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ALKYLATION OF ETHYL BROMOMALONATE BY ALKYLCOBALOXIMES *

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Summary

Allylcobaloximes react under very mild conditions with ethyl bromomalonate to yield allyl-substituted ethylmalonates in good yield In the case of crotyl-, 3,3 dimethyl, allyl- and cinnamyl-cobaloximes, the substitution occurs with total rearrangement of the allyl groups Similar rearrangements are observed during the reactions of propargyl- and allenylcobaloximes with $BrCH(CO_2Et)_2$ yielding allenyl- and propargyl-malonic esters respectively

Introduction

Alkylcobaloximes $R—Co(DmgH)_2Py$ ** have recently been shown to react with organic compounds which are considered to be good radical precursors polyhaloalkanes [1], diphenyl disulphide [2], diphenyl diselenide [2] and alkylsulphonyl chlorides [3] These reactions give the products $R—CCl_3$, R—SPh, R—SePh and $R—SO_2—R'$ respectively, but their mechanisms are not fully understood. It has been proposed that they proceed by a chain radical mechanism (e.g. Scheme 1 for the diphenyldisulphide reaction [2])

Scheme 1

Initiation: $R—Co(DmgH)_2Py \xrightarrow[\text{or } \Delta]{h\nu} Co(DmgH)_2Py$ + Organic products

Propagation $Co(DmgH)_2Py + C_6H_5—S—S—C_6H_5 \rightarrow C_6H_5—S—Co(DmgH)_2Py + C_6H_5—S$

$C_6H_5—S + R—Co(DmgH)_2Py \rightarrow C_6H_5—S—R + Co(DmgH)_2Py$

The inversion of configuration observed during the reaction of diphenyldi-

* Dedicated to Prof. Henri Normant on the occasion of his 72nd birthday

** Alkylcobaloximes $RCo(DmgH)_2Py$ = bis(dimethylglyoximato) alkylpyridinecobalt (III)

sulphide with optically active 2-octylcobaloxime and the rate increase produced by visible light irradiation are in agreement with this mechanism

In the present paper, we describe the results obtained in a study of the reactions between various alkylcobaloximes and ethyl bromomalonate this compound can be easily reduced to the free malonyl radical by reducing organometallic complexes such as $Fe(CO)_5$ [4] or iron (II) porphyrins [5] and an a priori reaction mechanism leading to the alkylmalonic esters may be envisaged (Scheme 2).

Scheme 2

Initiation: $R—Co(DmgH)_2Py \rightarrow Co^{\cdot}(DmgH)_2Py$ + Organic products

Propagation. $Co(DmgH)_2Py + BrCH(CO_2Et)_2 \rightarrow BrCo(DmgH)_2Py + {}^{\cdot}CH(CO_2Et)_2$

$${}^{\cdot}CH(CO_2Et)_2 + R—Co(DmgH)_2Py \rightarrow R—CH(CO_2Et)_2 + Co(DmgH)_2Py$$

In the case of allylcobaloximes the reaction was expected to give allyl-substituted malonates with high regioselectivity, by analogy with the reaction with $BrCCl_3$ [1]

Results and discussion

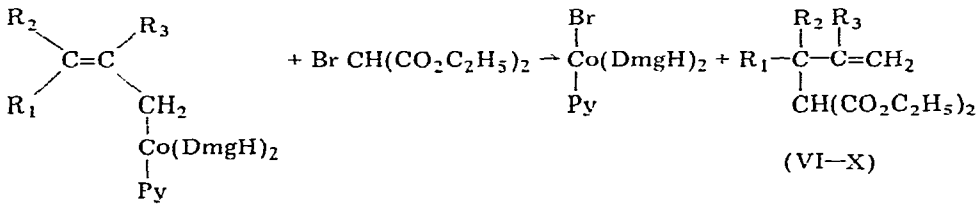
Reactions of allylcobaloximes with ethyl bromomalonate

Allylcobaloximes I to V react with ethyl bromomalonate in $CHCl_3$ at, or just above, room temperature to give ethyl allylmalonates VI to X (Scheme 3). Structures of the esters were assigned from their spectroscopic data, and the NMR spectra of esters VIII, IX and X in particular revealed the characteristic multiplets of a vinyl group $CH=CH_2$ · in the course of the reactions leading to these compounds there is a complete rearrangement of the allyl group initially present in the cobaloxime The allylmalonic esters are always accompanied by variable amounts of ethyl malonate but neither allylmalonic esters having an unrearranged allyl group nor products of diallylation could be detected. These results demonstrate the total regioselectivity of the reaction and are to be compared with those of Johnson et al. [1] for polyhaloalkanes

