_3$ (**4**) inherent to the radical pairs were detected. In the reaction with benzyl ethyl ether, **4** (R=$PhCH_2$) without noticeable CIDNP is produced about six times more than **4** (R=CH_3CH_2). No methyl α-benzyloxybutyrate is formed. The results indicate that the ethyl group is more easily cleaved than the benzyl *via* a non-radical path. Formation of an ylide intermediate $(PhCH_2)RO\overset{\oplus}{-}\overset{\ominus}{C}HCO_2CH_3$ (**1**, R=CH_3CH_2) followed by the Hoffmann type β-elimination of ethylene is the most reasonable explanation. Homolysis of the same ylide **1** is considered to give the radical pair **2** (R=CH_3CH_2). A similar process appears to lead solely to radical pairs **2** (R=$PhCH_2$, Ph) in the case of ylides lacking β-hydrogen. The potentiality of this ylide mechanism in the reactions of ethers is discussed.

In contrast to nearly random insertion of methylene into various C–H bonds, the reaction of electrophilic alkoxycarbonylcarbene with ethers is characterized by two types of reactions, namely, the insertion reaction into the C–O bonds and the displacement reaction of one of the alkyl groups. There are several *a priori* mechanisms conceivable for these reactions. A widely quoted one is the electrophilic attack of the carbene at the lone pair of electrons to form an ylide intermediate which then undergoes the Stevens rearrangement and/or the Hoffmann type β-elimination of an olefin (Scheme 1). However, the experimental supports so far obtained for the mechanism are limited and not conclusive.[1)]

Recent mechanistic studies disclosed the mechanism of the Stevens rearrangement of ammonium and sulfonium ylides;[2)] it is not a simple ionic intramolecular process but a homolysis-recombination one. Accordingly radical pairs $\overline{R\cdot\ \cdot CH(OR')CO_2R''}$ might play an important role in the present case and the inserted and/or displaced products might be derived from recombination and/or disproportionation or hydrogen abstraction after diffusion (broken lines, Scheme 1).



Scheme 1.

In order to confirm these possibilities, we chose the CIDNP technique which is considered to provide direct verification of intermediacy of radical pairs for a particular product of interest. A minor preference was given to the ESR method by which we can prove the presence of radical species but can not obtain anything definite about the manifold reaction paths. Methyl diazoacetate was allowed to react with benzyl ethers in the heated NMR probe. Benzyl ethers were selected because of their simple NMR spectra and their high boiling points sufficient to generate the carbene thermally, in spite of the complexity of the reaction caused by the addition of the carbene to the aromatic ring. Standard product analyses by means of VPC were also made to determine the composition of the products.

Results

CIDNP Spectra. The 60 MHz proton NMR spectra obtained during the course of thermal decomposition of *ca.* 10 vol % solutions of methyl diazoacetate (MDA) in dibenzyl, benzyl phenyl, and benzyl ethyl ethers at 180 °C are shown in Figs. 1a, 1b, and 1c, respectively. A strong emissive signal (denoted by E) is seen in the δ 2.9—3.1 region in each ether solution. By comparison of the chemical shifts with those of authentic samples, these emission signals are assigned to the *C*-benzyl methylene protons (A_2 parts of approximately A_2X patterns) of insertion products, methyl α-benzyloxyhydrocinnamate (**3a**), α-phenoxyhydrocinnamate (**3b**), and α-ethoxyhydrocinnamate (**3c**). The large difference in intensity of the lower and higher field halves is due to the superposition of multiplet effect of E/A phase on net emission. The enhanced absorption singlet (denoted by A) at higher field is assigned to the methyl protons of toluene. In addition we see enhanced abosprtion at the shoulder on the high-field side of the benzylic methylene proton signals of the solvent (Fig. 1a) and the corresponding

TABLE 1. PRODUCT ANALYSES OF THE REACTIONS OF METHYL DIAZOACETATE WITH DIBENZYL, BENZYL PHENYL, AND BENZYL ETHYL ETHERS BY VPC

