Preparation of Boron Tris(triflate). To 15 mL of SO_2ClF or 100 mL of Freon-113 placed into a 250-mL Schlenk flask cooled to −30 °C was added 9 mL (0.103 mol) of BCl_3. To the stirred solution cooled to −78 °C was added dropwise 26.4 mL (0.30 mol) of CF_3SO_3H over a period of 1 h. The temperature was maintained at −78 °C for 4–6 h and then slowly was allowed to warm up to room temperature within 4–6 h. At the end of this period, evolution of HCl ceased, and a clear colorless solution was obtained. Removal of the solvent in vacuum gave boron tris(triflate) as a white solid. Distillation at reduced pressure [68–73 °C (0.5 Torr)] gave pure boron tris(triflate) as a highly viscous compound, which subsequently solidifies (mp 43–45 °C). Preparations from BBr_3 were similarly carried out at 0 °C. The prepared boron tris(triflate) gave satisfactory elemental analysis. $B(O_3SCF_3)_3$MW calcd 458, found 454. Calcd: C, 7.8; S, 21.00; B, 2.36; F, 37.33. Found: C, 7.75; S, 21.07; B, 2.10; F, 37.20.

Preparation of Aluminum and Gallium Tris(triflate). Preparation of aluminum and gallium tris(triflate) from the corresponding trihalides and triflic acid were carried out according to the previously described procedure except that the reactions were run under mild reflux in Freon-113 solution for 10–12 h. At the end of this period, no further evolution of HX was observed. Removal of solvent under vacuum gave the triflates as white powders. The triflates were then washed several times with dry Freon-113 under dry nitrogen. Preparation of aluminum tris(triflate) from triethylaluminum was similarly carried out but at low temperature (−78 °C).

Preparation of Aluminum Triflate from Aluminum Carbide. A 100-mL stainless-steel autoclave equipped with a magnetic stirrer was charged with 1 g (7.0 mmol) of Al_4C_3 and 7.35 mL (83.4 mmol) of CF_3SO_3H diluted in 15 mL of Freon-113. The autoclave was then sealed and heated to 180–200 °C for 10–12 h. After depressurizing, the product was extracted several times with SO_2 or SO_2ClF. Removal of solvent gave aluminum tris(triflate) as a white powder.

Both aluminum and gallium tris(triflate) gave satisfactory elemental analyses. $Al(OSO_2CF_3)_3$ calcd: C, 7.99; S, 20.28; Al, 5.60; F, 35.32. Found: C, 7.48; S, 20.06; Al, 5.50; F, 35.20. $Ga(OSO_2CF_3)_3$ calcd: C, 6.97; S, 18.61; Ga, 13.40; F, 33.08. Found: C, 6.81; S, 18.40; Ga, 13.00; F, 33.16.

General Method for Alkylation and Acylation of Toluene and Benzene with $M(OSO_2CF_3)_3$ Catalysts. To a solution or suspension of $M(OSO_2CF_3)_3$ (5.5 mmol) in 25 mL of dichloromethane or nitromethane were added toluene (11.0 mmol) and benzene (55 mmol) under a dry nitrogen or argon atmosphere. The reaction flask was then placed in a constant-temperature bath at 25 °C. The corresponding alkyl or acyl halide (11 mmol) in the same solvent was added with vigorous stirring, and the reaction was allowed to proceed. The progress of the reaction was monitored by taking periodically samples and after usual workup (ice–$NaHCO_3$ quench and extraction with dichloromethane or nitromethane) by analyzing them by GC and GC–MS.

Preparative-scale experiments were similarly carried out with 10-fold amounts of the reagents. After usual workup, products were isolated by distillation (crystallization).

General Method of Isomerization of Isomeric Alkyltoluenes. To a well-stirred solution of $B(OSO_2CF_3)_3$ (3.0 mmol) in 25 mL of dichloromethane was added the corresponding isomeric alkyltoluene (6.0 mmol) under dry nitrogen or argon atmosphere. The reaction flask was then placed in a constant-temperature bath at 25 °C. Samples taken periodically, after usual workup (as described above), were analyzed by gas chromatography.

Acknowledgment. Support of our work by the National Institutes of Health and the National Science Foundation is gratefully acknowledged.

Registry No. BCl_3, 10294-34-5; BBr_3, 10294-33-4; $AlEt_3$, 97-93-8; $AlCl_3$, 7446-70-0; $AlBr_3$, 7727-15-3; AlI_3, 7784-23-8; $GaCl_3$, 13450-90-3; $GaBr_3$, 13450-88-9; GaI_3, 13450-91-4; Al_4C_3, 1299-86-1; CF_3SO_3H, 1493-13-6; $B(OTf)_3$, 64371-01-3; $Al(OTf)_3$, 75562-37-7; $Ga(OTf)_3$, 74974-60-0; methyl fluoride, 593-53-3; methyl chloride, 74-87-3; ethyl fluoride, 353-36-6; ethyl chloride, 75-00-3; ethyl bromide, 74-96-4; isopropyl chloride, 75-29-6; *tert*-butyl fluoride, 353-61-7; *tert*-butyl chloride, 507-20-0; acetyl chloride, 75-36-5; benzoyl chloride, 98-88-4; toluene, 108-88-3; benzene, 71-43-2; *o*-acetyltoluene, 577-16-2; *m*-acetyltoluene, 585-74-0; *p*-acetyltoluene, 122-00-9; *o*-benzoyltoluene, 131-58-8; *m*-benzoyltoluene, 643-65-2; *p*-benzoyltoluene, 134-84-9; *o*-methyltoluene, 95-47-6; *m*-methyltoluene, 108-38-3; *p*-methyltoluene, 106-42-3; *o*-ethyltoluene, 611-14-3; *m*-ethyltoluene, 620-14-4; *p*-ethyltoluene, 622-96-8; *o*-isopropyltoluene, 527-84-4; *m*-isopropyltoluene, 535-77-3; *p*-isopropyltoluene, 99-87-6; *m*-*tert*-butyltoluene, 1075-38-3; *p*-*tert*-butyltoluene, 98-51-1; *o*-*tert*-butyltoluene, 1078-92-6.

