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Cobaloximes. Part 2.[1] A Modified Schrauzer Synthesis for Base-sensitive Cobaloximes

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The generation of a cobaloxime(I) anion in dimethyl sulphoxide provides a clean, non-aqueous reagent of low basicity particularly useful for the synthesis of base-sensitive cobaloximes. The method has been applied to the synthesis of esters of (2,2-dicarboxypropyl)cobaloximes and their monothio-analogues.

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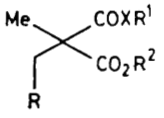
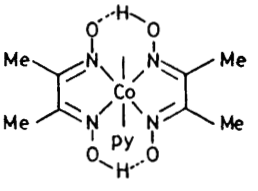
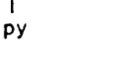
THE coenzyme-B_{12}-catalysed rearrangement of methylmalonylcoenzyme A to succinylcoenzyme A by methylmalonylcoenzyme A mutase is still poorly understood. A number of models for this rearrangement have been reported [2] but the exact nature of the process has not been determined. In an attempt to gain some insight into the reaction, we have synthesised a number of esters and thioesters (1) of (2,2-dicarboxypropyl)(pyridine)cobaloxime.† The preparation of these necessitated the development of a modified cobaloxime synthesis, since the strongly basic conditions of the conventional Schrauzer approach [3] caused decomposition of the malonyl functions. This paper reports the details of the new method. An alternative modification using sodium borohydride in dimethylformamide has recently been reported.[4]



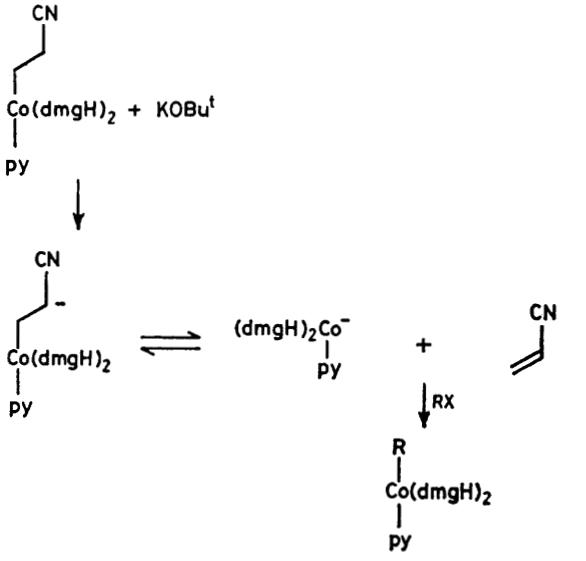
(1) R =  = 

(2) R = I

(7) a; R = OSO_2Me, $R^1 = R^2 = PhCH_2$, X = O
b; R = $OSO_2C_6H_4Me$-*p*, $R^1 = R^2 = PhCH_2$, X = O

The Schrauzer synthesis of cobaloximes involves the use of aqueous methanolic solvent at high pH. In order to avoid this we sought to generate the cobalt anion cleanly in a dipolar aprotic solvent. The method which finally proved most successful was to use the reversibility of the addition of a cobaloxime(I) anion to acrylonitrile (Scheme 1).[5] Thus, 2-cyanoethyl(pyridine)cobaloxime in dimethyl sulphoxide was treated with 1.1 equiv. of freshly sublimed potassium t-butoxide. The equilibrium mixture was swept with a vigorous stream of nitrogen and the t-butyl alcohol and acrylonitrile were collected in a cold trap. Removal of the volatile components was

† (2,2-Dicarboxypropyl)bis(dimethylglyoximato)pyridinecobalt(III).



SCHEME 1

complete in *ca.* 10 min. The resulting red solution of the potassium cobaloxime(I) salt in dimethyl sulphoxide was treated with 1—4 equiv. of the organic halide (quantity depending on the reactivity of the halide), and the reaction mixture was quenched with acetate buffer at pH 6. Conventional work-up gave cobaloximes in moderate (47—59%) yield (see Table). For simple alkyl halides

Synthesis of alkyl(pyridine)cobaloximes

Run no.	Alkylating agent	Equiv.	Yield (%)
1	CH_3I	2	55
2	CH_2I_2	1.2	58
3	$PhCH_2Br$	2.0	47
4	$PhCOCH_2Br$	2.0	59
5	cyclo-$C_6H_{11}Br$	4.0	58
6	$(EtO_2C)_2C(Me)CH_2I$	2.0	57
7	$(BuSCO)(EtO_2C)C(Me)CH_2I$	1.0	50
8	$(PhCH_2O_2C)_2C(Me)CH_2OTs$	1.3	0
9	$(PhCH_2O_2C)_2C(Me)CH_2OMs$	2.2	22 [a]
10	$(PhCH_2O_2C)_2C(Me)CH_2I$	1.0	35
11	$(t\text{-}BuO_2C)_2C(Me)CH_2I$	1.2	52

[a] The product was benzyl(pyridine)cobaloxime.