Types of products	Products	Yields (%) R=CH_2Ph	R=Ph	R=CH_2CH_3
Recombination	$PhCH_2CH(OR)CO_2CH_3$	6.9	2.7	9.4
	$RCH(OCH_2Ph)CO_2CH_3$	—	≪0.1	≪0.1
Escape	$PhCH_3$	2.8	0.6	2.1
	$ROCH_2CO_2CH_3$	3.1	0.2	0.9
Hoffmann-type	$PhCH_2OCH_2CO_2CH_3$	—	—	5.6
C-H insertion	$PhCH(OR)CH_2CO_2CH_3$	4.2	0.8	3.0
	$CH_3CH(OCH_2Ph)CH_2CO_2CH_3$	—	—	5.4
	$PhCH_2O(CH_2)_3CO_2CH_3$	—	—	1.6

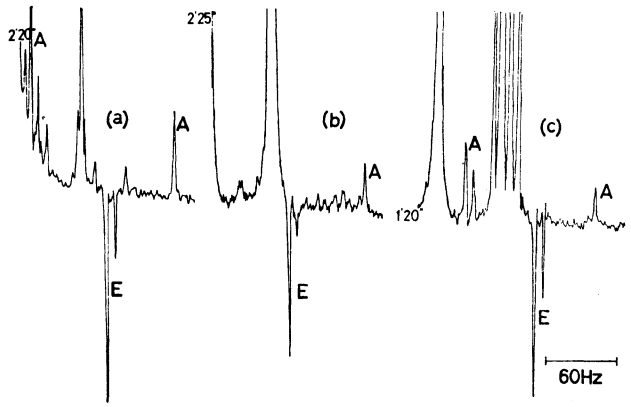


Fig. 1. The 60 MHz ^1H NMR spectra taken during thermal decomposition at 180 °C of *ca.* 10 vol% methyl diazoacetate in (a) dibenzyl ether, (b) benzyl ethyl ether, and (c) benzyl ethyl ether. The time when cw scanning of 600 Hz/200 s was started after insertion of the samples into the NMR probe is indicated.

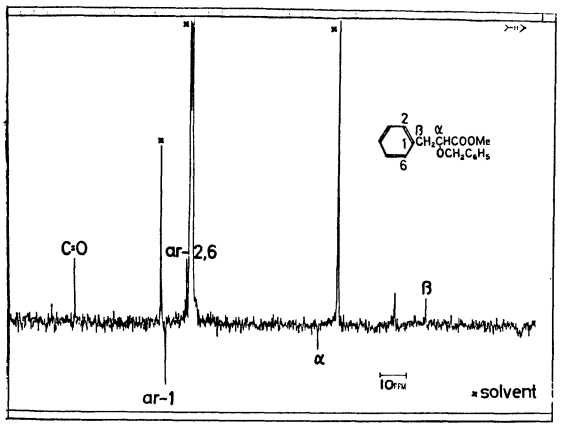


Fig. 2. The 20.1 MHz ^{13}C spectrum taken during the thermolysis at 170 °C of a 15 wt% solution of methyl diazoacetate in dibenzyl ether. The free induction decay signal was accumulated 1200 times on three portions of the batch solution.

enhanced absorption between the solvent signals (Fig. 1c). Their chemical shifts correspond to those of methine protons (X part of A_2X spins) of **3a** and **3c**. In the latter case, the lowest-field signal out of the triplet almost disappears as a result of the superposition of E/A multiplet effect. When the reactions are over,

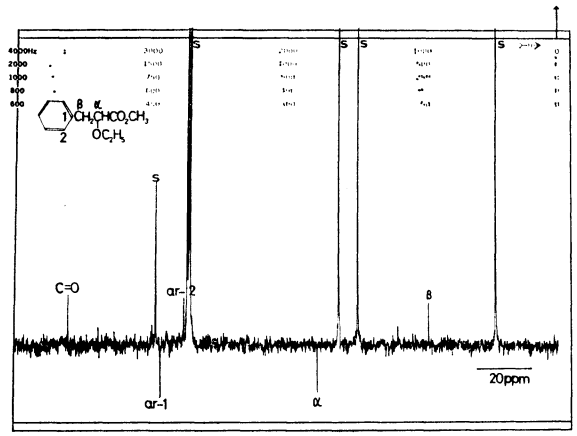


Fig. 3. The 20.1 MHz ^{13}C spectrum taken during the thermolysis at 170 °C of a 6 wt% solution of methyl diazoacetate in benzyl ethyl ether. The free induction decay signal was accumulated 2000 times on four portions of the batch solution. S denotes solvent signal.