Rearrangement of Suitably Constituted Aryl, Alkyl, or Vinyl Radicals by Acyl or Cyano Group Migration[1]

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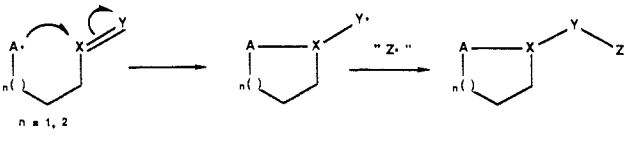
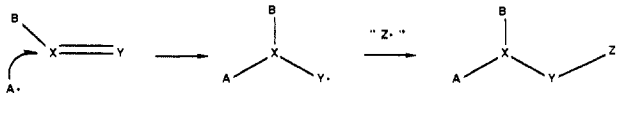
Abstract: Treatment of *o*-bromobenzyl acetoacetate (**14**) with tributyltin hydride affords the rearranged product **20** by a mechanism involving 1,4-acetyl migration in the aryl radical **15** via a cyclic intermediate **16**. Similarly, 1,4-cyano migration in the radical **22** derived from **21** affords rearranged product **24**. However, radicals, e.g., **26**, derived from cyclic keto esters give products formed both by 1,4-acyl migration and by H-atom transfer followed by 1,2-acyl migration. 1,2-Acyl migration in species containing a radical center exocyclic to a β-keto ester ring, e.g., **35** → **36**, provides a synthetically useful route to cyclic γ-keto esters. Examples of 1,4 or 1,5 migration of acyl or cyano groups to alkyl or vinyl radicals are given.

Early experimental investigations[3] of radical ring closures were designed mainly to reveal new insights into the factors affecting the intimate mechanism of homolytic addition processes. Not only did they afford a solid basis of kinetic data and related mechanistic information,[4] but they led to the recognition that intramolecular radical additions can often be carried out with highly predictable

Scheme I



Scheme II



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(2) Present address: Department of Chemistry, Imperial College, South Kensington, London SW7 2AY, U.K.

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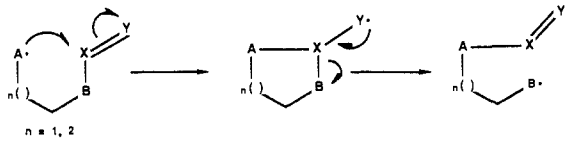
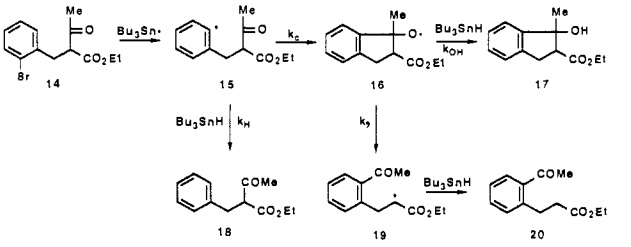
Scheme III



chemo-, regio-, and stereospecificity.[4c,5] This has provoked the development of a plethora of reactions of considerable synthetic utility,[6] many of which conform to the general equation of Scheme I, where A is a carbon-centered radical, either alkyl,[7] vinyl,[8] or aryl,[8h,9] X=Y represents a C=C or C≡C bond, Z includes hydrogen, halogen, allyl,[10] or nitrile,[8a,f,11] and the newly formed ring contains five or six atoms. In suitably constituted radicals containing more than one unsaturated group, the first ring closure may be followed by others to afford polycyclic products.[12] In a relatively few cases X=Y represents a C=O[12j,13] or C≡N bond.[12j,14]

The reactions represented by Scheme I are intramolecular analogues of the intermolecular process (Scheme II) in which the addition step is *either* essentially irreversible *or* in which the reaction with one of the reagents present is sufficiently rapid to trap the adduct radical before it undergoes β-fission.

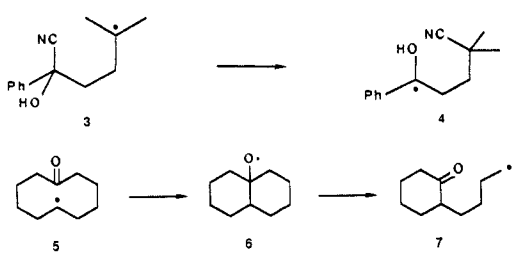
Scheme IV



If, however, the nature of the reactants were such that β-fission was fast relative to trapping of the adduct and proceeded selectively by loss of B•, the net outcome would be the transfer of X=Y from B to A.

When A and B reside within the same substrate molecule, and the reaction proceeds intramolecularly, it will afford rearranged products (Scheme III).

The transformations of Scheme III might be expected to proceed readily (a) when neither addition nor β-fission has a high barrier, (b) when the heat of formation of the A–X bond is greater than that of the B–X bond, and (c) when the reaction mixture contains no reagent capable of trapping the adduct sufficiently rapidly to preclude β-fission. Available data indicate that these criteria should be met when X=Y is a C=O or C≡N group and when both A• and B• are carbon-centered radicals, with the former being less thermodynamically stable than the latter. Thus, it is well-known that alkoxy or alkyliminyl radicals readily undergo β-fission,[15] while intramolecular homolytic additions to the cyano group[12j,14] and to the carbonyl group in both aldehydes[12j,13] and ketones[13d,16] have been described. Previous examples of transformations that incorporate the rearrangement of Scheme III include the reactions **1** → **2**,[13c] **3** → **4**,[17] and **5** → **7**.[18]



The homolytic intramolecular transfer of an acyl or cyano group according to the mechanism of Scheme III should be facilitated by factors that enhance the rate of either or both the addition and β-fission steps. Thus the rearrangement would be expected to proceed readily when A• is particularly reactive as is the case for aryl[19] or vinyl radicals[8i] or when β-fission is aided by the presence of a stabilizing substituent on B•. Although intramolecular additions to form three-membered rings usually occur more slowly than those affording five-membered rings, the ring strain in the former adducts would be expected to facilitate ring fission. Examples (e.g., **8** → **9**)[20m] have been previously recorded[20] and are

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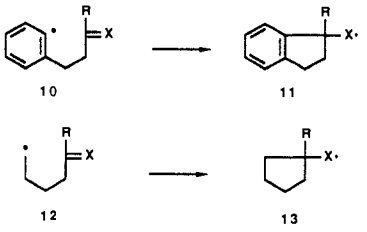
of possible biological significance since the coenzyme B_{12} promoted methylmalonyl-CoA to succinyl-CoA rearrangement is believed to involve a radical mechanism.[21]

8 9

In the present work we explore the mechanism and synthetic utility of reactions expected to conform to the general mechanism of Scheme III, in which A• is aryl, vinyl, or primary alkyl, B• is stabilized by an alkoxycarbonyl substituent, and X=Y is carbonyl or cyano. Some interesting new rearrangements have been uncovered, and some synthetically useful procedures have been developed.

