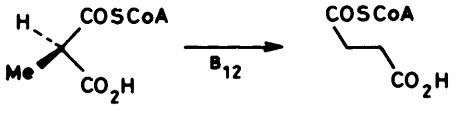
Reactions Potentially Related to Coenzyme B_{12} Dependent Rearrangements: Observations on the Radical [1,2]-Acyl and -Thiol Ester Migrations

Wayne M. Best, Anthony P. F. Cook, James J. Russell, and David A. Widdowson *
Department of Chemistry, Imperial College, London SW7 2AY

Reaction of 2-iodomethyl-2-methyl-3-oxo esters with tributyltin radicals, generated photochemically from hexabutylditin or tributyltin hydride in cyclohexane, or benzene–acetonitrile, resulted in a [1,2]-acyl migration in 10—63% yields dependent on the source of tin radical and substrate used. Radical migration was confirmed by the use of tributyltin deuteride. Thiol ester group migration was not observed. A new, highly efficient method for thiol ester synthesis is described.

Methylmalonyl CoA mutase brings about the rearrangement of (*R*)-methylmalonyl CoA to succinyl CoA by a coenzyme B_{12} dependent process (Scheme 1).[1] The mechanism for this

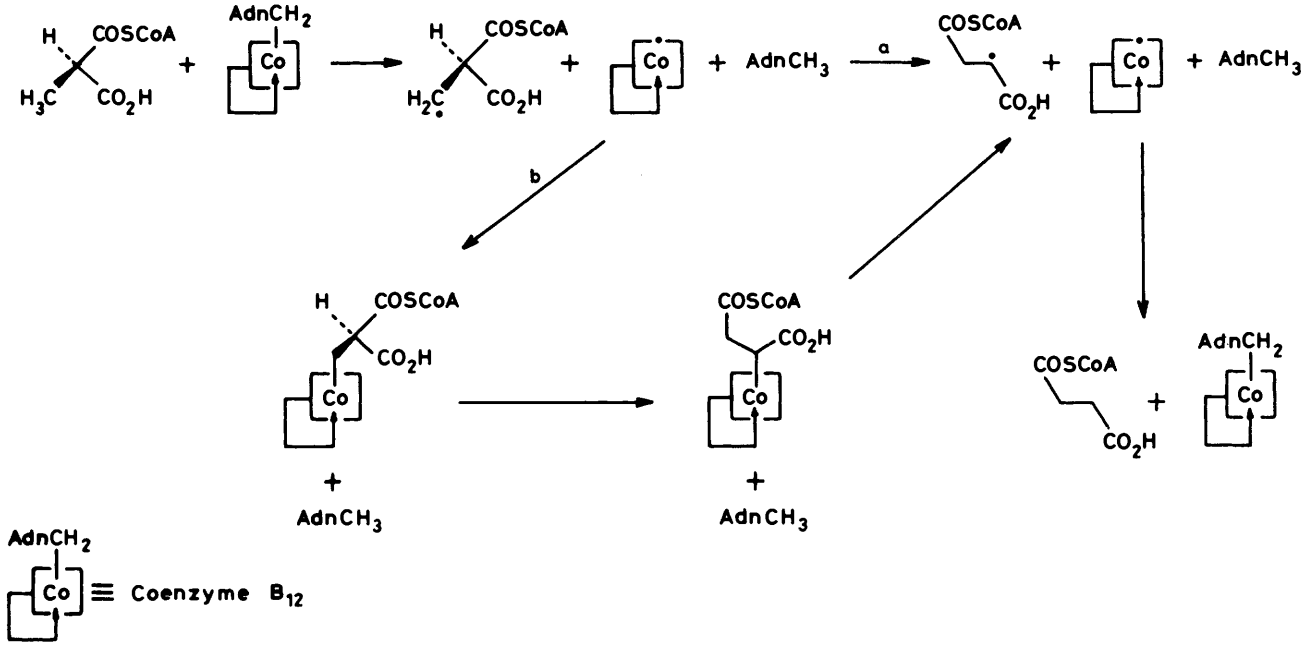


Scheme 1.

