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Photolyses of [2-Substituted 2-(alkoxycarbonyl)propyl]cobaloximes

Masaru Tada,* Shiro Akinaga, and Masami Okabe

Department of Chemistry, School of Science and Engineering, Waseda University, Shinjuku-ku, Tokyo 160

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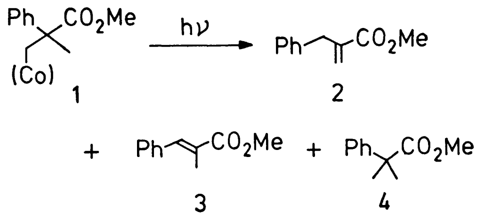
Synopsis. Photolysis of (2-methoxycarbonyl-2-phenylpropyl)cobaloxime (**1**) gives two phenyl-migrated products, methyl 2-methylene-3-phenylpropanoate and methyl *trans*-2-methyl-3-phenylpropenoate, and a hydrogen-abstracted product, methyl 2-methyl-2-phenylpropanoate. The alkoxycarbonyl groups do not migrate in the photolysis of either **1** or [2,2-bis(ethoxycarbonyl)propyl]cobaloxime.

Coenzyme B_{12}, 5′-deoxyadenosylcobalamin, is involved in 1,2-migration of the thioester group in an enzymatic system.[1] It is well known that organo-bis(dimethylglyoximato)(pyridine)cobalt(III), *R*-(Co) (organo-cobaloxime hereafter), is a good model compound of organo-cobalamin.[1] Photolysis of an organocobaloxime generates an organic radical and paramagnetic cobaloxime[2] which must be a reasonable mimicry of a pair of a substrate radical and paramagnetic cobalamin in an enzymatic system.[1]

In our previous studies[3,4] we photolyzed organocobaloximes having an acyl group at the *β*-position of the alkyl group attached to the cobalt atom, and observed acyl-migration in preference to alkyl, phenyl, and alkoxycarbonyl groups. This paper reports photolyses of [2-substituted 2-(alkoxycarbonyl)propyl]cobaloximes carried out to examine the migration ability of alkoxycarbonyl groups.

Results and Discussion

Photolysis of (2-methoxycarbonyl-2-phenylpropyl)cobaloxime (**1**) gave methyl 2-methylene-3-phenylpropanoate (**2**), methyl *trans*-2-methyl-3-phenylpropenoate (**3**), and methyl 2-methyl-2-phenylpropanoate (**4**) (Eq. 1); the results are summarized in Table 1.



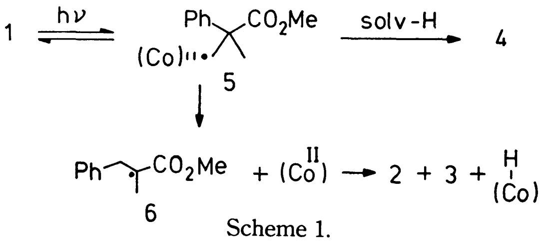
(1)

These results show that the phenyl group migrates in preference to the methoxycarbonyl group, and that no migration of the ester group takes place. The photolysis of **1** in chloroform is faster than in dichloromethane, which in turn is faster than in benzene. This indicates that the photolysis rate is dependent on the hydrogen-donating ability of the solvents. Since the formation of **2**, **3**, and **4** competes with the recombination of the radical pair **5** (Scheme 1), the faster rate of photolysis of **1** in chloroform is accounted for in terms of the faster hydrogen abstraction of **5**. The phenyl group migration is likewise competitive with the hydrogen abstraction. Thus, the photolysis of **1** in chloroform, a strong hydrogen donor,[5] gave only hydrogen-abstracted product **4**. On the other hand, the photolysis in benzene, having hardly any ability of hydrogen donation, gave only the phenyl-migrated products **2** and **3**.

Table 1. Photolysis of organo-cobaloxime 1

Solvent	Product yield/%[a)]		
	2	**3**	**4**
$CHCl_3$	Trace	0	84
CH_2Cl_2	21	15	30
C_6H_6	8	16	Trace

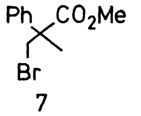
a) Yields after irradiation for 4 h (see Experimental section). Material balance was kept fairly well as examined on the basis of starting material.



Scheme 1.

The formation of the product having a methylene group is common in the photolysis of (2,2-disubstituted propyl)cobaloximes.[4] This is interpreted in terms of the steric hindrance on the hydrogen abstraction from **6** by cobaloxime(II).

The methoxycarbonyl group did not migrate in the reaction of the corresponding bromide **7** with tributyltin hydride. The reaction gave **4** and methyl 2-methyl-3-phenylpropanoate (**8**) formed by the radical migration of the phenyl group; **4** : **8**=77 : 23 (Bu_3SnH, 0.01 mol dm^{-3}) and 19 : 81 (Bu_3SnH, 0.001 mol dm^{-3}).



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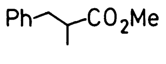

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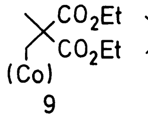

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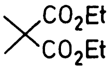

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The product composition depends on the concentration of tributyltin hydride, and this result shows that the direct hydrogen capture of the intermediate radical from tributyltin hydride competes with the radical rearrangement of the phenyl group.