Results and Discussion

Suitably constituted alkenylaryl radicals undergo ring closure more rapidly than do their alkenyl radical analogues. Thus, the rate constant for ring closure of the 2-(3-butenyl)phenyl radical **10a** ($k_c \sim 4 \times 10^8$ s^{-1} at 80 °C)[19] is more than 2 orders of magnitude greater than that ($k_c = 1.4 \times 10^6$ s^{-1} at 80 °C)[22] for the hexenyl radical **12a**. Factors that favor the cyclization of alkenylaryl radicals by comparison with alkenyl systems include the lower strain energies of the transition structures for the former. These, in turn, reflect the absence from aryl systems of the unfavorable nonbonded interactions involving the protons at C1 and C2 in alkenyl systems.[23] Also, it is possible that σ radicals such as aryl radicals are intrinsically more reactive than alkyl π radicals. Whatever the cause, the relatively high reactivity exhibited by aryl radicals for intramolecular addition to C=C bonds should be retained in analogous additions to C=O bonds. Consequently the ring closure, **10b** → **11b**, whatever its absolute rate, is likely to be more favorable than its alkyl radical counterpatt, **12b** → **13b**.



10 11

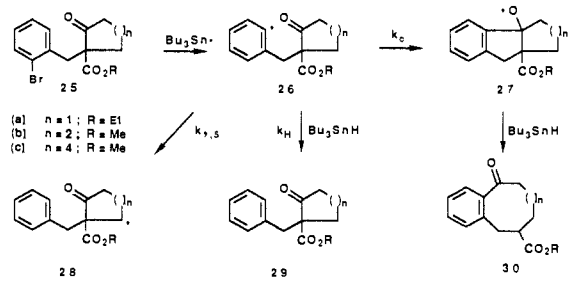
12 13

(a) R = H ; X = CH_2 (b) R = CH_3; X = O (c) R = CH_3 ; X = CH_2

Although exceptions have been noted, e.g., **6** → **7** at 80 °C,[18] alkoxy radicals usually undergo fragmentation by fission of the weakest β–γ bond. In view of the high dissociation energy of C–C_{aryl} bonds by comparison with C–C_{alkyl} bonds, the β-fission of **11b** to afford **10b** is unlikely. The most probable course of the reaction will be formation of an alkyl radical with opening of the newly formed ring, and this process should be facilitated by functionality that enhances the stability of the species so formed.

In the event these expectations were realized when the substituted acetoacetate **14** was treated with Bu_3SnH (0.05 M) at

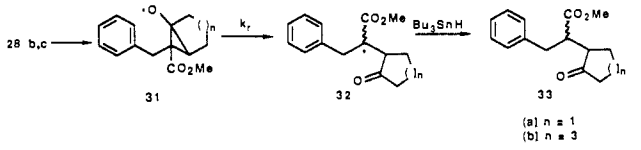
Scheme V



25 26 27

28 29 30

Scheme VI

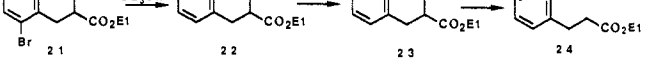


31 32 33

(a) n = 1
(b) n = 3

80 °C. The reaction afforded only the rearranged product **20** (26%) and the product **18** (65%) of direct reduction, the formation of which is consistent with the expected reaction Scheme IV. Also, in accord with this mechanism, which shows cyclization to be in direct competition with H transfer from stannane to **15**, the yield of **20** was increased to 38% by the use of more dilute (0.01 M) stannane. Accurate kinetic analysis of the system has not yet been completed. However, the present results, which give $k_c/k_H \simeq 10^{-2}$ s^{-1} at 80 °C, show ring closure to **15** to be considerably slower than that of the related alkenylaryl radicals **10a**, for which $k_c/k_H = 1.04$ M at 80 °C,[19] and **10c**, for which k_c/k_H is estimated to be about 0.35 M at 80 °C.[19] The failure of the reaction to afford the alcohol **17** is significant since the mechanism involves direct competition between its formation and β-fission to generate **19**. The results show that $k_f/k_{OH} > 0.1$. If k_{OH} has a value similar to that for the reaction of $Bu^tO^•$ with Bu_3SnH, then $k_f \geq 10^7$ s^{-1}. This appears to be considerably higher than the rate constant for β-fission of simple alkoxy radicals and reflects the stabilizing effect of the ethoxycarbonyl group on the radical formed. Separate experiments in these laboratories have shown that systems lacking this substituent undergo ring opening much more slowly.

Since suitable cyanoalkyl radicals readily undergo ring closure, the radical **22** was expected to undergo rapid rearrangement. In fact, treatment of the bromide, **21**, with Bu_3SnH (0.05 M) afforded mainly the rearrangement product **24** (59%) together with ethyl benzylcyanoacetate (12%) formed by direct reduction. The usual calculation based on the relative yields of rearranged and direct reduction product gives $k_c/k_H \sim 0.15$ M; i.e., the radical **22** undergoes rearrangement about 8 times more rapidly than its ketonic counterpart, **15**. By contrast with analogous cyanoalkyl ring closures,[12j,14] the reaction of **21** with Bu_3SnH afforded no cyclic imine; clearly, H-atom transfer from stannane to **23** occurs too slowly to compete with its ring opening.



21 22 23 24

The rearrangement by consecutive addition to the carbonyl group and β-fission of radicals (e.g., **26**) containing a cyclic β-keto ester moiety should afford ring expanded products by the mechanism of Scheme V. In the event treatment of the bromide **25a** with Bu_3SnH (0.05M) gave the expected rearrangement product **30a** in only 14% yield. The major product (75%) was that, **29a**, expected from direct reduction.

Application of the method to the cyclohexane derivative, **25b**, afforded four products, of which the major, **29b** (58%), contained an unrearranged skeleton. One minor product (21%) was found to be the ring-expanded compound, **30b**, while the other two (total 15%) were identified as the two diastereoisomers of the cyclopentanone derivative, **33a**.

In the case of the cyclooctanone, **25c**, the reaction afforded no ring-expanded product **30c**. Direct reduction gave **29c** in small

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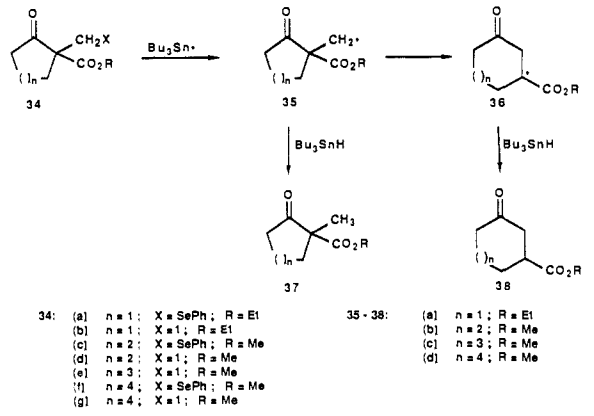
Scheme VII



yield (12%) but the major products (total 86%) were the two diastereoisomers of the ring-contracted compound **33b**.