(runs 1—5), the technique is not better than the Schrauzer method and is more cumbersome, but there are distinct advantages for base-sensitive substrates (see later).

The iodomethylmalonates (3) required were synthes-

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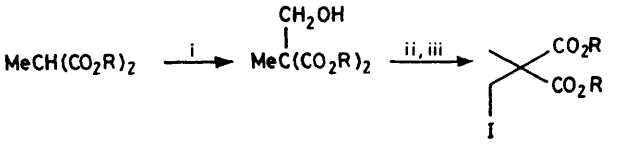
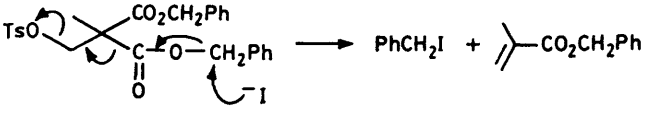
ised unexceptionally as depicted in Scheme 2. The esters (3; R = Et, $PhCH_2$, or CMe_3) were prepared from the corresponding methylmalonates *via* hydroxymethylation,[6] tosylation of the hydroxy-group and displacement of tosylate with iodide ion. In the case of the dibenzyl



(3)

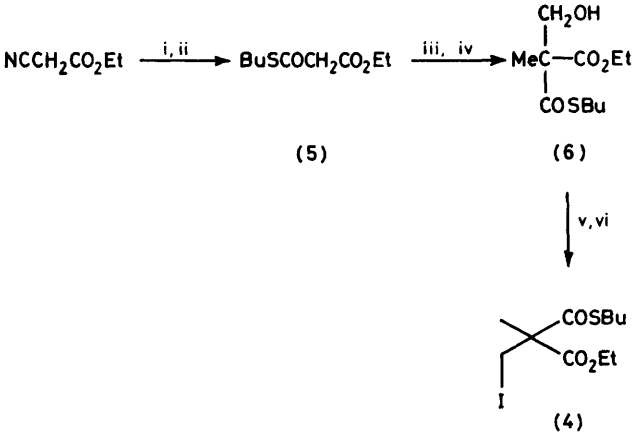
SCHEME 2 *Reagents*: i, $NaOEt–CH_2O$; ii, TsCl, py; iii, NaI–$(MeOCH_2)_2$, or $(PhO)_3P^+MeI^-$

ester (3; R = CH_2Ph), the direct displacement of tosylate with iodide occurred in very low yield, the predominant process being fragmentation to benzyl iodide and benzyl methacrylate (Scheme 3). However, iodination with triphenyl phosphite methiodide [7] afforded a 25% conversion into the iodomethylmalonate (2; X = O, $R^1 = R^2 = CH_2Ph$). This method was also superior for the synthesis of the t-butyl ester (2; X = O, $R^1 = R^2$ = t-Bu) in a yield of 68% as compared with 45% by tosylate displacement.



SCHEME 3

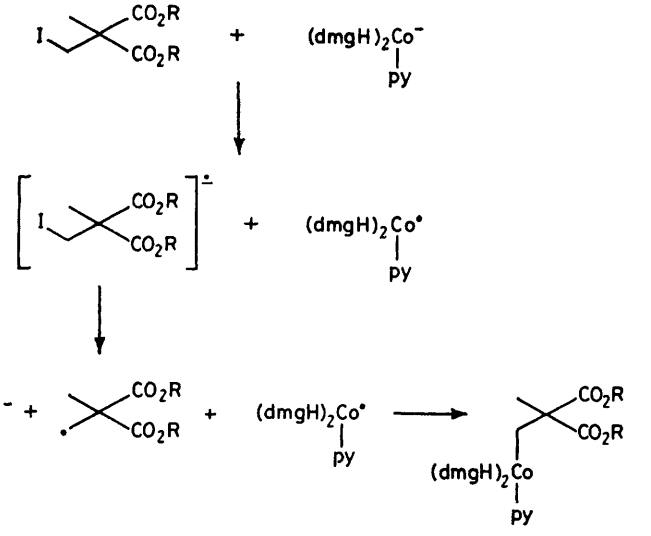
The monothioester (4) was obtained from ethyl cyanoacetate as shown in Scheme 4. Reaction with butane-1-thiol in the presence of hydrogen chloride and hydrolytic work-up gave the monothioester (5) (60%). Sequential alkylation with sodium hydride–methyl iodide and formaldehyde in the presence of a catalytic amount of sodium ethoxide gave the hydroxymethylmalonate (6) (60%). Tosylation (45%) and displacement of the tosylate group with iodide (52%) completed the synthesis.