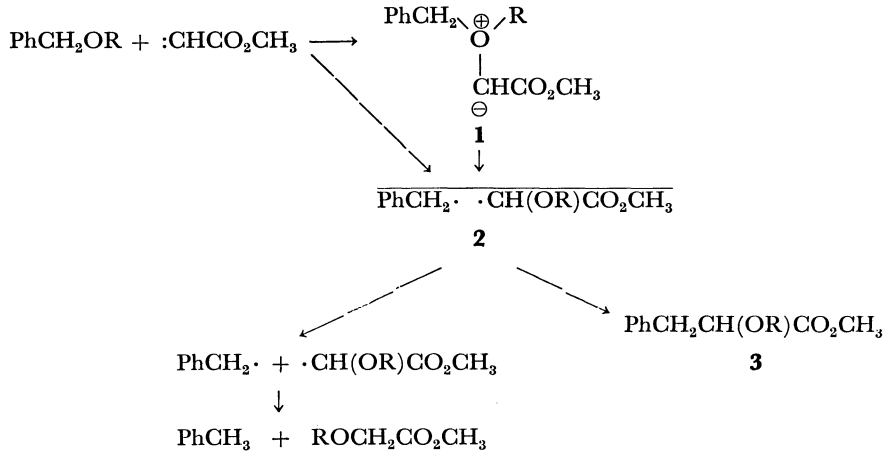
all the polarized signals collapse and nothing can be seen except those of the solvents unless the H_1 level and sensitivity of a spectrometer are increased.

The pulse Fourier transform ^{13}C spectra (20.1 MHz) taken during the course of thermolysis of MDA in dibenzyl and benzyl ethyl ethers are reproduced in Figs. 2 and 3, respectively. The spectra are time-averaged for *ca.* 800 s from 500 s after the start of the reaction (see Experimental). The emission signals at 10.8 and 68.5 ppm (down field from the benzylic carbon signal of solvent dibenzyl ether) are assigned to the α and aromatic C-1 carbon atoms of **3a** (Fig. 2). The enhanced absorption signals at −33.2, 56.9, and, 99.1 ppm are found to be due to the β, aromatic C-2 (C-6), and carbonyl carbon atoms of **3a**. Relativcly high intensity of polarized signals in spite of the low yield of **3a** (*vide infra*) as compared with those of solvent indicates a considerably large enhancement ($\sim 10^2$). The emission signals at 65.5 and 7.9 ppm (down field from the benzylic carbon signal of solvent benzyl ethyl ether) are due to aromatic C-1 and α-carbons of **3c** (Fig. 3). The enhanced absorption signals at 99.3, 56.8 and −33.1 ppm are assigned to the carbonyl, aromatic C-2 (C-6), and β-carbons, respectively, of **3c**.

Reaction Products. Table 1 shows the results of product analyses by VPC for the reaction of MDA in

Table 2. Theoretical and observed signs of CIDNP

Product	Nucleus	μ	ε	Δg	A_i	Signs	
						Theoret	Observed
$PhCH_2CHCO_2CH_3$ | OR	CH	−	+	+	−	A (+E/A)	A (+E/A)
	CH_2	−	+	−	−	E (+E/A)	E (+E/A)
	α-C	−	+	+	+	E	E
	β-C	−	+	−	+	A	A
	ar C-1	−	+	−	−	E	E
	ar C-2	−	+	−	+	A	A
	C=O	−	+	+	−	A	A
$PhCH_3$	CH_3	−	−	−	−	A	A



