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REACTIONS OF ORGANOCOBALT COMPLEXES WITH BROMOESTERS: REGIOSPECIFIC SYNTHESIS OF ALLYL- AND CYCLOPROPYLMETHYL-SUBSTITUTED MALONIC AND ACETOACETIC ESTERS

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Summary

Allyl(pyridine)cobaloximes $RCo(dmgH)_2Py$ (R = allyl) react readily with diethyldibromomalonate, diethylbromomethylmalonate and ethyl 2-bromo-acetoacetate to give the corresponding allyl-substituted esters. Transfer of the allyl group occurs with complete rearrangement in all but one cases. Buten-3-yl(pyridine)cobaloximes react with diethylbromomalonate giving cyclo-propylmethylmalonic esters.

We previously reported the reaction of various alkyl(pyridine)cobaloximes $RCo(dmgH)_2Py$ * with diethyl bromomalonate, leading to the formation of alkyl-substituted malonic esters in good yields [1]. These reactions are closely related by their characteristics and probably also mechanistically to other reactions of alkylcobaloximes with other compounds which can be considered as good free-radical precursors: polyhaloalkanes [2], sulphonyl chloride [3], disulphides and diselenides [4]. Apart from their mechanistic aspects, which remain largely obscure, these reactions exhibit interesting features for synthetic organic chemistry. When R = allyl, allenyl or propargyl, the reaction with diethylbromomalonate led to products in which the unsaturated R group had completely rearranged, indicating preferred attack of the malonyl entity on the carbon γ to the cobalt atom. This regiospecificity, together with the very mild conditions used and the reasonable yields obtained, suggest that these reactions

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

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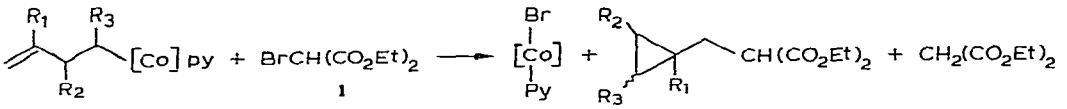
can have great synthetic utility. The purpose of this paper is to report extension of the reaction to other alkylcobaloximes, namely buten-3-ylcobaloximes, and to other bromodiesters and bromoketoesters.

Results and discussion

A — Reaction of buten-3-ylcobaloximes with diethyl bromomalonate

We have already shown that allyl-, allenyl-, and propargyl-cobaloximes readily react with $BrCH(CO_2Et)_2$, **1**, to give diethyl malonate substituted by allyl, propargyl and allenyl groups [1]. Buten-3-ylcobaloximes **2** to **5** also react with diethyl bromomalonate in $CHCl_3$ at 60° C to give organic products which were identified as the cyclopropylmethylmalonic esters **6** to **8** (Scheme 1). The



2, $R_1 = R_2 = R_3 = H$; 6
3, $R_1 = CH_3$, $R_2 = R_3 = H$; 7
4, $R_1 = H$, $R_2 = CH_3$, $R_3 = H$; 8a + 8b
5 $R_1 = R_2 = H$, $R_3 = CH_3$ 8a + 8b

Scheme 1

structures of these esters were assigned from their spectroscopic data. In particular, their NMR spectra exhibited the characteristic signals of cyclopropyl protons around $\delta = 0$ ppm. Compounds **4** and **5** react with $BrCH(CO_2Et)_2$ to give a mixture of two diastereoisomers, **8a** and **8b**: their NMR spectra show two doublets, at 0.33 and 0.28 ppm, which arise from the $CH—CH_3$ groups of the two isomers. The relative amounts of **8a** and **8b** are slightly different in the two reactions. It was not possible to deduce the precise geometry of **8a** and **8b** from the spectroscopic data available.

The only non-volatile product which was formed in detectable amounts in these reactions was diethyl malonate. There was no trace of malonic esters substituted by a buten-3-yl group, which demonstrates the total regiospecificity of these reactions. These results are comparable to those reported by Johnson et al. [5,6] for the reaction of butenylcobaloximes with $BrCCl_3$: in that case also the reaction products were cyclopropylmethyl derivatives resulting from the cyclisation of the buten-3-yl groups.