The mechanism of formation of **33a** and **33b** appears to involve rearrangement of the radicals, **28b** and **28c**, generated by 1,5-hydrogen-atom transfer from the aliphatic to the aromatic ring in **26b** and **26c**. Previous experiments in these laboratories have indicated that such transfers from alkyl to aryl centers occur readily with rate constants of the order of 10^7 s^{-1}.[24] In the case of the radical **26b**, the usual calculations show that $k_{1,5}/k_H$ is about 0.2 M. Since k_c/k_H for the radical **15** is estimated to be 0.01 M, it is not surprising that ring expansion competes inefficiently with rearrangement occurring via 1,5-H-atom transfer.

Schemes V and VI show that the final yield of ring-contracted products depends on the ease with which both 1,5-hydrogen-atom transfer and rearrangement of the resultant cyclic radical occur. The former will depend upon the strain energy generated in the attainment of conformations containing the approximately collinear disposition of the C–H–C centers required for efficient atom transfer.[4a,c] Inspection of models suggests that such strain will decrease with increasing flexibility of the aliphatic ring. Hence, 1,5-H-atom transfer should occur most readily in the radical, **26c**, containing the cyclooctanone ring and least readily in that, **26a**, containing the cyclopentanone moiety. The ease with which further rearrangement of **28** occurs should reflect ring strain both in the bicyclic alkoxy species, **31** (which may represent either an intermediate or a transition structure), and in the product radicals, **32**. Clearly, such factors do not present a substantial barrier to ring contraction of the eight-membered cyclic radical **28c**. However, they would be expected to disfavor rearrangement of the cyclohexyl radical **28b** and to preclude rearrangement of the cyclopentyl radical **28a**. In the case of each of the radicals **28a–c** intermolecular H transfer from stannane will afford the same products as those arising by direct reduction of **26a–c**. The occurrence of such an indirect route was detected by treatment of **25a** with Bu_3SnD when the **29a** produced was found by ^2H NMR to contain deuterium both on the aromatic ring and on the carbon adjacent to the ester carbonyl.

Since the relative proportions of **29b,c** formed by direct reduction of **26b,c** and by H-atom transfer to **28b,c** cannot be accurately determined from our present data, it is not possible to obtain firm rate constants for the ring-contraction step. However, if all of **29b** arises via **28b** and if the rate constant for the reaction of **28b** with Bu_3SnH is similar to that for cyclohexyl radical,[22] it can be shown that the rate constant k_r for the rearrangement **28b** → **32a** is at least 5×10^4 s^{-1} at 80 °C. Similarly, k_r for the ring contraction of **28c** must be about 1×10^6 s^{-1} at 80 °C.

The recognition that radicals such as **28b** and **28c** undergo ring contraction by acyl migration, even though formation of the intermediate radical (or transition structure) **31** must involve a considerable increase in strain energy, suggested that a similar acyl shift might occur readily in species containing an exocyclic radical center, such as **35**, to afford ring-expanded products by the mechanism of Scheme VII.

(24) Abeywickrema, A. N., unpublished observations.

Table I. Relative and Isolated Yields of Products from the Reaction of Iodo- or (Phenylseleno)methyl β-Keto Esters with Bu_3SnH[a]

substrate	product	rel yield,[b] %	isolated yield, %
34a	**37a**	2	
	38a	98	88
34b	**38a**		82
34c	**37b**	15	5
	38b	85	48
34d	**37b**	18	15
	38d	82	76
34e	**37c**	7	5
	38c	93	90
34f	**37d**	22	16
	38d	78	73
34g	**37d**	17	10
	38d	83	75
40a	**41a**	86	55
	42a	14	9

[a] Typical reaction conditions: AIBN/Bu_3SnH (ca. 0.2 M in benzene) added over 3 h to substrate (ca. 0.1 M) in benzene at 80 °C. Ratio AIBN/Bu_3SnH/substrate = 0.1/1.2/1.0. [b] Determined by GLC analysis of the crude reaction product.

To test this hypothesis, suitable substrates, **34a–g** (X = SePh or I), were prepared by alkylation of the appropriate cyclic β-keto esters with bromo- or chloro(phenylseleno)methane or diiodomethane. In the case of the former, the alkylation proceeded smoothly with DBU in DMF or sodium methoxide in methanol. However, the iodo compounds could only be obtained when alkylation was conducted with sodium hydride in DMSO.[20m] The yields of alkylated products were generally in the range 50–80%. Treatment of the cyclohexane derivative, **34d** (X = I) with Bu_3SnH (0.11 M) in boiling benzene gave some ring-expanded product, **38b**, but the yield was low (15%) and the major product (85%) was that, **37b**, formed by direct reduction. In terms of the expected mechanism (Scheme VII) the reaction **35b** → **36b** is too slow to compete effectively with H-atom transfer from Bu_3SnH under these conditions. Accordingly, we applied a technique whereby Bu_3SnH in dilute benzene solution containing AIBN as initiator was slowly added from a syringe pump to the iodide in boiling benzene. Under these conditions when Bu_3SnH is rapidly consumed as it is added and hence its effective concentration is very low, the rearrangement product, **38b**, was formed efficiently and only a trace of the direct reduction product, **37b**, could be detected. The yields of products obtained by similar treatment of suitable selenides and iodides are given in Table I.

A preliminary experiment indicated that this method could also be useful for the preparation of acyclic γ-keto esters. The iodide **40a** was prepared by iodomethylation of the acetoacetate ester **39a**. Treatment of the iodide **40a** with Bu_3SnH gave mainly the rearranged product **41a**, along with some of the direct reduction product **42a**. Widdowson and co-workers have previously reported the formation of **41a** when a solution of hexabutylditin was photolyzed in the presence of iodide **39a**.[20m] However, under their conditions the major reaction product was the direct reduction product **42a**, and only a small amount of the rearranged species **41a** was observed. There are conflicting reports in the literature regarding the ability of thioesters to undergo a 1,2 rearrangement of this type. Halpern has reported low levels of rearrangement to form the thioester **41b**, when the bromide **40b** was treated with highly dilute solutions of Bu_3SnH.[26] However, Kochi[27] and Widdowson[20m] have independently reported that radicals of this type do not undergo any rearrangement. The iodide **40c** was

(25) Shortly after a preliminary report of these results was published,[1] a communication by Dowd (Dowd, P.; Choi, S.-C. *J. Am. Chem. Soc.* **1987**, *109*, 3493) appeared reporting essentially the same results when the β-keto esters **34b,d,e,g** (X = Br) were treated with Bu_3SnH under high-dilution conditions. It was reassuring to see how closely both sets of results agreed.

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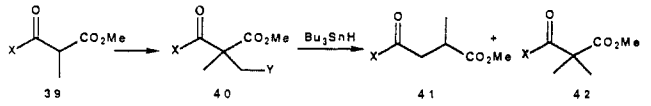
prepared by iodomethylation of the thioester **39b**. When **40c** was treated with Bu_3SnH using our high-dilution procedure, the major product (92–97% by GLC) was **42b**, formed by direct reduction. However, a small (3–8%) but measurable amount of the rearranged thioester, **41b**, was also observed.