biologically important reaction remains unknown and is a matter of considerable speculation.[2] Although it has been demonstrated that specifically the thiol ester (*S*-ester) group migrates in the process,[3] the precise means by which it does so is unresolved. Biochemical evidence is lacking on the precise nature of the migrating group and although a radical process is generally suggested,[2] an anionic mechanism cannot be totally eliminated.[4] The concomitant hydrogen migration is known to occur *via* transfer to and from the C-5′ position of the adenosyl ligand of the coenzyme (Scheme 2).[5] The mechanisms which encompass these facts fall into two categories: either B_{12} simply takes the role of a free radical initiator and the rearrangement is inherent in the nature of the derived radical under the steric and possibly mechanistic influence of the apoenzyme alone (Scheme 2a), or the substrate is bonded to the coenzyme and is reorganised within the co-ordination sphere of the cobalt atom (Scheme 2b). Within each of these categories, there are many possible variants and the true mechanism can only be unravelled ultimately by studies on the enzyme itself. However, the rarity of *in vitro* analogues of the process and the consequent lack of a firm chemical basis from which to describe the reaction, underlies the need for a continuing search for good examples of non-anionic [1,2]-acyl shifts. We describe here our results on tin radical initiated [1,2]-acyl migrations in systems designed to model the free radical process.

Earlier reports in the literature suggested that neither *O*-ester nor *S*-ester groups undergo [1,2]-free radical migration to any extent in malonate and thiomalonate systems.[6] Recently, however, Halpern has detected low levels of thiol ester migration in a tin radical-initiated reaction[7]. Although migrations of these groups have been claimed in organocobalt compounds[8] unambiguous evidence has not yet been reported. In contrast, a small number of acyl migrations in both organocobalt and simple organic compounds have been established[1,9] and a detailed study of the latter recently reported.[10]

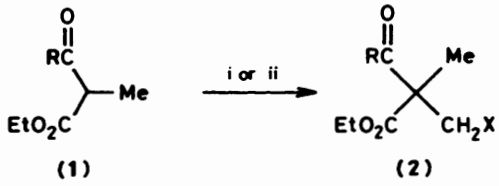
Previously we have described how MNDO calculations provide the sequence of migratory aptitudes toward [1,2]-free



Scheme 2.

radical migration: RCO > RSCO > ROCO.[11] The intermediate location of the thiol ester group led us to make a comparative study of acyl and thiol ester systems capable of [1,2]-free radical rearrangements. Previous relevant reports describe free radical generation under reducing (Bu_3SnH) conditions.[7,9] We have made similar observations and now extend them by means of a free radical generating method more conducive to longer free radical lifetimes.

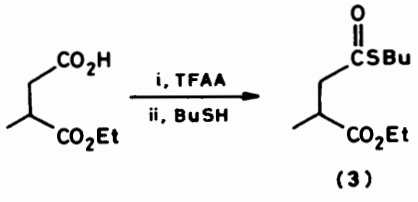
The thiol ester (1; R = SBu) was prepared by methods different from those previously reported.[12] Thus, *S*-butyl thiopropionate was treated with ethyl chloroformate in the presence of an equivalent of LDA to yield on acid work up and distillation *o*-ethyl *S*-butyl 2-methylmonothiomalonate (1; R = BuS) in 83% yield. Alternatively, the lithium enolate of ethyl propionate was treated with butyl chlorothioformate to give (1; R = BuS) in 92% yield. Oxo esters (2; R = Ph, Me, SBu, X = I) were prepared from (1) by a particularly mild and efficient iodomethylation procedure (Scheme 3). Thus



Scheme 3. *Reagents and conditions:* i, CH_2I_2–NaH–Me_2SO/room temp. (X = I) *or* ii, MeI–NaH–Me_2SO/room temp. (X = H)

oxo esters (1; R = Ph, Me, SBu) were treated with sodium hydride in DMSO and di-iodomethane at room temperature during 15—40 h to give the products (2; R = Ph, Me, SBu) in 71, 64, and 88% yield respectively.