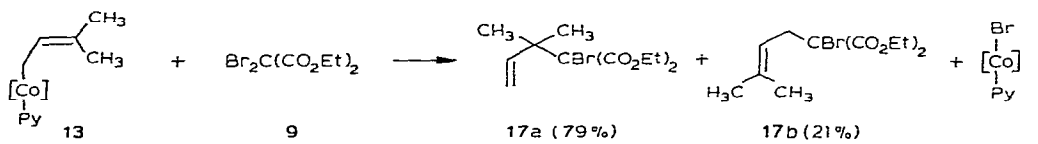
B — Reactions of allylcobaloximes with diethyl dibromomalonate, 9

Under the same experimental conditions, diethyl dibromomalonate, **9**, reacts rapidly with allylcobaloximes; the reaction products which are obtained depend on the amount of organocobalt complex used. With one equivalent of complex, malonic esters **14—17** were formed in reasonable yields (Scheme 2). Only negligible amounts of diallylmalonic esters were produced. With crotylcobaloxime **11**, the reaction occurred with total rearrangement of the crotyl group, leading to ester **15**. However, the reaction with 3,3-dimethylallylcobaloxime **13** did not prove to be very regiospecific, as it gave rise to a mixture of

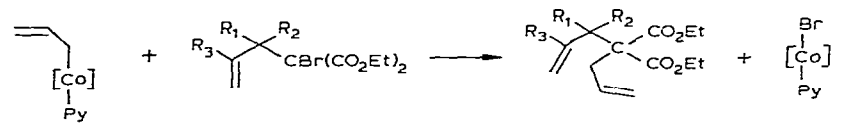
the two esters **17a** and **17b** in a ratio of 4/1 (total yield: 57%), the major product having the rearranged allylic substituent. The lack of regiospecificity observed in that case can be explained in terms of steric factors; the attack of the bulky bromomalonyl group on the γ carbon atom which bears two methyl substituents becomes slow so that the attack on the less hindered α carbon atom can compete with it.

Allylbromomalonic esters **14** and **15** react with another equivalent of allylcobaloxime **10** to give the malonic esters **18** and **19**, respectively, in which C(2) is substituted by two identical or non-identical allyl groups (Scheme 2).

10, $R_1 = R_2 = R_3 = H$; 9; 14
11 $R_1 = CH_3$, $R_2 = R_3 = H$; 15
12 $R_1 = R_2 = H$, $R_3 = CH_3$ 16



13 9 17a (79%) 17b (21%)

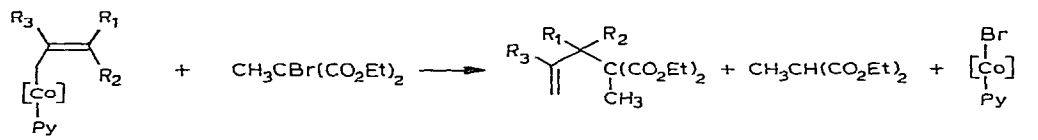


10 14, $R_1 = R_2 = R_3 = H$ 18
15, $R_1 = R_2 = H$, $R_3 = CH_3$ 19

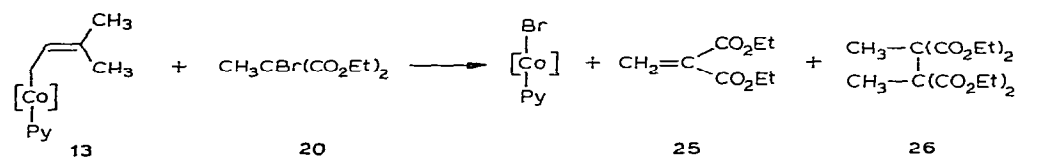
SCHEME 2

C — Reaction of allylcobaloximes with diethyl methylbromomalonate, 20

Using the same conditions, we observed reactions between diethyl 2-methyl-2-bromomalonate, **20**, and allylcobaloximes **10—12**, leading to the corresponding allylmethylmalonic esters **21—23** (Scheme 3). The reaction with



10, $R_1 = R_2 = R_3 = H$ 20 21 24
11, $R_1 = CH_3$, $R_2 = R_3 = H$ 22
12, $R_1 = R_2 = H$, $R_3 = CH_3$ 23



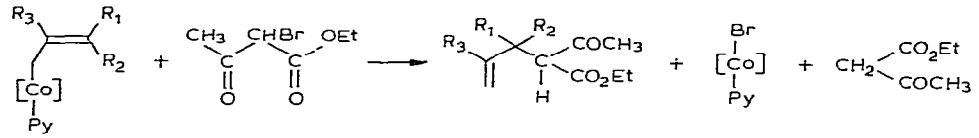
13 20 25 26

SCHEME 3

crotylcobaloxime, 11, occured with the same regiospecificity as that with monobromo- and dibromo-malonates. The only other product which was formed was diethyl methylmalonate, 24. It is interesting to note that no allylation of the methylmalonic ester was observed when 3,3-dimethylallylcobaloxime, 13, was used, and instead a mixture of esters 25 and 26 was obtained. This can be attributed to the bulkiness of both reagents.