39 40 41 42

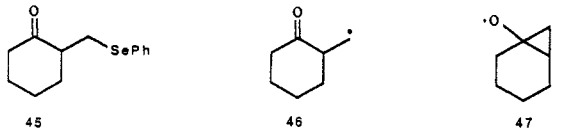
(a) X = Me; Y = I
(b) X = SEt; Y = Br
(c) X = SEt; Y = I

Cyclic β-keto esters are readily available, either by a Dieckmann condensation[28] or by α-alkoxycarbonylation of a cycloalkanone,[29] while the preparation of acyclic β-keto esters by alkylation of acetoacetate esters is one of the classical reactions of synthetic organic chemistry.[30] This procedure thus provides a convenient, flexible, and synthetically useful route to the γ-keto ester functionality from readily available starting materials, of particular interest for the preparation of relatively inaccessible cyclic γ-keto esters.

In experiments designed to afford mechanistic insights, the iodide **34d** was heated at 80 °C in sealed ampules with degassed solutions of known concentration of Bu_3SnH and AIBN in benzene, and the yields of **37b** and **38b** were determined by quantitative GLC. Substitution of the data (see Experimental Section) into the appropriate integrated rate equation[31] gave $k_c/k_H \simeq 0.0025 \pm 0.0006$ M, where k_c and k_H are the rate constants for conversion of **35b** into **36b** and **37b**, respectively. On the assumption that k_H is similar in value to the rate constant for the analogous reaction of the neopentyl radical,[22] k_c is about 2×10^4 s^{-1}. This is about some 3 orders of magnitude less than the rate constant for rearrangement of the somewhat similar all-carbon system, **43** → **44**.

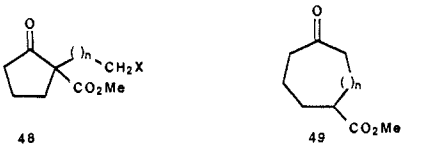
43 44

When the selenide **45**, prepared by Lewis acid catalyzed (phenylseleno)methylation of 1-((trimethylsilyl)oxy)cyclohexene,[32] was treated with Bu_3SnH under the same high-dilution conditions as had been successfully applied to cyclic keto ester derivatives such as **34c**, the only product formed was 2-methylcyclohexanone arising by direct reduction. The failure of the radical, **46**, to undergo rearrangement indicates that stabilization of the radicals formed by ring expansion affects the rate of the rearrangement reaction. The simplest explanation for this observation is that these rearrangements occur in one step; i.e., structures such as **31** and **47** represent transition states rather than true intermediates.



45 46 47

Rearrangements involving 1,4 or 1,5 transfer of acyl groups are expected to proceed more slowly than the 1,2 shifts described above, because of the greater loss of rotational freedom involved in formation of the transition complex. Nevertheless ring expansions can be accomplished, albeit in modest yield, by such reactions. Methyl 2-oxocyclopentane-1-carboxylate was alkylated with 1-bromo-3-chloropropane to give the chloropropyl compound **48a**. Exchange of chloride for iodide gave the substrate **48b**. Treatment of the iodide, **48b**, with Bu_3SnH in the usual way gave the cyclooctanone **49a** in 55% yield (GLC). The other reaction product was the direct reduction product **48c**. The higher homologue **48d** was prepared directly by alkylation of the keto ester with 1,4-dibromobutane. However, treatment of the iodide, **48d**, with Bu_3SnH gave only 5% of the cyclononanone, **49b**, and the major product was formed by direct reduction to give **48e**. Since both the rate of the ring closure of the intermediate radical and the rate of chain initiation should be increased by increase in temperature, the reaction was repeated in 130 °C in *tert*-butylbenzene. As expected the (GLC) yield of rearranged product, **49b**, was increased to 20%.

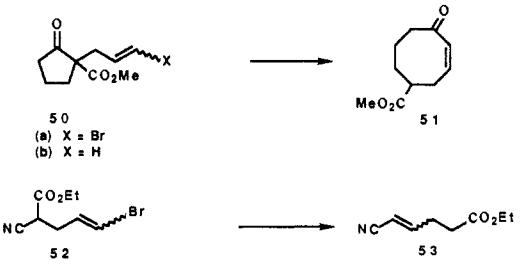


48 49

(a) n = 2; X = Cl
(b) n = 2; X = I
(c) n = 2; X = H
(d) n = 3; X = Br
(e) n = 3; X = H

(a) n = 2
(b) n = 3

Finally, we conducted some preliminary explorations of the rearrangement of vinyl radicals by acyl or cyano shifts. The substrates were prepared by alkylation of the corresponding β-keto ester or cyano ester with 1,3-dibromopropene. The formation of modest amounts of the ring-expanded ketone **51** (37% by GLC) and of the α,β-unsaturated nitrile **53** (*E*:*Z* ≃ 1:1, 32% isolated yield) by Bu_3SnH treatment of **50a** and **52**, respectively, suggests that such reactions could also be developed into synthetically useful procedures. The formation of **53** as a mixture of geometric isomers is at first surprising. Rearrangement of the vinyl radical formed from **52** should give only the *Z* isomer if the reaction is proceeding by an intramolecular rearrangement. Presumably the initial reaction product is solely the *Z* isomer, but this is isomerized under the reaction conditions by conjugate addition of $Bu_3Sn^{\bullet}$ radical present in the reaction mixture followed by bond rotation and β-elimination of $Bu_3Sn^{\bullet}$.



50 51

(a) X = Br
(b) X = H

52 53

Conclusion

The results presented above show that, in a number of different systems, acyl- and cyano-transfer rearrangements conforming to the general mechanism of Scheme III are possible. Significant amounts of rearranged material are observed when both the product radical is stabilized relative to the starting radical and the concentration of reagents (in our case Bu_3SnH) capable of trapping the initially formed radical is kept as low as possible. For transfer to an aryl radical, alkyl-to-aryl 1,5-hydrogen transfer is also a serious competitive side reaction. Comparison of the results for substrates **14** and **21** indicates that cyano groups are transferred more readily than acyl groups. 1,2-Acyl-transfer reactions, proceeding through a three-membered intermediate (or transition state?), occur significantly more rapidly than acyl transfers over a larger number of atoms. The procedure for carrying out 1,2-acyl-transfer reactions described herein constitutes a convenient and efficient synthetic route to γ-keto esters from readily available β-keto esters.