SCHEME 4 *Reagents*: i, BuSH–HCl; ii, H_2O; iii, NaH–MeI; iv, $NaOEt–CH_2O$; v, TsCl–py; vi, NaI–$(MeOCH_2)_2$

With these halides to hand, the synthesis of the malonylmethylcobaloximes (1) was attempted. In all cases, the simple Schrauzer synthesis failed. However, the newly developed method gave satisfactory yields (35—52%; Table, runs 7, 10, and 11) of the corresponding cobaloximes (1) on reaction of the cobalt(I) anion with the iodide precursors, despite the difficulty of attack of a bulky nucleophile at the neopentyl centre.

It is possible that this reaction is an electron-transfer process (Scheme 5) since the sulphonates (7a and b) gave



SCHEME 5

none of the required cobaloxime * (Table, runs 8 and 9). Mesylates, tosylates, and iodides show similar reactivity towards nucleophiles in general,[8] but of these, iodides are particularly susceptible to electron-transfer reactions.[9] Electron-transfer mechanisms in cobaloxime(I) anion alkylations have been suggested by others,[2,10] following similar observations with hindered alkylation agents.

This method for the generation and use of the cobaloxime(I) anion produces a reagent free from significant quantities of extraneous base and allows the synthesis of sensitive cobaloximes not readily accessible by previous techniques. Application of the method to other systems is in hand.

EXPERIMENTAL

Ethanol was purified by the magnesium method. Pyridine was purified by distillation from potassium hydroxide and stored over calcium hydride. 1,2-Dimethoxyethane was refluxed over and distilled from lithium aluminium hydride under nitrogen. Butane-1-thiol was dried over and distilled from dried calcium sulphate under nitrogen. Dimethylformamide and dimethyl sulphoxide were dried by reduced pressure distillation from calcium hydride. Benzene was dried and stored over sodium wire. Light petroleum refers to the fraction of b.p. 60—80 °C and was distilled before use.

* The benzyl ester tosylate (7b) did, however, give a benzylcobaloxime in low (22%) yield, presumably by a process analogous to Scheme 4.

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Diethyl p-*Tolylsulphonyloxymethyl(methyl)malonate*.—Diethyl hydroxymethyl(methyl)malonate [6] (6.12 g, 0.03 mol) was converted to the toluene-*p*-sulphonate with toluene-*p*-sulphonyl chloride and pyridine at 5 °C in the conventional manner. The product was purified by alumina (grade I) column chromatography with dichloromethane as eluant to give the *toluene*-p-*sulphonate* (8.79 g, 82%) as a colourless oil, suitable for conversion into the iodide. A sample purified by p.l.c. on silica, with ethyl acetate–light petroleum (1 : 3) as solvent, showed τ 2.1—2.8 (4 H, ABq), 5.8 (2 H, s), 5.9 (4H, q), 7.5 (3 H, s), 8.6 (3 H, s), and 8.8 (6 H, t); $\nu_{max.}$ (liq.) 3 000, 1 720, and 1 600 cm^{-1} (Found: C, 53.8; H, 6.2; S, 9.05. $C_{16}H_{22}O_7S$ requires C, 53.6; H, 6.2; S, 8.95%).