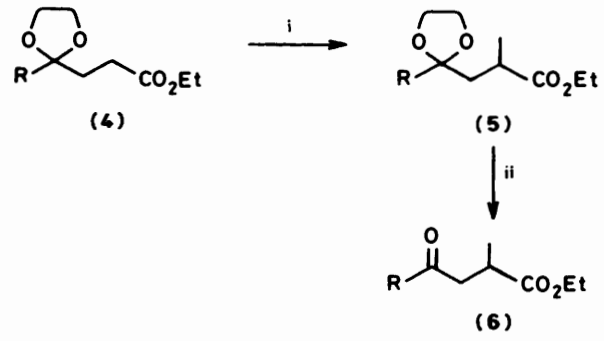
Authentic reduced rearranged materials were synthesized in order to permit product analysis by g.l.c. The products (2; R = Ph, Me, SBu, X = H) of the reduction of unrearranged substrates (2; R = Ph, Me, SBu, X = I) were readily available *via* methylation of the anions derived from (1; R = Ph, Me, SBu) (Scheme 3). The *S*-succinate (3) was obtained (90%) by thiol esterification of ethyl 2-methylsuccinate in the presence of trifluoroacetic anhydride (TFAA) as coupling reagent[13] in dichloromethane (Scheme 4). The use of TFAA in this capacity



Scheme 4.

has not previously been reported and it proved to be more efficient and technically simpler than any of the standard methods tried.[14] Rearrangement products (6; R = Ph, Me) were readily prepared (72, and 82% respectively) from the corresponding acetal esters (4; R = Ph, Me) (Scheme 5) by standard methods.[15]

With both the rearranged and unrearranged products to hand we proceeded to study the reactions of the substrates (2; X = I). The results of our studies using tin radical initiation in cyclohexane solvent, are presented in the Table. In the acyl series, we detected 10% of rearranged product (6; R = Ph) from (2; R = Ph, X = I) with tributyltin hydride (run 1, 36 h photolysis) and 23% from (2, R = Me, X = I) (run 4, 18 h photolysis). Halpern has reported[7] low levels of rearrangement of thiol esters under slightly different conditions, others report



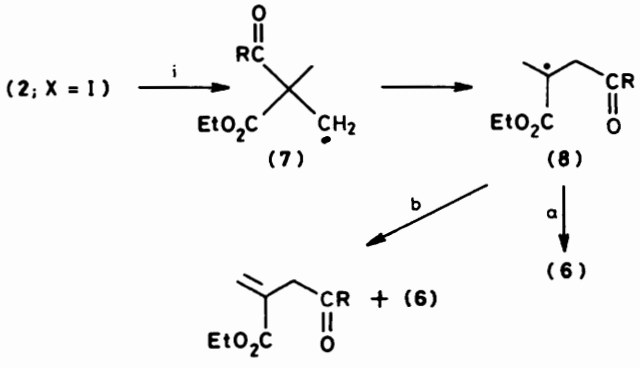
Scheme 5. *Reagents and conditions:* i, LDA–MeI; ii, H_3O^+–SiO_2 gel.

none[6] and we can detect none (by g.l.c.) in the crude product (Table, run 6). It appeared therefore that the [1,2]-migration was slow relative to hydrogen abstraction by the substrate radical (from tin hydride and/or solvent) and we adopted hexabutylditin as a non-hydrogenating source of tributyltin radicals.[16] Photolysis (125 W high-pressure Hg lamp/pyrex) of hexabutylditin (1 molar equivalent) in the presence of the iodo compound (2; R = Ph, X = I) in cyclohexane solution to complete consumption of substrate (run 2) gave a low yield (21% of volatile products) which consisted of rearranged species (6; R = Ph) (15%) and reduced (deiodinated) substrate (2; R = Ph, X = H) (6%). The bulk of the product was shown by mass and n.m.r. spectroscopy to contain organotin. Product stannylation could be largely avoided by the use of ≤0.5 equivalents of the tin reagent (run 3). Under these conditions a high mass balance (91%) of reduced/rearranged product was obtained, again predominantly rearranged (63%). In the acetyl series (2; R = Me, X = I) (runs 4,5) product yields were consistently lower, whatever the reactant ratio, but the ratio of rearranged to unrearranged materials was approximately the same as in the analogous phenyl series (runs 1,3).

The hexabutylditin reaction was extended to the thiol ester substrate (2; R = SBu, X = I) but still no rearrangement was detectable (run 7).