Experimental Section

General Methods. Unless otherwise noted all reactions were run under a positive pressure of dry nitrogen in flasks that were oven dried and were allowed to cool under a stream of nitrogen. ^1H NMR spectra were recorded on Varian XL-200 or XL-300 spectrometers operating at 200

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or 300 MHz, respectively. All chemical shifts are reported in δ, parts per million (ppm) downfield from tetramethylsilane (TMS). Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Coupling constants are reported in hertz (Hz). ^{13}C NMR spectra were recorded on the Varian XL-300 spectrometer operating at 75.4 MHz as solutions in $CDCl_3$ and are reported in ppm relative to the central line (assigned 77.0 ppm downfield relative to TMS) of the triplet due to the solvent carbon signal. Assignment of the hydrogen substitution of each carbon was made by use of the DEPT pulse sequence.[33] Infrared spectra were measured on a Perkin-Elmer 683 spectrophotometer and were obtained as liquid films on sodium chloride plates, as chloroform solutions in 0.5-mm path length sodium chloride cells, or as Nujol mulls. Mass spectra were recorded on a VG-Micromass 7070F medium-resolution mass spectrometer operating at 70 eV. The molecular ion and significant fragment ions in the electron impact mass spectra are reported as the mass/charge ratios (m/e), followed by their realtive ion intensities as ratios of the base peak (100%). High-resolution mass spectrometry (for exact mass measurements) was carried out on an MS-902 high-resolution mass spectrometer. Gas–liquid chromatographic (GLC) analyses were performed on a Varian 6000 chromatograph equipped with a flame ionization detector and coupled to a Hewlett-Packard 3390A recorder/integrator using either a 2 m × 1.5 mm 2% OV-17 on Gaschrom Q (60–80 mesh) packed column (column A) or a 25 m × 0.2 mm vitreous silica capillary column (SGE25QC2/BPI-1.0) (column B) with helium as the carrier gas.

Ajax Grade 923 (0.07–0.15 mm) silica gel was used for column chromatography. Flash chromatography was carried out by following the method of Still[34] using Merck Kieselgel 60 (230–400 mesh) silica gel. Medium-pressure liquid chromatography (MPLC) was carried out with Merck prepacked LiChroprep Si 60 (40–60 μm) columns.

The following abbreviations were used in the body of the text: AIBN (azobis(isobutyronitrile)), Bu_3SnH (tributyltin hydride), DBU (1,8-diaza[5.4.0]bicyclo-7-undecene), DMF (dimethylformamide), DMSO (dimethyl sulfoxide), ether (diethyl ether), LDA (lithium diisopropylamide), NaH (sodium hydride), and THF (tetrahydrofuran).

THF was freshly distilled from sodium/benzophenone ketyl prior to use. DMSO and DMF were distilled under reduced pressure from calcium hydride and were stored over 4-Å molecular sieves. Benzene (Ajax) and dichloromethane (Ajax) were used as supplied as the analytical grade reagent and were stored over 4-Å molecular sieves. Bu_3SnH (Aldrich) was stored under nitrogen in the freezer. NaH (Aldrich) was used as a 50% dispersion in mineral oil, and weights were recorded for the dispersion. *o*-Bromobenzyl bromide,[35] methyl 2-oxocyclohexane-1-carboxylate,[29] methyl 2-oxocycloheptane-1-carboxylate,[29] methyl 2-oxocyclooctane-1-carboxylate,[29] bromo(phenylseleno)methane,[36] chloro(phenylseleno)methane,[37] methyl 2-methyl-3-oxobutanoate (**39a**),[38] methyl 2,2-dimethyl-3-oxobutanoate (**42a**),[38] *O*-methyl *S*-ethyl 3-methylmonothiosuccinate (**41b**),[20m,39] 1-((trimethylsilyl)oxy)cyclohexene,[40] and (*E*,*Z*)-1,3-dibromopropene[41] were prepared by the literature methods. All other starting materials were commercially available.

In the body of the text a compound was described as being identical with an authentic sample if the two compounds were indistinguishable by their spectral data (^1H and ^{13}C NMR, IR, and MS) and if they had the same GLC retention time relative to an internal standard. A compound was described as corresponding by GLC analysis to an authentic sample if the two compounds had the same GLC retention time relative to an internal standard and if addition of a sample of the authentic compound resulted in peak enhancement. Organic solutions that had been in contact with water were dried over anhydrous magnesium sulfate. Concentration under reduced pressure implies the removal of solvent on a Büchi rotary evaporator operating at water pump pressure.

Ethyl 2-Acetyl-3-(2-bromophenyl)propionate (14). General Alkylation Procedure A. An ethanolic solution of sodium ethoxide was prepared by the addition of sodium (0.5 g, 22 mmol) to dry ethanol (20 mL). Ethyl acetoacetate (10.4 g, 80.0 mmol) was added to the reaction mixture, and the solution was stirred for 10 min at room temperature. *o*-Bromobenzyl bromide (5 g, 20 mmol) was added, and the reaction mixture was heated under reflux for 15 h. The mixture was concentrated under reduced pressure and the residue was taken up in ether (100 mL). The ether solution was washed with water (50 mL) and was dried. The residue after removal of solvent under reduced pressure was purified by fractional distillation to afford 5.16 g (86%) of the alkylation product **14** as a colorless oil: bp 118 °C/0.9 mmHg; ^1H NMR (200 MHz) δ 7.2 (4 H, m), 4.12 (2 H, q, J = 7.1 Hz), 3.97 (1 H, t, J = 7.1 Hz), 3.28 (2 H, m), 2.21 (3 H, s), 1.17 (3 H, t, J = 7.1 Hz); IR (neat) 1740, 1710 cm^{-1}. Anal. Calcd for $C_{13}H_{15}BrO_3$: C, 52.19; H, 5.05. Found: C, 52.32; H, 5.00.

Ethyl 2-Cyano-3-(2-bromophenyl)propionate (21). Following standard procedure A, ethyl cyanoacetate (7.5 g, 66 mmol) was alkylated with *o*-bromobenzyl bromide (5 g, 20 mmol). Fractional distillation of the residue isolated after workup afforded 2.32 g (41%) of the alkylation product **21** as a clear oil, bp 110–118 °C/0.05 mmHg, which solidified on standing to form a white solid: mp 38–40 °C; ^1H NMR (200 MHz) δ 7.32 (4 H, m), 4.25 (2 H, q, J = 7.1 Hz), 3.93 (1 H, m), 3.47 (1 H, m), 3.25 (1 H, m), 1.26 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 165.2 (s), 134.8 (s), 133.1 (d), 131.7 (d), 127.9 (d), 129.6 (d), 124.2 (s), 115.8 (s), 63.0 (t), 37.4 (d), 36.1 (t), 13.9 (q); IR (neat) 2250, 2200, 1740 cm^{-1}. Anal. Calcd for $C_{12}H_{12}BrNO_2$: C, 51.09; H, 4.24; N, 4.96. Found: C, 50.64; H, 4.29; N, 4.96.