Bildingmaier *et al.*[6] reported that the photochemical decomposition of [2,2-bis(ethoxycarbonyl)propyl]cobaloxime (**9**) gave diethyl methylsuccinate without reproducibility, *via* the migration of the ethoxycarbonyl group, and diethyl dimethylmalonate (**10**). However, we did not detect the migrated product in the photolyses of **9** after several trials even under the same conditions as reported by Bildingmaier *et al.*[6] On a photolysis of **9** in the same procedure as for the photolysis of **1** for

90 min, **9** gave **10** in 100% (chloroform), 82% (dichloromethane), 34% (ethanol), and 18% (acetonitrile) yields. The photolysis in benzene gave diethyl benzylmethylmalonate (**11**) in addition to **10** only in low yield. Material balance was kept fairly well as examined on the basis of the residual starting cobaloxime **9**. The rate of the photolysis thus depends on the hydrogen-donating ability of the solvent.[5)]

In conclusion the photolyses of [2-substituted 2-(alkoxycarbonyl)propyl]cobaloximes **1** and **9** cause no migration of the alkoxycarbonyl groups. The ester group seems to have the least or no ability for the radical rearrangement. Thus no ester group is any good mimicry of the (alkylthio)carbonyl group in methylmalonyl-CoA. Study on the migration property of the (alkylthio)carbonyl group is currently under way at our laboratory.

Experimental

The Preparation of Methyl 3-Bromo-2-methyl-2-phenylpropanoate (7). To a suspension of sodium hydride (55% oil dispersion) (1.86 g, 21.5 mmol) in 20 cm^3 of anhydrous 1,2-dimethoxyethane was added a solution of methyl 2-phenylproanoate (3.54 g, 21.5 mmol) in 5 cm^3 of anhydrous 1,2-dimethoxyethane under N_2. After the mixture had been refluxed for 5 h, excess dibromomethane (5 cm^3, 70 mmol) was added dropwise. The reaction mixture was refluxed for 15 h, cooled to room temperature, neutralized with acetic acid, and evaporated. After addition of water (50 cm^3) to the residue, the mixture was extracted with ether (50 cm^3×3). The combined etheral extracts were washed with water and dried over anhydrous sodium sulfate. After removal of the solvent the residue was distilled under reduced pressure to give 2.96 g (54%) of methyl 3-bromo-2-methyl-2-phenylpropanoate (**7**), bp 84—87 °C/1070 Pa. Found: C, 51.35; H, 5.11%. Calcd for $C_{11}H_{13}BrO_2$: C, 51.38; H, 5.10%. IR (CCl_4) 1740 and 699 cm^{-1}; ^{1}HNMR (CCl_4) δ=1.77 (s, 3H), 3.68 (d, 1H, J=10 Hz), 3.77 (s, 3H), 4.11 (d, 1H, J=10 Hz), and 7.50 (s, 5H).

The Preparation of (2-Methoxycarbonyl-2-phenylpropyl)cobaloxime (1). The organo-cobaloxime **1** was prepared from the bromide **7** (10 mmol) and cobaloxime (I) (15 mmol) in methanol (30 cm^3) in the conventional manner.[7)] Recrystallization from methanol yielded pure **1** (70%), mp 120 °C (decomp). Found: C, 53.09; H, 5.69; N, 12.67%. Calcd for $C_{24}H_{32}N_5O_6Co$: C, 52.85; H, 5.91; N, 12.84%. IR ($CHCl_3$) 1711, 1560, 1450, and 1084 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.67 (s, 3H), 1.86 (d, 1H, J=10 Hz), 1.97 (s, 6H), 2.03 (s, 6H), 2.75 (d, 1H, J=10 Hz), 3.63 (s, 3H), 7.30—7.65 (m, 7H), 7.78—8.00 (m, 1H), and 8.70—8.85 (m, 2H).

The Photolysis of the Organo-cobaloxime 1. A solution of the organo-cobaloxime **1** (6×10^{-3} mol dm^{-3}) in an appropriate solvent (see Table 1) was placed in a Pyrex tube and immersed in an ultrasonic bath with argon bubbling from a syringe needle for 30 min. The solution was then irradiated externally for 4 h with a 450-W high pressure Hg lamp mounted in a rotary irradiation apparatus (Rikosha RH-400), the distance between the lamp and the reaction tube being *ca.* 5 cm. The reaction mixture was condensed and the residue was placed on a Florisil column and eluted with chloroform to give methyl 2-methylene-3-phenylpropanoate (**2**),[8)] methyl *trans*-2-methyl-3-phenylpropenoate (**3**),[9)] and methyl 2-methyl-2-phenylpropanoate (**4**).[10)] Elution with chloroform–ethyl acetate (1 : 1) gave the residual starting organo-cobaloxime. The results are summarized in Table 1. The products **2**, **3**, and **4** were identified by comparison with authentic samples.

The Reaction of the Bromide 7 with Tributyltin Hydride. A mixture of tributyltin hydride (1.6 mmol), the bromide **7** (0.4 mmol), and AIBN (trace) in benzene (160 cm^3) was refluxed for 4 h under N_2. A concentrate of the reaction mixture was passed through a short column of silica gel with chloroform and further purified by preparative TLC (silica gel) using benzene. The products were **4** and methyl 2-methyl-3-phenylpropanoate (**8**) (**4** : **8**=77 : 23, 75% yield). The product **8** was identified by comparison with an authentic sample.[11)]

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