D — Reactions of allylcobaloximes with ethyl 2-bromoacetoacetate, 27

Ethyl 2-bromoacetoacetate, 27, was prepared cleanly and in good yield by bromination of ethyl acetoacetate by *N*-bromosuccinimide. Reaction of 27 with the two allylcobaloximes 10 and 13 under standard conditions ($CHCl_3$ solvent, 60°C) lead to the corresponding allyl-substituted acetoacetic esters 28 and 29 (Scheme 4). With 13, the reaction again occured with complete isomer-



10, $R_1 = R_2 = R_3 = H$ 27 28 30

13, $R_1 = R_2 = CH_3$, $R_3 = H$ 29

SCHEME 4

isation of the 3,3-dimethylallyl group. The only by-product formed was ethyl acetoacetate, 30. No *O*-allylation product was observed.

Conclusion

The results demonstrate that allylcobaloximes readily react with a variety of bromodiesters or bromoketoesters to give products in which the bromine atom has been replaced by allyl groups, total rearrangement of the allyl group being observed as a rule. The good yields obtained in most cases and the regiospecificity of these reactions demonstrate the synthetic utility of these reactions; in particular they seem of interest for the synthesis of malonic esters or acetoacetic esters substituted by secondary or tertiary allyl groups which are practically impossible to make by the classical synthetic methods [7].

Further studies are in progress in our laboratory to extend these allylations to other organic molecules which can be considered as good free radical precursors and also to obtain deeper insight into the mechanism of the reactions.

Experimental

Allyl- and buten-3-yl-cobaloximes were prepared by published methods [8]. Commercial (Fluka) diethyl 2-bromomalonate containing 6% diethyl malonate was used without further purification. Diethyl 2,2-dibromomalonate was prepared according to Teichmann and al. [9].

IR spectra were measured in chloroform solution on a Beckman Acculab 5 spectrophotometer. ^1H NMR spectra were obtained at 90 MHz on a Perkin-Elmer R-32 spectrometer using $CDCl_3$ as solvent and TMS as internal reference. Mass spectra were measured on a Hewlett Packard instrument.

Ethyl 2-bromoacetoacetate

To a solution of 0.1 mol of ethyl acetoacetate in 10 ml of acetone, 0.1 mol of *N*-bromosuccinimide was added slowly at room temperature. The mixture was stirred for 15 minutes with careful control of the temperature. After removal of succinimide by filtration, the solvent was removed under vacuum and the remaining solid was washed several times with hexane. The hexane extract was washed with water to remove HBr, and evaporated under vacuum to leave an oily residue (yield 76%). This oil (which was homogeneous by GLC and NMR) was distilled under reduced pressure.

$B.p._{0.3}$ = 50—53°C. Lit. [10] $B.p._{0.5}$ = 72°C. IR (cm^{-1}): ν(C—H) 2980, ν(C=O) 1710, ν(C—Br) 540. NMR: δ 4.77 (s, 1 H, C*H*Br), 4.28 (q, 2 H, OCH_2CH_3), 2.41 (s, 3 H, CH_3CO) and 1.3 ppm (t, 3 H, OCH_2CH_3). Mass spectrum (*m/e*): 208, 206 (M^+), 43.

General procedure for the reactions between alkylcobaloximes and bromoesters

In a typical reaction, 1 mmol of alkylcobaloxime and 1.5 mmol of bromoester were added to 6 ml of degassed $CHCl_3$ in the dark. The solution was warmed at 60°C. The mixture was chromatographed on a silica gel CC7 column. Elution by CH_2Cl_2 gave a crude separation of the organic products from bromo(pyridine)cobaloxime. Pure products were obtained by chromatography on an alumina (activity 1) column (eluant: hexane/ethylacetate 95/5).

Diethyl cyclopropylmethylmalonate, 6. (Yield 12%, reaction time 21 h): IR (cm^{-1}): ν(C—H) 2990, 2960, ν(C=O) 1720; NMR: δ 4.22 (q, 4 H, OCH_2CH_3), 3.47 (t, 1 H, $CH(CO_2Et)_2$), 1.83 (t, 2 H, CH_2CH) 1.30 (t, 6 H, OCH_2CH_3), 0.75 (m, 1 H, cyclopropane) and 0.11—0.47 ppm (m, 4 H, cyclopropane); mass spectrum (*m/e*): 215 (*M* + 1), 160, 141, 115, 87, 55, 41.