Crude yields of ethyl allylmalonates ranged between 50 and 80% and a study of the influence of temperature and of bromomalonate concentration was carried out with 3,3-dimethylallylcobaloxime IV in order to define the best experimental conditions. An increase in the reaction temperature (Table 1) from 20 to 60°C resulted in a decrease in the yield of ester IX. On the other hand, an increase of the ratio ethyl bromomalonate/complex IV gave an increase in the yield of ethyl malonate with respect to ester IX (Table 2). Thus the best yields of the latter compound were obtained by running the reaction at room temperature with equal concentrations of ethyl bromomalonate and allylcobaloximes

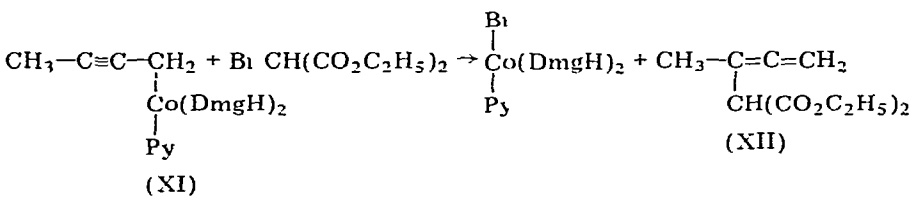
Irradiation of the reaction mixture with visible light from a tungsten lamp resulted in an increase of the reaction rate. For example compound IV is completely converted into a mixture of ester IX (69%) and ethyl malonate after 17

SCHEME 3

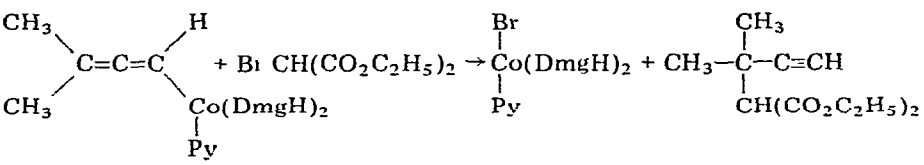


(I—V) (VI—X)

I, VI $R_1 = R_2 = R_3 = H$, II, VII $R_1 = R_2 = H$, $R_3 = CH_3$, III VIII $R_1 = R_3 = H$, $R_2 = CH_3$, IV, IX $R_1 = R_2 = CH_3$, $R_3 = H$, V, X $R_1 = R_3 = H$, $R_2 = C_6H_5$



(XI) (XII)



(XIII) (XIV)

TABLE 1

INFLUENCE OF TEMPERATURE ON THE YIELD OF ESTER IX IN THE REACTION OF COMPLEX IV (0 2 mmol) WITH ETHYL BROMOMALONATE (0 3 mmol) IN CHLOROFORM

Temp (°C)	Reaction time	Ester IX (%)	Ethyl malonate (%)
20	2 days	83	17
40	6 hours	75	25
60	30 min	70	30

TABLE 2

INFLUENCE OF THE CONCENTRATION OF ETHYL BROMOMALONATE ON THE YIELD OF ESTER IX IN THE REACTION WITH COMPLEX IV (0 2 mmol) IN CHLOROFORM AT 60°C

Concn of ethyl bromomalonate (mmol)	Ester IX (%)	Ethyl malonate (%)
0 2	70	30
0 4	68	32
0 6	66	33
0 8	64	35

h of irradiation at 0°C whereas at that temperature no reaction takes place in the absence of light

The most important by-product of these reactions is ethyl malonate which could be formed either (a) by reduction of the malonyl radical to malonate anion followed by protonation, or (b) by abstraction by the malonyl radical of a hydrogen atom from a suitable hydrogen donor (Scheme 4)

Scheme 4

$$BrCH(CO_2Et)_2 \xrightarrow{Co(DmgH)_2Py} BrCo(DmgH)_2Py + CH(CO_2Et)_2$$

$$CH(CO_2Et)_2 \xrightarrow[(a)]{+e^- +H^+} CH_2(CO_2Et)_2$$

$$CH(CO_2Et)_2 \xrightarrow[(b)]{+QH\ -\ Q} CH_2(CO_2Et)_2$$

In order to choose between these two possibilities, the reaction of complex IV with ethyl bromomalonate was carried out in deuterated methanol, CH_3OD Ethyl malonate from this reaction contained no deuterium, as shown by NMR spectroscopy, which is in favor of pathway (b) for the formation of ethyl malonate *