Finally, in order to establish unambiguously that the initial product of rearrangement was the derived radical and not an ionic species, substrate (2; R = Me, X = I) was treated with tributyl tin deuteride (run 8). The products (6; R = Me) and (2; R = Me, X = H) were isolated as their 2,4-dinitrophenylhydrazones and shown by mass and n.m.r. spectroscopy to be the monodeuterio species derived from [2-^{2}H]-(6; R = Me) and 2-[Me-$^2H_1$]-(2; X = H).

We have now established that [1,2]-acyl migration can be effected under unambiguously homolytic conditions when reduction of the intermediate radical (7) is suppressed (Scheme 6). The choice of solvent is crucial since hydrogen abstraction by



Scheme 6. *Reagents and conditions:* i, Bu_6Sn_2/*hν*: a, Solvent: cyclohexane; b, solvent: MeCN–C_6H_6

Table.

Run	Substrate (2; X = I)	Conc. ($\times 10^{-3}$ M)	Initiator	Mol. ratio[a]	Yield[b,c] Rearranged	Yield[b,c] Unrearranged
1	R = Ph	7.23	Bu_3SnH	1:1	10	68
2	R = Ph	11.6	$(Bu_3Sn)_2$	1:1	15	6
3	R = Ph	7.38	$(Bu_3Sn)_2$	1:0.4	63[d]	28[d]
4	R = Me	8.33	Bu_3SnH[e]	1:1	23	72
5	R = Me	4.70	$(Bu_3Sn)_2$	1:0.4	32[d]	14
6	R = SBu	7.02	Bu_3SnH	1:1	0	>99
7	R = SBu	7.02	$(Bu_3Sn)_2$	1:0.4	0[d]	>99
8	R = Me	8.13	Bu_3SnD	1:1.01	34	59
9	R = Ph	33.3[f]	$(Bu_3Sn)_2$	1:0.5	*g*	0

[a] Ratio, substrate: organotin compound. [b] Absolute yields determined, after 36 h photolysis, by g.l.c. using naphthalene as internal standard and response factors calculated from authentic specimens. [c] The products were also isolated and fully characterised. [d] Yield based on hexabutylditin. [e] Photolysis time 18 h. [f] Solvent acetonitrile–benzene (1:1). [g] Absolute yields not determined. The volatile products consisted of a 1:1 mixture of ethyl 2-methyl-4-oxo-4-phenylbutyrate (**6**; R = Ph) and ethyl 2-methylene-4-oxo-4-phenylbutyrate.

the initially formed radical must not compete with rearrangement, but the system is simplified if the product radical is finally quenched by the solvent. Cyclohexane proved to be particularly useful in this respect. When the reaction was run in acetonitrile–benzene and such quenching prohibited (run 9), although no unrearranged product was observed, the rearranged radical (**8**; R = Ph) disproportionated to (**6**; R = Ph) and its dehydro-analogue (Scheme 6b). Interestingly, only the *exo*-methylene isomer was detectable (by n.m.r. spectroscopy) in the initial product mixture.

Our results reinforce the findings of the previous studies[6] which demonstrated the inability of thiocarbonyl groups to undergo [1,2]-migration under unassisted free radical conditions and are clearly at a variance with Halpern's results. Our conditions, which produce a high proportion of rearrangement in the acyl series, {[$Bu_3SnSnBu_3$] < [substrate]}, approximate to Halpern's limiting conditions,[7] {[Bu_3SnH] < [substrate]}, yet we observe no migration in cyclohexane, or acetonitrile–benzene. The theoretical prediction of the relative free radical migratory aptitude of RCO > RSCO is thus confirmed but the free radical system alone does not adequately model the enzymic rearrangement. It follows that the thiol ester migration in the mutase must involve considerable assistance from the apoenzyme, the coenzyme or both. We are currently studying systems aimed at mimicking these effects.

Experimental

Column chromatography was carried out on silica gel 60H (Merck No. 7736). Commercial reagents and solvents were purified by standard methods; ether refers to diethyl ether. ^1H N.m.r. spectra were recorded 60 MHz, (Varian EM-360); 90 MHz (Perkin-Elmer R32); or 250 MHz, (Bruker WH 250 spectrometer). G.l.c. traces were recorded on either a Perkin-Elmer Sigma 1B or a Varian 6000 instrument fitted with a 2 m column; 15% Carbowax 20M on Chromasorb W 80/100.