Diethyl (1-methylcyclopropyl)methylmalonate, 7. (Yield 74%, reaction time 27 h): IR (cm^{-1}): ν(C—H) 3000; ν(C=O) 1710; NMR: δ 4.22 (9, 4 H, OCH_2CH_3), 3.58 (t, 1 H, $CH(CO_2Et)_2$), 1.98 (d, 2 H, CH_2CH), 1.32 (t, 6 H, OCH_2CH_3), 1.08 (s, 3 H, CH_3cyclopropane) and 0.32 ppm (d, 4 H, cyclopropane); mass spectrum (*m/e*): 228 (M^+), 160, 55, 41.

Diethyl (2-methylcyclopropyl)methylmalonate, 8a + 8b. (Yield 83%, reaction time 21 h, ratio 8a/8b = 3/1 (from 4)) IR (cm^{-1}); ν(C—H) 2950, 2920, ν(C=O) 1720, NMR: δ 4.22 (q, 4 H, OCH_2CH_3), 3.43 (t, 1 H, $CH(CO_2Et)_2$), 1.83 (t, 2 H, CH_2CH), 1.30 (t, 6 H, OCH_2CH_3), 1.01, 1.09 (d, 3 H, CH_3cyclopropane *cis* and *trans*) and —0.21 to 0.9 ppm (m, 5 H, CH cyclopropane); mass spectrum (*m/e*); 228 (M^+), 160, 155, 87, 55. The same products 8a and 8b (yield 71%, reaction time 21 h, ratio 8a/8b = 7/3) were obtained from 5.

Diethyl 2-bromo,2-allylmalonate, 14. (Yield 81%, reaction time 20 minutes): IR (cm^{-1}): ν(C—H) 2980, ν(C=O) 1730, ν(C=C) 1635, ν(C—Br) 630; NMR: δ 5.82 (m, 1 H, $CH=CH_2$), 5.19 (m, 2 H, $CH=CH_2$), 4.33 (q, 4 H, OCH_2CH_3), 3.01 (d, 2 H, CH_2CH) and 1.29 ppm (t, 6 H, OCH_2CH_3); mass spectrum (*m/e*): 199, 153, 125, 53, 29.

Diethyl 2-bromo,2(1-methylallyl)malonate, 15. (Yield 74%, reaction time 20 minutes) IR (cm^{-1}): ν(C—H) 2990, ν(C=O) 1730, ν(C=C) 1640, ν(C—Br) 650; NMR: δ 5.90 (m, 1 H, $CH=CH_2$), 5.13 (m, 2 H, $CH_2=CH$), 4.25 (q, 2 H, OCH_2CH_3), 3.10 (m, 7 lines, 1 H, $CHCH_3$), 1.29 (t, 6 H, OCH_2CH_3) and 1.22 ppm (d, 3 H, CH_3CH); mass spectrum (*m/e*): 240, 238, 213, 212, 210, 167, 121.

Diethyl 2-bromo,2(2-methylallyl)malonate, 16. (Yield 77%, reaction time 5 h) IR (cm^{-1}): ν(C—H) 2990, ν(C=O) 1730, ν(C=C) 1640, ν(C—Br) 640; NMR: 4.91 (m, 2 H, CH_2=C), 4.29 (q, 4 H, OCH_2CH_3), 3.08 (s, 2 H, CH_2CBr), 1.79 (s, 3 H, CH_3C=C) and 1.29 ppm (t, 6 H, OCH_2CH_3).

Diethyl 2-bromo,2(1,1-dimethylallyl)malonate, 17a. (Yield 45%, reaction time 1 h) IR (cm^{-1}): ν(C—H) 2990, ν(C=O) 1735, ν(C=C) 1640, ν(C—Br) 650; NMR: δ 6.37 (m, 1 H, CH=C), 5.12 (m, 2 H, CH_2=C), 4.27 (q, 4 H, OCH_2CH_3), 1.42 (s, 6 H, $(CH_3)_2C$) and 1.25 ppm (t, 6 H, OCH_2CH_3); mass spectrum (*m/e*): 293, 291, 240, 238, 69.

Diethyl 2-bromo,2(3,3-dimethylallyl)malonate, 17b. (Yield 12%, reaction time 1 h) IR (cm^{-1}): ν(C—H) 2990, ν(C=O) 1735, ν(C=C) 1640, ν(C—Br) 650; NMR: δ 4.88 (m, 1 H, CH=C), 4.27 (q, 4 H, OCH_2CH_3), 3.03 (m, 2 H, CH_2CBr), 1.69 (d, 6 H, $(CH_3)_2C$=), and 1.25 ppm (t, 6 H, OCH_2CH_3); mass spectrum (*m/e*): 293, 291, 240, 238, 69.