Reactions of propargyl- and allenyl-cobaloximes with ethyl bromomalonate

Reactions of cobaloxime (I) with propargyl halides lead, depending on their structures, either to allenyl- or to propargyl-cobaloximes [6]

3-Methylpropargylcobaloxime XI reacts with ethyl bromomalonate to give the allenylmalonic ester XII as major product Allenylcobaloxime XIII under the same conditions yields the propargylmalonic ester XIV. In all cases, irradiation with visible light produced an acceleration of the reaction As for allylcobaloximes, substitution of cobalt by the malonyl group occurs with complete rearrangement of the propargyl or allenyl group

Mechanism of the reactions between ethyl bromomalonate and allylcobaloximes

The similarity between the reactions described in this paper and the reactions of allylcobaloximes with $BrCCl_3$ [1] suggest identical mechanisms for these allyl transfer reactions Further support for the mechanism shown in Scheme 2 is provided by the following experimental data

(a) When the reaction between ethyl bromomalonate and complex IV was carried out at 60°C in the presence of the radical traps galvinoxyl- or tri-tert-butyl-phenol [8], decomposition of compound IV was observed but only traces of the allylmalonic ester IX were formed

(b) The first step of the propagation phase (Scheme 2) involves reaction between cobaloxime (II) and ethyl bromomalonate This reaction can be performed by preparing cobaloxime (II) in situ and adding ethyl bromomalonate

* The hydrogen donor QH is not $CHCl_3$ since no deuterium incorporation was observed when the reactions were carried out in $CDCl_3$.

One of the reaction products was bromocobaloxime ($BrCo(DmgH)_2Py$) (yield 36%) in agreement with the proposed mechanism

This mechanism rationalises most of the features of these reactions but does not account for the high regioselectivity observed with complexes III, IV and V A similar pathway can be envisaged for the reaction of allenyl- or propargylcobaloximes However, we have no experimental evidence for the formation, during thermolysis or photolysis of these compounds, of cobaloxime (II), the initiating entity of the chain mechanism, whereas such evidence does exist in the case of allylcobaloximes [9]

Conclusion

The results reported herein demonstrate the synthetic value of these reactions Several methods have been proposed to prepare allylmalonates which are important intermediates in the synthesis of barbiturates Allylation of sodium malonate by allyl halides has been widely used [10] and more recently other reactions, which involve transition metal salts or complexes, have been reported e g allylation of ethyl malonate by alkenes in the presence of Mn^{III} (or Co^{III}) and Cu^{II} salts [11], and nucleophilic attack of sodium malonate on π-allyl complexes of Ni^{II} [12] or Pd^{II} [13] These reactions give rise, in most cases, to mixtures in which the product having the most substituted double bond is predominant The reactions of allylcobaloximes with ethyl bromomalonate provide an alternative method of synthesis of allylmalonic esters and its interest lies in the possibility of preparing compounds in which the malonyl group is bound to secondary or tertiary carbon atoms

Experimental

Chemicals and instrumentation

Allyl-, allenyl- and propargyl-cobaloximes were known compounds which were prepared by treating pyridinecobaloxime (I) with allylic or propargylic halides from commercial sources Ethyl bromomalonate (Fluka), containing 6% ethyl malonate, was used without further purification Infrared spectra of reaction products were recorded neat with a Beckman Acculab 6 spectrophotometer ^1H NMR spectra at 90 MHz were measured with a Perkin—Elmer R-32 spectrometer in $CDCl_3$ solution containing 1% TMS Mass spectra were obtained with an AEI MS 50 spectrometer (ICSN - Gif-sur-Yvette, France)

General procedure for the reactions between ethyl bromomalonate and alkylcobaloximes

In a typical reaction, 1 mmol of alkylcobaloxime and 1 5 mmol of ethyl bromomalonate were added to 6 ml of degassed $CHCl_3$ in the dark The mixture was left at room temperature for 48 h under nitrogen and then passed through a column of Silica gel CC7. Elution by CH_2Cl_2 allowed a crude separation of the organic products. unreacted ethyl bromomalonate, ethyl malonate and ethyl allylmalonate from bromopyridinecobaloxime The reaction yields were deduced from the integration curve of the NMR spectra of the mixtures of organic products. Pure allyl, propargyl- and allenyl-malonates were obtained

either by chromatography on an alumina (activity 1) column (eluant hexane and hexane/ethyl acetate 95/5) or by preparative thin-layer chromatography on Silica gel (Merck F-254) (eluant hexane/ethyl acetate 1/1)