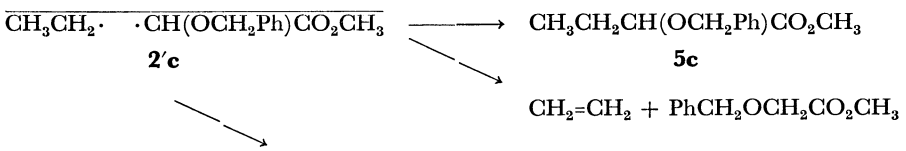
Scheme 2.

dibenzyl, benzyl phenyl, and benzyl ethyl ethers, respectively, at 170 °C for 1 h. The products are classified with respect to the type of reaction from which they were derived. All the possible C–H insertion products are formed in moderate yields.[3] The mass balance is not satisfactory since the main reaction of methoxycarbonylcarbene to give norcaradiene or cycloheptatriene derivatives *via* the addition to the aromatic rings is not taken into account. Peaks probably due to these products appear near or beyond the peaks due to the products analysed. Most values are accurate within 10%, some exceeding the limit because of the low yield and/or incomplete separation of the VPC peaks.

Discussion

All the spectral results are consistent with the formation of the singlet geminate radical pairs $\overline{PhCH_2\cdot\ \cdot CH(OR)CO_2CH_3}$ (**2**, **a**; R=$PhCH_2$, **b**; R=Ph, **c**; R=CH_3CH_2) followed by cage recombination to give the C–O insertion products **3**. The signs of net polarization (Γ_{ne}+ for absorption and−for emission) are given by $\Gamma_{ne}=\mu\varepsilon\Delta g A_i$ according to the first order treatment of Kaptein,[4] where μ, ε and A_i labels indicate the multiplicity of the precursor (−for singlet precursor), the type of the products (+for cage recombination) and the sign of hyperfine coupling of the nucleus i under consideration, respectively. Radicals $\cdot CH(OR)CO_2CH_3$ are assumed to have a *g*-value not far from 2.0036 of analgous radical $\cdot CH(OH)CO_2H$,[5] while the *g*-value of benzyl radical is 2.0025.[6] The methylene protons of insertion products **3**, for example, reside in the component of the pair which has a smaller *g*-value, their hyperfine coupling constant being negative (−16.3 gauss).[7] Their polarization is predicted to be emission when the insertion products are formed by the cage recombination (ε, +) of the singlet radical pair (μ, −). Similarly the polarization of the carbonyl carbons of **3** which are on the component with larger *g*-value of the radical pairs and possess negative hyperfine coupling constants[8] is considered to be an ehnanced absorption (Γ_{ne}=−−+−=+). The agreement between the theory and the observed signs of CIDNP is satisfactory (Table 2). There is no doubt about the intermediacy of radical pairs **2** for the formation of the insertion products.

The product distributions also support the above conclusion. Toluene and $ROCH_2CO_2CH_3$ (**4**) are formed in less than one fourth the amount of the insertion products **3** and are quite natural as escape products of radical pairs **2**. Their formation is difficult to justify by other routes. The observed enhanced absorption of the methyl protons of toluene is consistent with such a mode of formation (Table 2). Emission is expected for the methylene protons of $ROCH_2CO_2CH_3$ but can not be detected. The question is now where the radical pairs **2** come from.



Scheme 3.

Two alternatives are possible, namely, direct abstraction of an alkoxy group OR by the carbene or homolysis of the oxonium ylides **1** which in turn are formed by electrophilic attack of the carbene at the lone pair of electrons (Scheme 2). A clue to the proper selection can be found from Table 1.

Benzyl phenyl ether gives each type of products in fairly lower yields as compared with those of other ethers. The reduced reactivity corresponds to the lower nucleophilicity of the lone pair of electrons of the oxygen atom and to the higher reactivity at the aromatic rings of phenyl ethers. Actually the reactions of dichlorocarbene with phenoxides and anisoles at the ring give phenol aldehydes and tropone derivatives, respectively.[9] Products derived from insertion into the O–R bond ($R \neq CH_2Ph$) are not detected.