Diethyl diallylmalonate, 18. (Yield 80%, reaction time 4 h) IR (cm^{-1}): ν(C—H) 2950, 2920, ν(C=O) 1720, ν(C=C) 1630; NMR: δ 5.71 (m, 2 H, CH=C), 5.14 (m, 4 H, CH_2=C), 4.21 (q, 4 H, OCH_2CH_3), 2.65 (d, 4 H, CH_2-CH=) and 1.24 ppm (t, 6 H, OCH_2CH_3); mass spectrum (*m/e*): 199, 167, 41.

Diethyl 2-allyl,2(2-methylallyl)malonate, 19. (Yield 95%, reaction time 1 h) IR (cm^{-1}): ν(C—H) 2950, 2920, ν(C=O) 1720, ν(C=C) 1640; NMR: δ 5.73 (m, 1 H, CH=CH_2), 5.10 (m, 2 H, CH_2=CH), 4.82 (m, 2 H, CH_2=C), 4.17 (q, 4 H, OCH_2CH_3), 2.70 (s, 2 H, CH_2CCH_3), 2.67 (d, 2 H, CH_2CH), 1.67 (s, 3 H, CH_3-C=C) and 1.24 ppm (t, 6 H, OCH_2CH_3).

Diethyl 2-methyl,2-allylmalonate, 21. (Yield 79%, reaction time 5 h) IR (cm^{-1}): ν(C—H) 3000, ν(C=O) 1720, ν(C=C) 1640; NMR: δ 5.72 (m, 1 H, CH=C), 5.13 (m, 2 H, CH_2=C), 4.16 (q, 4 H, OCH_2CH_3), 2.62 (d, 2 H, CH_2C=), 1.31 (s, 3 H, CH_3) and 1.24 (t, 6 H, OCH_2CH_3).

Diethyl 2-methyl,2(1-methylallyl)malonate, 22. (Yield 37%, reaction time 1 h) IR (cm^{-1}): ν(C—H) 2980, ν(C=O) 1720, ν(C=C) 1680; NMR: δ 5.85 (m, 1 H, CH=C), 5.09 (m, 2 H, CH_2=C), 4.20 (q, 4 H, OCH_2CH_3), 2.94 (m, 1 H, $CHCH_3$), 1.35 (s, 3 H, CH_3), 1.25 (t, 6 H, OCH_2CH_3) and 1.08 ppm (d, 3 H, CH_3CH); mass spectrum (*m/e*): 183, 174, 155, 137, 128, 55.

Diethyl 2-methyl,2(2-methylallyl)malonate, 23. (Yield 52%, reaction time 1.5 h) IR (cm^{-1}): ν(C—H) 2990, ν(C=O) 1720, ν(C=C) 1640; NMR: δ 4.79 (m, 2 H, CH_2=C), 4.17 (q, 4 H, OCH_2CH_3), 2.69 (s, 2 H, CH_2C=C), 1.67 (s, 3 H, CH_3C=C), 1.40 (s, 3 H, CH_3) and 1.24 ppm (t, 6 H, OCH_2CH_3), mass spectrum (*m/e*): 228 (M^+), 183, 155, 55.

Ethyl 2-allylacetoacetate, 28. (Yield 36%, reaction time 30 min) IR (cm^{-1}): ν(C—H) 3000, 2950, ν(C=O) 1740, 1700, ν(C=C) 1630; NMR: δ 5.76 (m, 1 H, CH=C), 5.10 (m, 2 H, CH_2=C), 4.29 (q, 2 H, OCH_2CH_3), 3.38 (t, 1 H, $CHCH_2$) 2.53 (t, 2 H, CH_2C=), 2.15 (s, 3 H, CH_3C=O) and 1.27 ppm (t, 3 H, OCH_2CH_3).

Ethyl 2(1,1-dimethylallyl)acetoacetate, 29. (Yield 47%, reaction time 1 h) IR (cm^{-1}): ν(C—H) 3000, 2960, ν(C=O) 1740, 1700, ν(C=C) 1630; NMR: δ 6.06 (m, 1 H, CH=C), 5 (m, 2 H, CH_2=C), 4.16 (q, 2 H, OCH_2CH_3), 3.42 (s, 1 H, CHC), 2.17 (s, 3 H, CH_3C=O), 1.25 (t, 3 H, OCH_2CH_3) and 1.20 ppm (s, 6 H, CH_3); mass spectrum (*m/e*): 169, 130, 87, 85, 45, 43, 41.

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