O-Ethyl S-Butyl 2-Methylmonothiomalonate (**1**; R = BuS).—(a) Butyl thiopropionate (4.386 g, 30 mmol) in tetrahydrofuran (THF) (30 ml) was added over a period of 10 min to a solution of LDA (63 mmol) in THF (250 ml) at −78 °C. After 10 min, ethyl chloroformate (3.25 g, 30 mmol) in THF (60 ml) was added slowly over 30 min to the stirred solution. After 40 min, glacial acetic acid (3.6 g 60 mmol) was added in THF (10 ml). The THF was evaporated and sufficient water added to dissolve the precipitated amine salt. The resulting mixture was extracted with light petroleum–ether (1:1; 4 × 20 ml). The organic fractions were combined, washed sequentially with water, saturated aqueous sodium hydrogen carbonate and brine, dried, and evaporated. Distillation of the residue gave *O*-ethyl *S*-butyl 2-methylmonothiomalonate (**1**; R = BuS) (5.43 g, 83%), b.p. 72—74 °C at 0.15 mmHg (lit.,[12] 66 °C/0.08 mmHg); δ_H (250 MHz, $CDCl_3$) 0.92 (3 H, t, *J* 7.2 Hz), 1.27 (3 H, t, *J* 7.1 Hz), 1.32—1.63 (4 H, m), 1.43 (3 H, d, *J* 7.1 Hz), 2.92 (2 H, t, *J* 7.2 Hz), 3.62 (1 H, q, *J* 7.1 Hz), and 4.20 (2 H, q, *J* 7.1 Hz); $\nu_{max.}$(neat) 1 740 and 1 685 cm^{-1}.

(b) Ethyl propionate (204 mg, 2 mmol) in THF was added to a solution of lithium di-isopropylamide (LDA) (4 mmol) at −78 °C. After 10 min, *S*-butyl chlorothioformate[17] (310 mg, 2 mmol) in THF (5 ml) was added over 20 min. After a further 40 min, glacial acetic acid (0.24 g, 4 mmol) was added and the reaction mixture worked up as before except that the crude product was chromatographed over silica gel (eluant, light petroleum–ether 125:1—40.1) to give the ester (**1**; R = BuS) (400 mg, 92%), spectroscopically identical with the above product.

Ethyl 2-Benzoyl-2-iodomethylpropionate (**2**; R = Ph, X = I).—Ethyl 2-benzoylpropionate[18] (**1**; R = Ph) (3.0 g, 15 mmol) in Me_2SO (20 ml) was treated with a suspension of sodium hydride in oil (60%; 0.64 g, 16 mmol). The mixture was stirred until homogeneous and di-iodomethane (2.0 ml, 25 mmol) was added. The solution was stirred overnight before being worked up by ether extraction. The crude product was chromatographed over silica gel. Elution with ethyl acetate–light petroleum (1:9) gave *ethyl 2-benzoyl-2-iodomethylpropionate* (**2**; R = Ph, X = I) as a colourless liquid (3.57 g, 71%); δ (250 MHz; $CDCl_3$) 1.10 (3 H, t, *J* 7.1 Hz), 1.65 (3 H, s), 3.65 and 3.76 (2 H, ABq, *J* 10.3 Hz), 4.15 (1 H, A*B*X_3, *J* 7.1 and 10.4 Hz), 4.19 (1 H, *A*BX_3, *J* 7.1 and 10.4 Hz), 7.37—7.55 (3 H, m), 7.80—7.85 (2 H, m); *m/z* 346 (M^+, 0.2%), 105 (100), and 77 (17); $\nu_{max.}$(neat) 1 730 and 1 680 cm^{-1} (Found: C, 45.05; H, 4.5; I, 36.9; $C_{13}H_{15}IO_3$ requires C, 45.11; H, 4.37; I, 36.66%).