Diethyl Iodomethyl(methyl)malonate.—The foregoing toluene-*p*-sulphonate (7 g, 0.02 mol) was added to a solution of sodium iodide (50 g, 0.33 mol) in 1,2-dimethoxyethane (400 ml), and the mixture was refluxed in the dark under nitrogen for 90 h. The solvent was removed by distillation and the residue washed thoroughly with benzene. The solution obtained on filtration was concentrated to yield an orange oil, which was purified by passing it, in the dark, down a 30 cm alumina (grade III) column, eluting with benzene. The eluate was concentrated to give *diethyl iodomethyl(methyl)malonate* (5.1 g, 80%) as a pale yellow oil. A pure sample was prepared by p.l.c. on silica gel with ethyl acetate–light petroleum (1 : 3) as solvent. All operations were performed in light from a photographic red safety lamp, and the sample was submitted for immediate analysis; τ 5.9 (4 H, q), 6.5 (2 H, s), 8.5 (3 H, s), and 8.8 (6 H, t); $\nu_{max.}$ (liq.) 3 000 and 1 730 cm^{-1}; $\lambda_{max.}$ (cyclohexane) 200, 220, and 255 nm (Found: C, 34.3; H, 4.7; I, 40.6. $C_9H_{15}IO_4$ requires C, 34.4; H, 4.81; I, 40.4%).

Dibenzyl Hydroxymethyl(methyl)malonate.—A portion (10 drops) of a solution of sodium benzyl oxide (0.1 g, 4 mmol)] in benzyl alcohol (50 ml) was added to a stirred suspension of paraformaldehyde (4.5 g, 0.05 mol) in dibenzyl methylmalonate [11] (43 g, 0.145 mol), and the mixture was stirred at 60 °C for 30 min. The resulting clear solution was dissolved in ether (100 ml) and washed with 2N-hydrochloric acid (50 ml) and water (2 × 50 ml). The solution was dried over anhydrous sodium sulphate–potassium carbonate and concentrated to give dibenzyl hydroxymethyl(methyl)-malonate (43.5 g, 92%) as a colourless oil, characterised by analysis of its tosylate and mesylate derivatives; τ 2.8 (10 H, s), 5.0 (4 H, s), 6.2 (2 H, s), 7.2 (1 H, s, D_2O-exchangeable), and 8.6 (3 H, s); $\nu_{max.}$ (liq.) 3 500, 3 000, and 1 735 cm^{-1}.

Dibenzyl p-*Tolylsulphonyloxymethyl(methyl)malonate*.—Dibenzyl hydroxymethyl(methyl)malonate (7 g, 0.02 mol) was converted into the toluene-*p*-sulphonate in the conventional manner. The product was recrystallised from benzene–light petroleum (1 : 6) to yield a white *solid* (6.5 g, 67%), m.p. 50—51 °C; τ 2.2—2.8 (4 H, ABq), 2.7 (10 H, s), 5.0 (4 H, s), 5.7 (2 H, s), 7.6 (3 H, s), and 8.5 (3 H, s); $\nu_{max.}$ ($CHCl_3$) 3 000, 1 740, and 1 600 cm^{-1} (Found: C, 64.9; H, 5.55; S, 6.8. $C_{26}H_{26}O_7S$ requires C, 64.6; H, 5.45; S, 6.65%).

Dibenzyl Iodomethyl(methyl)malonate.—*Method* 1. The foregoing toluene-*p*-sulphonate (4.8 g, 0.01 mol) was treated with sodium iodide (15 g, 0.10 mol) in 1,2-dimethoxyethane (300 ml) for 90 h as already described, to give a red oil (4.5 g). This was purified by p.l.c. on silica (hexane as solvent) and yielded benzyl iodide (R_F 0.9) and benzyl methacrylate (R_F 0.4), identified spectroscopically. No dibenzyl iodomethyl(methyl)malonate was detected under the foregoing conditions, which were necessary for complete reaction of the tosylate. When the reaction mixture was worked up after 24 h, p.l.c. with toluene as solvent gave a small amount of a pale yellow oil identified as dibenzyl iodomethyl-(methyl)malonate; τ 2.6 (10 H, s), 4.8 (4 H, s), 6.4 (2 H, s), and 8.4 (3 H, s); $\nu_{max.}$ (liq.) 3 000, 1 740, and 1 500 cm^{-1}.