The yields of insertion products **3a** and **3c** do not differ much in dibenzyl and benzyl ethyl ethers. However, methyl benzyloxyacetate is formed in the latter nearly twice as much as in the former (Table 1). Methyl benzyloxyacetate is produced in a greater amount as compared with methyl ethoxyacetate (**4c**) in benzyl ethyl ether even if the lower yield of the latter than that of toluene may partly be an artefact.[10] The results indicate that the ethyl group is more easily cleaved than benzyl. The apparent cleavage of the benzyl group is actually due to diffusion of the radical pairs **2** (*vide supra*). However, cage disproportionation of radical pair $\overline{CH_3CH_2\cdot \cdot CH(OCH_2Ph)CO_2CH_3}$ (**2'c**) and/or hydrogen abstraction by $\cdot CH(OCH_2Ph)CO_2CH_3$ after diffusion from **2'c** (Scheme 3) can not be the origin of cleavage of the ethyl group for the following reasons.

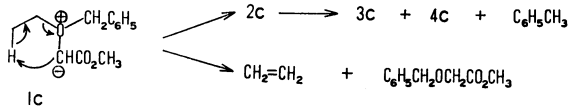
First of all, the cage recombination product methyl α-benzyloxybutyrate (**5c**) of the radical pair **2'c** is absent (*vide supra*). If **2'c** were formed, it could have recombined to give **5c** in a detectable amount as judged from the amount of the disproportionation and/or escape product, methyl benzyloxyacetate. The radical pair **2'c** is, therefore, considered not to be formed.

In order to find a rationale, let us have recourse to thermochemical data. From the standard heats of formation of radicals,[11] the dissociation energy of O–benzyl bond is estimated to be smaller by *ca.* 15 kcal/mol than that of the O–alkyl bond in benzyl alkyl ethers or benzyl dialkyl oxonium ions:

$$\begin{aligned} &D(PhCH_2\text{-}\overset{\oplus}{O}R_2) - D(PhCH_2R\overset{\oplus}{O}\text{-}R) \\ &\approx D(PhCH_2\text{-}OR) - D(PhCH_2O\text{-}R) \\ &= \Delta H_f^\circ(PhCH_2\cdot) + \Delta H_f^\circ(RO\cdot) - \Delta H_f^\circ(PhCH_2O\cdot) \\ &\quad - \Delta H_f^\circ(R\cdot) \\ &\approx -15\ \text{kcal/mol} \end{aligned} \quad (1)$$

The cleavage of the O–benzyl bond to give **2c** is, therefore, considered to be easier than that of the O–alkyl bond to give **2'c**, whether they occur at the same time with the attack of the carbene at oxygen or in oxonium ylide **1c**.

Secondly no CIDNP of methyl benzyloxyacetate and ethylene expected to arise in the cage disproportionation of **2'c** is observed. Thus, formation of the ylide intermediate **1c** followed by the Hoffmann type β-elimination of ethylene by a non-radical path gives a reasonable explanation for the easy cleavage of the ethyl group. Homolysis of the same ylide is considered to give the radical pair **2c** (Scheme 4).



Scheme 4.

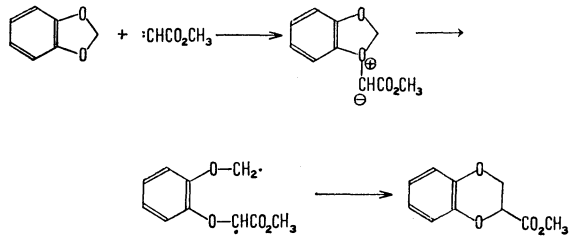
Similarly in dibenzyl and benzyl phenyl ethers the carbene attacks at oxygen to give ylide intermediates **1a** and **1b**. However, a possible path for their disappearance is restricted to the dissociation to the radical pairs **2a** and **2b**, respectively. Formation of methyl benzyloxyacetate in benzyl ethyl ether is only an additional pathway of dissipation of oxonium ylide which becomes available for **1c** because of the presence of hydrogen at β-carbon.