Photochemical reactions

0.2 mmol of alkylcobaloxime and 0 3 mmol of ethyl bromomalonate were dissolved in 0.7 ml degassed $CDCl_3$ in an NMR tube filled with N_2 and closed by a serum cap. The tube was irradiated in a Pyrex vessel cooled at 0° C, by two 300 W tungsten lamps The reactions were followed by measuring the NMR spectrum of the mixture at regular intervals

Ethyl allylmalonate (VI) (yield 50%) was identified by comparison of its NMR spectrum with that of an authentic sample and by its mass spectrum *m/e* 200 (M^+), 155, 127.

Ethyl (2-methyl) allylmalonate (VII) (yield 71%)· IR (cm^{-1}) ν(CH) 3040, ν(C=O) 1735, ν(C=C) 1650; NMR δ 4 79, 4 72 (2s, 2H, C=CH_2) 4 18 (q, 4H, O—CH_2), 3.53 (t, 1H, $CH(CO_2C_2H_5)_2$), 2 62 (d, 2H, CH_2—CH), 1.75 (s, 3H, CH_3—C=) and 1 27 ppm (t, 6H, O—CH_2—CH_3), mass spectrum *m/e* 214 (M^+), 159, 141, 55.

Ethyl (1-methyl) allylmalonate (VIII) (yield 60%)· IR (cm^{-1}) ν(CH) 3010, ν(C=O) 1730, ν(C=C) 1650, NMR. δ 5 83 (m, 1H, CH=C), 5 10 (m, 2H, CH_2=C), 4.22 (q, 4H, O—CH_2), 3 28 (d, 1H, $CH(CO_2C_2H_5)_2$), 2 95 (m, 1H, $CH(CH_3)$), 1 28 (t, 6H, O—CH_2—CH_3) and 1 12 ppm (d, 3H, CH_3(CH)), mass spectrum *m/e*: 214 (M^+), 169, 160, 141, 55

Ethyl (1,1-dimethyl) allylmalonate (IX) (yield 75%) IR (cm^{-1}) ν(CH) 3035, ν(C=O) 1740, ν(C=C) 1635; NMR· δ 6.08 (q, 1H, CH=C), 5.00 (m, 2H, CH_2=C), 4.16 (q, 4H, O—CH_2), 3.30 (s, 1H, $CH(CO_2C_2H_5)_2$), 1 26 (t, 6H, O—CH_2—CH_3) and 1 26 ppm (s, 6H, $(CH_3)_2C$); mass spectrum *m/e* 228 (M^+), 183, 160, 155, 69.

Ethyl (1-phenyl) allylmalonate (X) (yield 52%). IR (cm^{-1}) ν(CH) 3010, ν(C=O) 1725, ν(C=C) 1500, 1600, 1635, NMR. δ 7.22 (s, 5H, C_6H_5), 6 00 (m, 1H, CH=C), 5.10 (m, 2H, CH_2=C), 4 21 (q, 4H, O—CH_2), 3.85 (m 2H, —CH—CH—) and 1 27 ppm (t, 3H, O—CH_2—CH_3), mass spectrum *m/e* 276 (M^+), 203, 117, 91.

Ethyl (3-methyl) allenylmalonate (XII) (yield 70%). IR (cm^{-1}) ν(C=O) 1740, ν(C=C=C) 1960; NMR·δ 4.70 (m 8 lines, 2H, CH_2=C, J 1 6 Hz, J 3 Hz), 4 14 (q, 4H, O—CH_2), 4.01 (t, 1H, $CH(CO_2C_2H_5)_2$, J 1.6 Hz), 1.82 (t, 3H, CH_3—C; J 3 Hz) and 1 30 ppm (t, 6H, O—CH_2—CH_3), mass spectrum *m/e* 212 (M^+), 167, 139, 110, 65.

Ethyl (1,1-dimethyl) propargylmalonate (XIV) (yield 30%)· IR (cm^{-1})· ν(CH) 3105, ν(C=O) 1745; NMR·δ 4 22 (q, 4H, O—CH_2), 3 42 (s, 1H, $CH(CO_2C_2H_5)_2$), 2.19 (s, 1H, HC≡C), 1.46 (s, 6H, $(CH_3)_2C$) and 1.29 ppm (t, 6H, O—CH_2—CH_3), mass spectrum *m/e*: 226 (M^+), 181, 160, 153, 67

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