Method 2. Triphenyl phosphate methiodide (3.62 g, 8 mmol), prepared by the method of Rydon [7] and stored under ether, was added to dibenzyl hydroxymethyl(methyl)-malonate (2.70 g, 8 mmol), and *N*,*N*-dimethylformamide (10 ml) was then added. The resulting solution was warmed to 60 °C for 90 min and stored at room temperature overnight. The mixture was poured into water (100 ml) and extracted with ether (3 × 100 ml). The combined ethereal solutions were washed with 2N-sodium hydroxide (2 × 100 ml), and water (3 × 100 ml), and dried over anhydrous potassium carbonate. The solution was concentrated and the red oil obtained was chromatographed over an alumina (grade III) column and eluted with carbon tetrachloride. Benzyl iodide was eluted first, followed by *dibenzyl iodomethyl(methyl)malonate* (0.89 g, 25%), showing spectral data identical with those of the product obtained by Method 1 (Found: M^+, 438.0318. $C_{19}H_{19}IO_4$ requires M, 438.0329).

Di-t-butyl Hydroxymethyl(methyl)malonate.—Di-t-butyl methylmalonate [12] (21.8 g, 0.095 mol) was mixed with paraformaldehyde (3 g, 0.033 mol) and a catalytic quantity of sodium ethoxide in ethanol, and warmed to 60 °C for 30 min. The resulting clear solution was dissolved in ether (100 ml), and washed with 2N hydrochloric acid (50 ml), water (2 × 50 ml), and saturated aqueous sodium hydrogencarbonate (50 ml). The solution was dried over anhydrous potassium carbonate and concentrated, to give as a colourless oil di-t-butyl hydroxymethyl(methyl)malonate (23.4 g, 95%), τ 6.2 (2 H, s), 7.2 (1 H, s, D_2O exchangeable), 8.4 (18 H, s), and 8.5 (3 H, s); $\nu_{max.}$ (liq.) 3 500, 3 000, and 1 720 cm^{-1}.

Di-t-butyl p-*Tolylsulphonyloxymethyl(methyl)malonate*.—Di-t-butyl hydroxymethyl(methyl)malonate (6 g, 0.023 mole) was converted into the toluene-*p*-sulphonate in the conventional manner. The usual work-up gave an oil which crystallised on addition of light petroleum. The product was recrystallised from methanol to give a white solid (5.4 g, 57%), m.p. 73—74 °C; τ 2.0—2.6 (4 H, ABq), 5.6 (2 H, s), 7.5 (3 H, s), 8.6 (18 H, s), and 8.7 (3 H, s); $\nu_{max.}$ ($CHCl_3$) 3 540, 2 920, 1 730, and 1 600 cm^{-1} (Found: C, 58.2; H, 7.45; S, 7.9. $C_{20}H_{30}O_7S$ requires C, 58.0; H, 7.3; S, 7.7%).

Di-t-butyl Iodomethyl(methyl)malonate.—Triphenyl phosphite methiodide [7] (4.84 g, 0.011 mol) was treated similarly with di-t-butyl hydroxymethyl(methyl)malonate (2.78 g, 0.011 mol) in *N*,*N*-dimethylformamide (10 ml). Work-up as before gave an orange oil which was chromatographed over an alumina (grade III) column, with benzene as eluant. Concentration of the iodide-containing fractions yielded *di-t-butyl iodomethyl(methyl)malonate* (2.68 g, 68%) as a pale yellow oil, τ 6.4 (2 H, s), 8.5 (18 H, s), and 8.6 (3 H, s); $\nu_{max.}$ (liq.) 2 890 and 1 730 cm^{-1} (Found: M^+, 370.0649. $C_{13}H_{23}IO_4$ requires M, 370.0643).

O-*Ethyl* S-*Butyl Thiomalonate*.—Ethyl cyanoacetate (31 g, 0.27 mol) was dissolved in benzene (100 ml) and the solution saturated with dry hydrogen chloride at 0 °C. Butane-1-thiol (26 g, 0.28 mol) was added and dry hydrogen chloride bubbled through the mixture at 0 °C for a further 2 h. Distillation left a white solid, which was refluxed gently with water (80 ml) for 30 min. The oil layer was removed and

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the aqueous phase extracted with ether (3 × 100 ml). The organic phases were combined, washed with water (3 × 100 ml), and dried over anhydrous sodium sulphate. Concentration followed by distillation at 98 °C and 2.5 mmHg gave O-*ethyl* S-*butyl thiomalonate* (35 g, 60%). A sample purified by redistillation showed τ 5.8 (2 H, q), 6.6 (2 H, s), 7.0 (2 H, t), and 8.2—9.0 (10 H, m); $\nu_{max.}$ (liq.) 3 000, 1 740, and 1 690 cm^{-1} (Found: C, 52.8; H, 8.0. $C_9H_{16}O_3S$ requires C, 52.9; H, 7.9%).