Path **1→3** is formally [1,2]sigmatropy to the anionic center. The process is forbidden as a concerted reaction with respect to orbital symmetry. Prior dissociation to radical pairs may be favored. The same rationale is widely used to explain the general radical nature of the Stevens rearrangement.[2] In contrast, path **1c** to methyl benzyloxyacetate *via* Hoffmann-type β-elimination of ethylene is formally [2,3]sigmatropy including anionic center. Six electrons are involved in a cyclic array of orbitals, the reaction being allowed as a concerted reaction. This may be the reason for the path being effectively competitive with path **1c→3c**.[12]

While chemical yields of the C–O insertion products are not necessarily high for the benzyl ethers, the insertion reaction is often of preparative value. The mechanistic information we obtained above together with the survey on the successful reaction types for insertion[1] reveal that there are three structural features governing the C–O insertion reaction.

Firstly it is small ring ethers which lead effectively to ring-enlarged products as a result of the C–O insertion of the carbene. Relief of the ring strain is considered to be responsible for the weak C–O bond. In contrast, displacement products and the corresponding olefins are almost exclusively formed in the case of acyclic ethers, especially when there are β-hydrogen

atoms available. In small ring ethers, the β-hydrogen atoms, if present, can not take part in conformation **1c** necessary for the displacement reaction. Lower steric demand for electrophiles of the oxygen atom in small ring ethers as compared to acyclic ethers should also be taken into account. There are many examples of higher reactivity or basicity of tetrahydrofuran when compared to diethyl ether.[13] Attempt to detect CIDNP for these high-yield insertion products of cyclic ethers has been unsuccessful. As an example the CH_2CH moiety of product **6**[14] appears in the δ 4.1—4.9 region as an approximate A_2X pattern, showing normal increase in its absorption signals during the course of formation in an NMR probe. The negative result does not necessarily rule out the homolysis-recombination mechanism of the intermediate oxonium ylide. Singlet 1,6-biradicals are formed instead of radical pairs. Exchange coupling between the unpaired electrons in **7** is estimated to be too large to allow the appearance of CIDNP.[15] On the other hand, internal recombination to give the C–O insertion product is expected to be efficient, resulting in a high yield of **6**.



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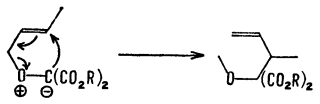
Secondly, a high yield of C–O insertion is found in allyl ethers. The C–O insertion is accompanied by allyl inversion as shown in the following.[1c]



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The transition state is aromatic with 6π electrons in a cyclic array of five atomic orbitals; the reaction is rationalized to be efficient.

Thirdly, phenyl ethers are disfavored with respect to reactivity to give insertion products. In addition to the enhanced reactivity at the aromatic ring and the β-elimination of the alkyl chain, if structurally possible, displacement of the methyl group takes place indicating the inertness of the C(aryl)–O bond towards carbene insertion.[16]

$$PhOCH_3 + :CHCO_2R \longrightarrow PhOCH_2CO_2R$$

Experimental

General Procedure for Measuring CIDNP Spectra. ^1H NMR spectra were measured on a Hitachi R-20B Spectrometer (60 MHz). Cw sweep of 200 or 400 s/600 Hz was employed. The pulse Fourier transform ^{13}C NMR spectra were obtained on a Varian CFT-20 spectrometer (20.1 MHz). The free induction decay signals, obtained by application of a short radio frequency pulse of 8 μs width, acquisition time of 1.023 s and 8K data points over the 4000 Hz spectral width, were accumulated a few thousand times on several portions of a batch solution (400—500 times for each portion). Pulse delay of 1 s was taken in the case of dibenzyl ether. As an internal lock, a capillary of dimethyl sulfoxide-d_6 was fixed concentrically at the center of a sample tube of 8 mm o.d. The reaction was started by introducing the sample tube containing *ca.* 5—15 wt or vol% solution of MDA in ethers to the NMR probe preheated at 170—180 °C. Under these conditions the half-life of MDA is less than 5 min. The assignment of the signals was made by comparison of their chemical shifts with those of the authentic samples under the experimental conditions.