Ethyl 2-Acetyl-2-iodomethylpropionate (**2**; R = Me, X = I).—Ethyl 2-methylacetoacetate[19] (**1**; R = Me) (3.0 g, 21 mmol) in Me_2SO (25 ml) was treated with a suspension of sodium hydride in oil (60%; 1.0 g, 25 mmol). The mixture was stirred until homogeneous and di-iodomethane (4.0 ml, 50 mmol) was added. The solution was stirred overnight before being worked up by ether extraction. The crude product was chromatographed over silica gel. Elution with ethyl acetate–

light petroleum (1:9) gave *ethyl 2-acetyl-2-iodomethylpropionate* (**2**; R = Me, X = I) as a colourless liquid (3.8 g, 64%); δ (250 MHz; $CDCl_3$) 1.30 (3 H, t, *J* 7.1 Hz), 1.49 (3 H, s), 2.23 (3 H, s), 3.48 and 3.62 (2 H, ABq, *J* 10.3 Hz), 4.23 (1 H, A*B*X_3, *J* 7.1 and 11 Hz), 4.26 (1 H, *A*BX_3, *J* 7.1 and 11 Hz); *m/z* 284 (M^+, 2%), 115 (92), 87 (38), 69 (40), 43 (100), 41 (22), and 29 (16); $\nu_{max.}$(neat) 1 715 cm^{-1} (Found: C, 34.0; H, 4.8; I, 44.85. $C_8H_{13}IO_3$ requires C, 33.82; H, 4.61; I, 44.67%).

O-Ethyl S-Butyl 2-Iodomethyl(2-methyl)monothiomalonate (**2**; R = SBu, X = I).—*O*-Ethyl *S*-butyl 2-methylmonothiomalonate (**1**; R = SBu) (5.40 g, 25 mmol) in Me_2SO (35 ml) was treated with a suspension of sodium hydride in oil (1.2 g, 60%, 30 mmol). The mixture was stirred until homogeneous and diiodomethane (5.0 ml, 60 mmol) was added. The reaction was stirred at room temperature for 40 h and worked up by dilution with water and ether extraction. The crude product was chromatographed over silica gel. Elution with ethyl acetate–light petroleum (1:19) gave *O*-ethyl *S*-butyl 2-iodomethyl(2-methyl)monothiomalonate (**2**; R = SBu, X = I)[12] as a colourless liquid (7.80 g, 88%); δ (250 MHz; $CDCl_3$) 0.92 (3 H, t, *J* 7.1 Hz), 1.28 (3 H, t, *J* 7.1 Hz), 1.30—1.63 (4 H, m), 1.61 (3 H, s), 2.93 (2 H, t, *J* 7.1 Hz), 3.56 and 3.71 (2 H, ABq, *J* 10.1 Hz), 4.22 (1 H, A*B*X_3, *J* 7.1 and 10.4 Hz), and 4.24 (1 H, *A*BX_3, *J* 7.1 and 10.4 Hz), *m/z* 358 (M^+, 14%), 269 (20), 241 (50), 169 (27), 115 (60), 87 (27), 69 (45), 57 (89), 41 (100), and 29 (99); $\nu_{max.}$(neat) 1 675 and 1 740 cm^{-1}.

Thiol Ester Synthesis; *O-Ethyl S-Butyl 3-Methylmonothiosuccinate* (**3**).—2-Methylsuccinic acid monoethyl ester[20] (410 mg, 3 mmol) in dichloromethane (10 ml) was treated with trifluoroacetic anhydride (0.42 ml, 3 mmol) at room temperature. After 10 min, butanethiol (270 mg, 3 mmol) was added and the mixture was refluxed for 4 h. An excess of saturated aqueous potassium carbonate was added and the reaction mixture was extracted with ether. The extract was dried and evaporated and the residue yielded, on short-path distillation at 0.02 mmHg, *O-ethyl S-butyl 3-methylmonothiosuccinate* (630 mg, 90%); δ (250 MHz; $CDCl_3$) 0.91 (3 H, t, *J* 7.2 Hz), 1.20 (3 H, d, *J* 7 Hz), 1.25 (3 H, t, *J* 7.1 Hz), 1.30—1.65 (4 H, m), 2.63 (1 H, dd, *J* 18.4 and 8.9 Hz), 2.82—3.04 (4 H, m), and 4.14 (2 H, q, *J* 7.1 Hz); *m/z* 187 (16%), 157 (16), 143 (95), 115 (100), 87 (40), 57 (26), 43 (33), and 41 (28); $\nu_{max.}$(neat) 1 735 and 1 692 cm^{-1}. A small sample was further purified by h.p.l.c. and distillation (Found: C, 57.1; H, 8.9; S, 13.8. $C_{11}H_{20}SO_3$ requires C, 56.87; H, 8.68; S, 13.80%).