O-*Ethyl* S-*Butyl* (*Methyl*)*thiomalonate*.—A solution of *O*-ethyl *S*-butyl thiomalonate (7.6 g, 0.037 mol) in benzene (50 ml) was added under nitrogen to a stirred suspension of benzene-washed sodium hydride (1.68 g, 0.04 mol; 57% oil dispersion) in benzene (50 ml). When hydrogen evolution had ceased, iodomethane (5.2 g, 0.037 mol) was added and the mixture stirred at room temperature overnight. The resulting suspension was filtered, and the solid residue was washed with benzene. The filtrate and washings were shaken with water (2 × 100 ml), aqueous 10% sodium disulphite (2 × 100 ml), and water (3 × 100 ml). After drying (Na_2SO_4), the solution was concentrated and the residual oil distilled at 66 °C and 0.08 mmHg to give *O*-ethyl *S*-butyl (methyl)thiomalonate (5 g, 62%), τ 5.8 (2 H, q), 6.6 (1 H, q), 7.2 (2 H, t), and 8.2—9.2 (13 H, m); $\nu_{max.}$ (liq.) 3 000, 1 740, and 1 690 cm^{-1}.

O-*Ethyl* S-*Butyl* p-*Tolylsulphonyloxymethyl*(*methyl*)*thiomalonate*.—*O*-Ethyl *S*-butyl hydroxymethyl(methyl)thiomalonate (3.2 g, 0.013 mol) was converted into the toluene-*p*-sulphonate in the conventional manner. The crude product was chromatographed over alumina (grade III) with dichloromethane as eluant to yield an almost colourless oil, (2.3 g, 45%), suitable for conversion into the iodide. A sample prepared by p.l.c. on silica, with benzene–cyclohexane (2 : 1) as solvent, showed τ 2.2—3.0 (4 H, ABq), 5.8 (2 H, s), 5.9 (2 H, q), 7.2 (2 H, t), 7.6 (3 H, s), and 8.4—9.4 (13 H, m); $\nu_{max.}$ (liq.) 2 900, 1 720, 1 670, and 1 590 cm^{-1} (Found: C, 53.8; H, 6.7; S, 15.9. $C_{18}H_{26}O_6S_2$ requires C, 53.7; H, 6.5; S, 15.9%).

O-*Ethyl* S-*Butyl* *Iodomethyl*(*methyl*)*thiomalonate*.—The foregoing toluene-*p*-sulphonate (2.0 g, 0.005 mol) was treated with sodium iodide (7.5 g, 0.050 mol) in 1,2-dimethoxyethane (50 ml) as already described. The crude product was purified by chromatography on alumina (grade III), with benzene as eluant. O-*Ethyl* S-*butyl iodomethyl*(*methyl*)*thiomalonate* (0.95 g, 52%) was isolated as a yellow oil. A sample prepared by p.l.c. on silica, with benzene–cyclohexane (2 : 1) as solvent, showed τ 5.8 (2 H, q), 6.5 (2 H, ABq), 7.2 (2 H, t), and 8.3—9.3 (13 H, m); $\nu_{max.}$ (liq.) 2 900, 1 720, and 1 660 cm^{-1}; $\lambda_{max.}$ (cyclohexane) 240 nm (Found: C, 37.1; H, 5.65; I, 35.3; S, 9.0. $C_{11}H_{19}IO_3S$ requires C, 36.9; H, 5.35; I, 35.4; S, 8.95%).

Generation and Reactions of Cobaloxime(I) *Anions; (Malonylmethyl)cobaloxime Syntheses*.—*General procedure*. Potassium t-butoxide (60 mg, 0.54 mmol) was added to a solution of β-cyanoethyl(pyridine)cobaloxime [13] (211 mg, 0.5 mmol) in dimethyl sulphoxide (50 ml). Volatile material was removed into a cold trap by passing a vigorous stream of nitrogen for 10 min. The halogeno-compound (1—2 mmol) was then added with a syringe. The deep red colour of pyridinecobaloxime(I) anion was rapidly discharged. The mixture was stirred at room temperature overnight and poured into pH 6.0 acetate buffer (250 ml). Conventional work-up and recrystallisation from methanol gave the alkyl(pyridine)cobaloxime. Simple alkylcobaloximes prepared by this method are listed in the Table.