VPC Analyses. VPC analyses were carried out on a Shimadzu GC-4A instrument equipped with an FID detector under nitrogen flow rate of 60 ml/min. A 3 m glass column of 4 mm i.d. packed with 10% polyethylene glycol 20 M on 60/80 mesh Uniport B and a 1.5 m glass column of the same diameter packed with 20% diethylene glycol stearate on 60/80 mesh Uniport B were used. The samples for VPC analyses were prepared separately from those for NMR study by heating the sample solutions in glass ampoules in an oil bath at 170 °C for a longer period (1 h) to ensure the completion of the reactions and to avoid the loss of low boiling materials. Molar ratios of dibenzyl, benzyl phenyl, and benzyl ethyl ethers to MDA were 12.9, 12.8, and 13.3, respectively. Identification of VPC components was carried out by comparison of the retention time with that of authentic samples. All the quantitative analyses were carried out by using an internal standard, bromobenzene in most cases. The C–H insertion product was not sufficiently separated from other components of unknown origin to determine the yield accurately, and the same detector response as for the corresponding C–O insertion product was assumed.

Starting Materials. Commercial dibenzyl and benzyl phenyl ethers were purified by distillation. Benzyl ethyl ether was prepared from benzyl chloride and ethanol by the standard method to give clear liquid; bp 183 °C (lit,[17] 189 °C). MDA was obtained by the same procedure as for the corresponding ethyl ester.[18]

Authentic Samples for Identification of Reaction Products. Methyl Benzyloxy-, Phenoxy- and Ethoxyacetates. Free acids were prepared according to literature[19-21] and esterified with methanol and sulphuric acid. Their boiling points are 112 °C/3 mmHg, 130 °C/5 mmHg (lit,[22] 245 °C) and 57—58 °C/29 mmHg (lit,[23] 148 °C/734 mmHg), respectively.

Most insertion products into the C–O or C–H bonds were prepared by the coupling of appropriate hydroxy and halogen compounds promoted by silver oxide.[24] The general procedure is as follows. To a water cooled mixture of 50 mmol of a hydroxy compound and 150 mmol of a halide was added portionwise 75 mmol of silver oxide under vigorous stirring. In some cases exothermic reactions took place. The mixture was gradually heated up to *ca.* 100 °C and maintained at the temperature for 6 h under stirring. Its color turned grey from black due to the formation of silver halide. With the aid of diethyl ether the solid was filtered off and the concentrated filtrate was chromatographed on silica gel with hexane–ether as an eluent. Further purification was performed by preparative TLC. 10—80% Yields were obtained based on hydroxy compounds. Reactants, bp's, NMR spectra, and the results of elemental analyses are summarized in Table 3.

Commercially unavailable reactants were prepared as follows. α-Hydroxyhydrocinnamic acid was prepared from phenylacetaldehyde[25] and esterified with methanol and

Table 3. Authentic samples prepared by the silver oxide-promoted alkylation of alcohols with halides ($ROH + R'X \xrightarrow{Ag_2O} ROR'$) and their boiling points, analytical and ^1H NMR data