Similarly prepared were butyl thioacetate (95%), butyl thiopropionate (96%), butyl thioisobutyrate (97%) and *O*-ethyl *S*-phenyl 3-methylthiosuccinate (95%), δ (60 MHz; CCl_4) 1.17 (3 H, d), 1.25 (3 H, t), 2.23—3.3 (1 H, m), 4.10 (2 H, q), and 7.33 (5 H, s); $\nu_{max.}$(neat) 1 730 and 1 710 cm^{-1}.

O-Ethyl S-Butyl Dimethylmonothiomalonate (**2**; R = SBu, X = H).—*O*-Ethyl *S*-butyl 2-methylmonothiomalonate (2.18 g, 10 mmol) in Me_2SO (15 ml) was treated with a suspension of sodium hydride in mineral oil (600 mg, 60%, 15 mmol). The mixture was stirred until homogeneous and methyl iodide (1.25 ml, 20 mmol) was added. The resulting solution was stirred overnight before being worked up by dilution with water and ether extraction. Chromatography of the crude product over silica gel [eluant, ethyl acetate–light petroleum (1:19)] followed by distillation (b.p. 104 °C/1 mmHg) gave *O-ethyl S-butyl dimethylmonothiomalonate* (**2**; R = SBu, X = H) as a colourless liquid (2.03 g, 88%; δ (250 MHz; $CDCl_3$) 0.92 (3 H, t, *J* 7.2 Hz), 1.26 (3 H, t, *J* 7.1 Hz), 1.32—1.62 (4 H, m), 1.48 (6 H, s), 2.90 (2 H, t, *J* 7.2 Hz), and 4.18 (2 H, q, *J* 7.1 Hz); *m/z* 232 (M^+, 2%), 187 (8), 143 (75), 116 (64), 115 (100), 88 (24), 87 (72), 59 (24), 57 (46), 41 (38), and 29 (47); $\nu_{max.}$(neat) 1 685 and 1 742 cm^{-1} (Found: C, 56.6; H, 8.75; S, 13.45. $C_{11}H_{20}O_3S$ requires C, 56.87; H, 8.68; S, 13.80%).

Photolysis Experiments: Typical Procedure.—The iodide (**1**; R = Ph, Me, SBu) and either tributyltin hydride (1 mol equiv.) or hexabutylditin (0.4 mol equiv.) was dissolved in spectroscopic grade cyclohexane (40 ml) in a Pyrex flask. The solution was rigorously degassed by applying a freeze, pump, thaw cycle five times, and exchanging the atmosphere for dry, oxygen-free, nitrogen. The contents of the sealed flask were photolysed using a high-pressure mercury lamp for 18—36 h depending on the iodide. At the end of the reaction a white to yellow precipitate of tributyltin iodide had been deposited. An accurately weighed sample of naphthalene (5—20 mg) was added to the photolysate as an internal g.l.c. standard. The product distribution was analysed by g.l.c. Retention times relative to naphthalene (oven temperature 180 °C); ethyl 2-acetyl-2-methylpropionate (**2**; R = Me, X = H) 0.294 ± 0.001, ethyl 2-methyl-4-oxopentanoate (**6**; R = Me) 0.504 ± 0.01 and ethyl 2-methyl-4-oxo-4-phenylbutyrate (**6**; R = Ph) 6.27 ± 0.01. The solvent was evaporated and the residue treated with ether–ethanolic potassium fluoride. The mixture was diluted with light petroleum and the precipitate filtered off. The solvents were evaporated and the products separated by column chromatography. The isolated materials were chromatographically and spectroscopically identical with authentic specimens.