Ethyl 1-(2-Bromobenzyl)-2-oxocyclopentane-1-carboxylate (25a). Following standard procedure A, ethyl 2-oxocyclopentane-1-carboxylate (12.5 g, 80.0 mmol) was alkylated with *o*-bromobenzyl bromide (5.0 g, 20.0 mmol). The residue isolated from workup of the reaction mixture was purified by fractional distillation to afford 5.52 g (85%) of the title compound **25a** as a pale yellow oil: bp 190 °C/4.5 mmHg; ^1H NMR (200 MHz) δ 7.2 (4 H, m), 4.19 (2 H, q, J = 7.1 Hz), 3.55 and 3.32 (2 H, AB q, J = 14.3 Hz), 1.6–2.5 (6 H, m), 1.26 (3 H, t, J = 7.1 Hz); ^{13}C NMR δ 214.5 (s), 170.8 (s), 136.7 (s), 132.9 (d), 131.4 (d), 128.4 (d), 127.5 (d), 126.3 (s), 61.6 (t), 61.4 (s), 38.1 (t), 37.5 (t), 31.7 (t), 19.7 (t), 14.0 (q); IR (neat) 1750, 1710 cm^{-1}. Anal. Calcd for $C_{15}H_{17}BrO_3$: C, 55.40; H, 5.27. Found: C, 55.11; H, 5.79.

Methyl 1-(2-Bromobenzyl)-2-oxocyclohexane-1-carboxylate (25b). Following standard procedure A, methyl 2-oxocyclohexane-1-carboxylate (4.15 g, 26.6 mmol) was alkylated with *o*-bromobenzyl bromide (5.31 g, 21.3 mmol) to afford the impure product as a heavy oil, bp 120 °C/0.05 mmHg. The crude product was purified by MPLC (10% ethyl acetate/hexane) to afford 2.65 g (60%) of the title compound **25b** as a white solid: mp 50–51 °C; ^1H NMR (200 MHz) δ 7.13 (4 H, m), 3.69 (3 H, s), 3.47 and 3.24 (2 H, AB q, J = 14.3 Hz), 1.5–2.6 (8 H, m); ^{13}C NMR δ 206.5 (s), 171.2 (s), 136.4 (s), 132.9 (d), 132.1 (d), 128.3 (d), 127.0 (d), 125.8 (s), 61.8 (s), 52.3 (q), 41.1 (t), 38.7 (t), 35.3 (t), 27.4 (t), 22.4 (t); IR (Nujol) 1745, 1710 cm^{-1}. Anal. Calcd for $C_{15}H_{17}BrO_3$: C, 55.40; H, 5.27. Found: C, 55.73; H, 5.45.

Methyl 1-(2-Bromobenzyl)-2-oxocyclooctane-1-carboxylate (25c). Following standard procedure A, methyl 2-oxocyclooctane-1-carboxylate (4.0 g, 21.7 mmol) was alkylated with *o*-bromobenzyl bromide (4.34 g, 17.4 mmol) to yield, after recrystallization of the crude product from ether/hexane, 4.7 g (77%) of the alkylation product **25c** as a white crystalline solid: mp 78–80 °C; ^1H NMR (200 MHz) δ 7.16 (4 H, m), 3.61 (3 H, s), 3.57 and 3.25 (2 H, AB q, J = 14.7 Hz), 1.1–2.7 (12 H, m); ^{13}C NMR δ 210.9 (s), 171.8 (s), 136.9 (s), 132.9 (d), 131.5 (d), 128.2 (d), 127.1 (d), 125.8 (s), 63.4 (s), 52.2 (q), 39.2 (t), 36.1 (t), 29.7 (t), 27.9 (t), 25.9 (t), 24.9 (t), 23.3 (t); IR (Nujol) 1740, 1700 cm^{-1}. Anal. Calcd for $C_{17}H_{21}BrO$: C, 57.80; H, 5.90. Found: C, 58.12; H, 6.07.

Reaction of 14 with Bu_3SnH. A deoxygenated solution of bromide **14** (100 mg, 0.33 mmol), AIBN (3 mg, 0.02 mmol), and Bu_3SnH (117 mg, 0.40 mmol) in benzene (8.0 mL) ($[Bu_3SnH]_0$ = 0.05 M) was heated under reflux for 2 h. The solvent was removed under reduced pressure and the residue was purified by MPLC (30% ethyl acetate/hexane) to afford 48 mg (65%) of **ethyl 2-acetyl-3-phenylpropionate (18)** as a clear oil: bp 155–158 °C/13 mmHg (lit.[42] bp 156–160 °C/13 mmHg); ^1H NMR (200 MHz) δ 7.19 (5 H, m), 4.14 (2 H, q, J = 7.1 Hz), 3.78 (1 H, t, J = 7.6 Hz), 3.15 (2 H, d, J = 7.6 Hz), 2.18 (3 H, s), 1.20 (3 H, t, J = 7.1 Hz). Further elution afforded 19 mg (26%) of **ethyl 3-(2-acetylphenyl)propionate (20)** as a clear liquid: bp 140 °C/13 mmHg; ^1H NMR (200 MHz) δ 7.7 (1 H, m), 7.31 (3 H, m), 4.11 (2 H, q, J = 7.1 Hz), 3.17 (2 H, t, J = 7.8 Hz), 2.64 (2 H, t, J = 7.8 Hz), 2.60 (3 H, s), 1.22 (3 H, t, J = 7.1 Hz); IR (neat) 1730, 1680 cm^{-1}. Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.97; H, 7.31.

The experiment was repeated with bromide **14** (200 mg, 0.67 mmol), Bu_3SnH (234 mg, 0.80 mmol), AIBN (7 mg), and benzene (80 mL) ($[Bu_3SnH]_0$ = 0.01 M). By following the same workup and purification procedure described above, the reaction afforded 87 mg (59%) of the open-chain keto ester **18** and 56 mg (38%) of the rearranged ester **20**.