(a) *With diethyl iodomethyl*(*methyl*)*malonate*. This experiment was performed on a 2.5 mmol scale, using diethyl iodomethyl(methyl)malonate (1.6 g, 5 mmol) and a nitrogen sweep time of 20 min. The product was recrystallized from methanol to give (2,2-bisethoxycarbonylpropyl)(pyridine)-cobaloxime (780 mg, 57%).

(b) *With* O-*ethyl* S-*butyl iodomethyl*(*methyl*)*thiomalonate*. This experiment was performed in the same manner as in (a) but with *O*-ethyl *S*-butyl iodomethyl(methyl)thiomalonate (890 mg, 2.5 mmol) as alkylating agent. The product was recrystallised from acetonitrile to give [2-*butylthio*-(*carbonyl*)-2-*ethoxycarbonylpropyl*](*pyridine*)*cobaloxime* (74 mg, 50%); τ 1.4—2.8 (5 H, m), 5.8 (2 H, q), 7.3 (2 H, t), 7.85 (6 H, s), 7.90 (6 H, s), 8.0 (2 H, s), and 8.6—9.2 (13 H, m); $\nu_{max.}$ ($CHCl_3$) 3 000, 1 720, 1 675, 1 610, and 1 570 cm^{-1} (Found: C, 47.9; H, 6.1; N, 11.7; S, 6.65. $C_{24}H_{38}CoN_5O_7S$ requires C, 48.1; H, 6.35; N, 11.7; S, 5.35%)

(c) *With dibenzyl* p-*tolylsulphonyloxymethyl*(*methyl*)*malonate*. When the reaction was carried out on a 0.5 mmol scale using the toluene-*p*-sulphonate (300 mg, 0.62 mmol), no conversion was observed after 48 h.

(d) *With dibenzyl methylsulphonyloxymethyl*(*methyl*)*malonate*. The reaction was repeated with the methanesulphonate (430 mg, 1.1 mmol) as alkylating agent. After 72 h, the mixture was worked up in the standard manner. The solid obtained was recrystallised from methanol and identified as benzyl(pyridine)cobaloxime (51 mg, 22%) by comparison with the product obtained previously.

(e) *With dibenzyl iodomethyl*(*methyl*)*malonate*. When pyridinecobaloxime(I) anion, generated from β-cyanoethyl-(pyridine) cobaloxime (800 mg, 1.9 mmol) in the usual manner, was treated with dibenzyl iodomethyl(methyl)malonate (887 mg, 2 mmol) and the mixture was worked up after 4 h, an orange solid was obtained. This was recrystallised from acetonitrile and identified as (2,2-*bisbenzyloxycarbonylpropyl*)(*pyridine*)*cobaloxime* (450 mg, 35%); τ 1.4—2.8 (5 H, m), 2.7 (10 H, s), 5.0 (4 H, ABq, *J* 6.5 Hz), 7.85 (2 H, s), 7.9 (12 H, s), and 8.6 (3 H, s); $\nu_{max.}$ ($CHCl_3$) 2 900, 1 725, and 1 605 cm^{-1} (Found: C, 56.4; H, 5.85; N, 10.5. $C_{32}H_{38}CoN_5O_8$ requires C, 56.6; H, 5.65; N, 10.3%).

(f) *With di-t-butyl iodomethyl*(*methyl*)*malonate*. Pyridinecobaloxime(I) anion was generated from β-cyanoethyl-(pyridine)cobaloxime (4.04 g, 0.095 mol) and treated with di-t-butyl iodomethyl(methyl)malonate (4.28 g, 0.115 mol). The mixture was stirred overnight and then worked up in the usual manner. The solid obtained was recrystallised from acetonitrile and identified as (2,2-*bis-t-butoxycarbonylpropyl*)(*pyridine*)*cobaloxime* (3 g, 52%); τ 1.4—2.8 (5 H, m), 7.8 (12 H, s), 8.0 (2 H, s), 8.6 (18 H, s), and 8.8 (3 H, s); $\nu_{max.}$ ($CHCl_3$) 2 900, 1 720, and 1 605 cm^{-1} (Found: C, 51.1; H, 6.9; N, 11.5. $C_{26}H_{42}CoN_5O_8$ requires C, 51.4; H, 7.0; N, 11.4%).

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