Photolysis of Ethyl 2-Acetyl-2-iodomethylpropionate (**2**; R = Me, X = I) *with Tributyltin Deuteride.*—The iodo keto ester (**2**; R = Me, X = I) (185 mg, 0.65 mmol) and tributyltin deuteride (>99%) (188 mg, 0.64 mmol) were dissolved in spectroscopic grade cyclohexane (80 ml) degassed as described above and photolysed for 18 h. Addition of the naphthalene internal standard and g.l.c. analysis revealed two major products, ethyl 2-acetyl-2-methylpropionate (**2**; R = Me, X = H) (60 mg, 59%) and ethyl 2-methyl-4-oxopentanoate (**6**; R = Me) (35 mg, 34%). The position and yield of deuterium incorporation was determined from a spectroscopic analysis of the corresponding 2,4-dinitrophenylhydrazones, which were separated by p.l.c. (ether–light petroleum, 1:19; multiple elution); ethyl 2-acetyl-2-methylpropionate 2,4-DNP derivative: δ ($CDCl_3$; 250 MHz) 1.27 (3 H, t, *J* 7.1 Hz), 1.51 (5 H, s), 2.05 (3 H, s), 4.19 (2 H, q, *J* 7.1 Hz), 7.95 (1 H, d, *J* 9.8 Hz), 8.32 (1 H, dd, *J* 9.8 and 2.3 Hz), 9.13 (1 H, d, *J* 2.3 Hz), and 11.06 (1 H, br s); *m/z* 339 (100%). Ethyl 2-methyl-4-oxopentanoate 2,4-dinitrophenylhydrazone: δ($CDCl_3$; 90 MHz) 1.26 (3 H, t, *J* 7 Hz), 1.28 (3 H, s), 2.08 (3 H, s), 2.54 (1 H, d, *J* 17 Hz), 2.87 (1 H, dd, *J* 17 Hz), 4.13 (2 H, q, *J* 7 Hz), 7.96 (1 H, d, *J* 10 Hz), 8.25 (1 H, dd, *J* 10 and 2 Hz), 9.00 (1 H, d, *J* 2 Hz), and 11.00 (1 H, br s); *m/z* 339 (100%).

Photolysis of Ethyl 2-Benzoyl-2-iodomethylpropionate with Hexabutylditin in Acetonitrile–Benzene.—Ethyl 2-benzoyl-2-iodomethylpropionate (492 mg, 2 mmol) was photolysed with hexabutyliditin (600 mg, 1 mmol) according to the general procedure previously described except that acetonitrile–benzene (1:1) (60 ml) was used as solvent. Work-up as described above followed by short-path (Kugelrohr) distillation of each chromatographic fraction gave, in addition to unchanged starting material, ethyl 2-methyl-4-oxo-4-phenylbutyrate; δ ($CDCl_3$; 250 MHz) 1.25 (3 H, t, *J* 7.2 Hz), 1.28 (2 H, d, *J* 7.2 Hz), 3.00 (1 H, dd, *J* 4.9 and 16.3 Hz), 3.05—3.18 (1 H, m), 3.48 (1 H, dd, *J* 7.2 and 16.3 Hz), 4.15 (2 H, q, *J* 7.2 Hz), 7.40—7.60 (3 H, m), and 7.93—8.00 (2 H, m); $\nu_{max.}$(neat) 1 729 and 1 686 cm^{-1}; *m/z* 220 (M^+, 4%), 175 (18), 146 (15), 121 (15), 105 (100), and 77 (36), identical with an authentic specimen and ethyl 2-methylene-4-oxo-4-phenylbutyrate, δ ($CDCl_4$; 60 MHz) 0.7—1.8 (3 H, m), 3.9 (2 H, s), 4.18 (2 H, q), 5.62 (1 H, s), and 6.30 (1 H, s). This compound was further characterised by isomerisation

to the more stable (*E*)-ethyl 2-methyl-4-oxo-4-phenylbut-2-enoate; δ (250 MHz; $CDCl_3$) 1.36 (3 H, t, *J* 7.1 Hz), 2.19 (3 H, d, *J* 1.5 Hz), 4.31 (2 H, q, *J* 7.1 Hz), 7.46—7.63 (3 H, m), 7.72 (1 H, q, *J* 1.5 Hz), and 7.95—7.99 (2 H, m); $\nu_{max.}$(neat) 1 720, 1 670, and 1 265 cm^{-1}; *m/z* 218 (M^+, 16%), 173 (17), 172 (49), 145 (22), 144 (20), 105 (100), and 77 (40) (Found: C, 71.4; H, 6.6. $C_{13}H_{14}O_3$ requires C, 71.54; H, 6.47%).

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