ROR′	ROH	R′X	Bp (°C/mmHg)	NMR (CCl_4, δ)	Elemental analyses (%) Found C	Found H	Calcd C	Calcd H
$PhCH_2CH(OCH_2Ph)CO_2CH_3$	$PhCH_2CH(OH)CO_2CH_3$	$PhCH_2Br$	—	2.95(d, 2H), 3.61(s, 3H), 3.98(q, 1H), 4.40(ABq, 2H, J=15 Hz), 7.11(s, 10H)	75.63	6.60	75.53	6.71
$PhCH(OCH_2Ph)CH_2CO_2CH_3$	$PhCH(OH)CH_2CO_2CH_3$	$PhCH_2Br$	147/3	2.26—3.15(m, 2H), 3.59(s, 3H), 4.30 (ABq, 2H, J=12 Hz), 4.75(q, 1H), 7.18(s, 5H), 7.27(s, 5H)	75.77	6.94		
$PhCH(OPh)CH_2CO_2CH_3$	PhOH	$PhCHBrCH_2CO_2CH_3$	—	2.45—3.22(m, 2H), 3.63(s, 3H), 5.56 (q, 1H), 6.6—7.5(m, 10H)	74.68	6.37	74.98	6.29
$PhCH(OCH_2Ph)CO_2CH_3$	$PhCH(OH)CO_2CH_3$	$PhCH_2Br$	151/3	3.61(s, 3H), 4.51(ABq, 2H, J=12 Hz), 4.81(s, 1H), 7.0—7.6(m, 10H)	75.10	6.32		
$PhCH_2CH(OCH_2CH_3)CO_2CH_3$	$PhCH_2CH(OH)CO_2CH_3$	CH_3CH_2I	—	1.13(t, 3H, J=7 Hz), 2.90(d, 2H), 3.1—3.7(m, 2H), 3.61(s, 3H), 3.88 (q, 1H), 7.15(s, 5H)	69.47	7.81	69.31	7.74
$PhCH(OCH_2CH_3)CH_2CO_2CH_3$	$PhCH(OH)CH_2CO_2CH_3$	CH_3CH_2I	124/12	1.18(t, 3H, J=7 Hz), 2.18—2.93 (m, 2H), 3.33(q, 2H, J=7 Hz), 3.60 (s, 3H), 4.64(q, 1H), 7.24(s, 5H)	69.09	7.51		
$CH_3CH(OCH_2Ph)CH_2CO_2CH_3$	$CH_3CH(OH)CH_2CO_2CH_3$	$PhCH_2Br$	106/4	1.21(d, 3H), 2.16—2.78(m, 2H), 3.59 (s, 3H), 3.91(m, 1H), 4.45(s, 2H), 7.21(s, 5H)	69.04	7.79		
$CH_3CH_2CH(OCH_2Ph)CO_2CH_3$	$CH_3CH_2CH(OH)CO_2CH_3$	$PhCH_2Br$	106/5	0.8—1.1(m, 3H), 1.4—2.1(m, 2H), 3.67(s, 3H), 3.77(t, 1H), 4.46(ABq, 2H, J=12 Hz), 7.24(s, 5H)	69.10	7.69		

sulphuric acid to give methyl α-hydroxyhydrocinnamate, an oil, bp 99 °C/3 mmHg. Methyl β-hydroxyhydrocinnamate was obtained by the same procedure as for the corresponding ethyl ester.[26] Bromination with phosphorous tribromide gave methyl β-bromohydrocinnamate, an oil, bp 115 °C/4 mmHg. Reduction of methyl acetoacetate with sodium borohydride gave methyl β-hydroxybutyrate, an oil, bp 82 °C/26 mmHg. Propionaldehyde cyanohydrin prepared according to the method of Letch and Linstead[27] was hydrolyzed with concd hydrochloric acid. Esterification of the resulting acid with methanol and sulphuric acid gave methyl α-hydroxyburyrate, an oil, bp 58 °C/18 mmHg.

Methyl α-Phenoxyhydrocinnamate. To a stirred suspension of 50 mmol sodium phenoxide in 70 ml of benzene was added dropwise a solution of 50 mmol of methyl α-bromohydrocinnamate (an oil obtained by esterification of the free acid,[28] bp 100 °C/2.5 mmHg) in benzene, and the mixture was refluxed for 4 h. The cooled mixture was treated as usual and purified by column chromatography on silica gel and preparative TLC to give an oil, bp 144 °C/3 mmHg. NMR(CCl_4, δ); 3.15(d, 2H), 3.57(s, 3H), 4.41(t, 1H), *ca.* 6.2—6.7 (m, 5H), 7.18(s, 5H). Anal. Found: C, 75.63; H, 6.60. Calcd for $C_{17}H_{18}O_3$; C, 75.53; H, 6.71%.

Methyl γ-Benzyloxybutyrate. γ-Benzyloxybutyric acid was prepared by a procedure similar to that of Reppe *et al.*.[29] Esterification with diazomethane gave a clear oil, bp 112 °C/5 mmHg. NMR(CCl_4, δ): *ca.* 1.6—2.6(m, 4H), 3.44 (t, 2H, J=6 Hz), 3.58(s, 3H), 4.42(s, 2H), 7.22(s, 5H). Treatment of the ester with ammonia in a methanol gave the corresponding amide, mp 81—82 °C (benzene-cyclohexane). Anal. Found: C, 68.52; H, 7.97; N, 7.39%. Calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25%.

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