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Reaction of 21 with Bu_3SnH. A solution of bromide **21** (100 mg, 0.36 mmol), AIBN (4 mg, 0.024 mmol), and Bu_3SnH (124 mg, 0.43 mmol) in deoxygenated benzene (8.5 mL) ($[Bu_3SnH]_0$ = 0.05 M) was heated under reflux for 1 h. TLC and GLC analysis (column A, 170 °C) of the reaction mixture indicated that two products had been formed. The benzene was removed under reduced pressure. The residue was diluted with ether (10 mL) and was stirred overnight with 40% acetic acid/water (4 mL). The layers were separated and the aqueous phase was extracted with ether. The combined ether layers were washed with water and were dried. After removal of the solvent under reduced pressure, the residue was subjected twice to MPLC (30% ethyl acetate/hexane) to afford 51 mg of a mixture of the two reaction products. GLC analysis (column A, 210 °C) of the mixture indicated that the two components, **ethyl 2-cyano-3-phenylpropionate** and **ethyl 3-(2-cyanophenyl)propionate** (**24**), were present in the ratio 17:83. Physical and spectral data for the major component, nitrile **24**: ^1H NMR (200 MHz) δ 7.5 (4 H, m), 4.13 (2 H, q, J = 7.1 Hz), 3.18 (2 H, t, J = 7.6 Hz), 2.71 (2 H, t, J = 7.6 Hz), 1.23 (3 H, t, J = 7.1 Hz); IR (neat) 2220, 1740 cm^{-1}. Anal. Calcd for $C_{12}H_{13}NO_2$: C, 70.92; H, 6.45. Found: C, 70.83; H, 6.22.

The experiment was repeated with a solution of bromide **21** (100 mg, 0.36 mmol), Bu_3SnH (517 mg, 1.78 mmol), and AIBN (20 mg, 0.12 mmol) in benzene (1.8 mL) ($[Bu_3SnH]_0$ = 1.0 M). By following the same workup and purification procedure used above, the reaction afforded 44 mg of a 93:7 mixture of the direct reduction product and nitrile **24**. Spectral data for the major reaction component, ethyl 2-cyano-3-phenylpropionate: bp 150 °C/13 mmHg (lit.[43] bp 165–173 °C/15 mmHg); ^1H NMR (200 MHz) δ 7.31 (5 H, m), 4.23 (2 H, q, J = 7.1 Hz), 3.72 (1 H, m), 3.23 (2 H, m), 1.26 (3 H, t, J = 7.1 Hz).

Reaction of 25a with Bu_3SnH. A solution of bromide **25a** (200 mg, 0.62 mmol), Bu_3SnH (215 mg, 0.74 mmol), and AIBN (6 mg, 0.037 mmol) in deoxygenated benzene (14.8 mL) was heated under reflux for 2 h. The solvent was removed under reduced pressure and the residue was purified by MPLC (20% ethyl acetate/hexane) to afford 113 mg (75%) of **ethyl 1-benzyl-2-oxocyclopentane-1-carboxylate** (**29a**) as a clear liquid: bp 174 °C/13 mmHg (lit.[42] bp 186–190 °C/14 mmHg); ^1H NMR (200 MHz) δ 7.22 (5 H, m), 4.17 (2 H, q, J = 7.1 Hz), 3.16 (2 H, d, J = 6.1 Hz), 1.5–2.5 (6 H, m), 1.25 (3 H, t, J = 7.1 Hz). Further elution afforded 21 mg (14%) of **ethyl 10-oxo-5,6,7,8,9,10-hexahydrobenzocyclooctene-6-carboxylate** (**30a**) as a clear oil: ^1H NMR (200 MHz) δ 7.80 (1 H, d, J = 7.6 Hz), 7.2–7.4 (3 H, m), 4.17 (2 H, q, J = 7.1 Hz), 2.7–3.6 (5 H, m), 1.7–1.8 (4 H, m), 1.28 (3 H, t, J = 7.1 Hz); ^{13}C NMR δ 205.2 (s), 174.6 (s), 139.9 (s), 137.4 (s), 132.0 (d), 131.9 (d), 128.4 (d), 127.1 (d), 60.7 (t), 44.1 (d), 43.5 (t), 35.9 (t), 26.6 (t), 21.9 (t), 14.3 (q); IR (neat) 1730, 1690, 1665 cm^{-1}. Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 72.95; H, 7.31.

Reaction of 25b with Bu_3SnH. A solution of bromide **25b** (250 mg, 0.77 mmol), Bu_3SnH (269 mg, 0.92 mmol), and AIBN (8 mg, 0.05 mmol) in deoxygenated benzene (18.5 mL) was heated under reflux for 1 h. The benzene was removed under reduced pressure and the residue was purified by MPLC (20% ethyl acetate/hexane) to afford 109 mg (58%) of **methyl 1-benzyl-2-oxocyclohexane-1-carboxylate** (**29b**) as a clear oil: ^1H NMR (200 MHz) δ 7.20 (5 H, m), 3.63 (3 H, s), 3.56 and 2.85 (2 H, AB q, J = 13.7 Hz), 1.4–2.5 (8 H, m); IR (neat) 1740, 1710 cm^{-1}. Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 73.03; H, 7.17. Further elution afforded 39 mg (21%) of **methyl 11-oxo-6,7,8,9,10,11-hexahydro-5*H*-benzocyclononene-6-carboxylate** (**30b**) as a clear oil: ^1H NMR (200 MHz) δ 7.33 (4 H, m), 3.66 (3 H, s), 3.18 (2 H, m), 2.84 (2 H, m), 2.59 (1 H, m), 1.6–2.1 (6 H, m); ^{13}C NMR δ 210.6 (s), 175.3 (s), 142.8 (s), 136.3 (s), 131.2 (d), 130.4 (d), 126.7 (d), 126.3 (d), 51.7 (q), 45.8 (d), 42.1 (t), 33.1 (t), 26.5 (t), 25.7 (t), 23.9 (t); IR (neat) 1740, 1730, 1690, 1665 cm^{-1}. Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 73.32; H, 7.52. Further elution afforded 29 mg (15%) of an inseparable mixture of the two diastereoisomers of **2-(1-carbomethoxy-2-phenylethyl)cyclopentanone** (**33a**) as a colorless oil: ^1H NMR (200 MHz) δ 7.22 (5 H, m), 3.63 (1.5 H, s), 3.59 (1.5 H, s), 2.7–3.4 (2 H, m), 1.5–2.5 (8 H, m); ^{13}C NMR δ 219.2 (s), 218.2 (s), 174.6 (s), 139.0 (s), 138.8 (s), 129.0 (d), 128.8 (d), 128.6 (d), 128.4 (d), 51.6 (q), 50.1 (d), 48.9 (d), 47.7 (d), 46.5 (d), 38.2 (t), 38.1 (t), 35.9 (t), 35.7 (t), 27.2 (t), 25.7 (t), 20.6 (t), 20.5 (t); IR (neat) 1735 (broad) cm^{-1}. Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 73.19; H, 7.22.

Reaction of 25c with Bu_3SnH. A solution of bromide **25c** (250 mg, 0.71 mmol), Bu_3SnH (247 mg, 0.85 mmol), and AIBN (7 mg, 0.04 mmol) in deoxygenated benzene (17 mL) was heated under reflux for 3 h. The solvent was removed under reduced pressure and the residue was purified by MPLC (20% ethyl acetate/hexane) to afford 23 mg (12%) of **methyl 1-benzyl-2-oxocyclooctane-1-carboxylate** (**29c**) as a colorless oil: ^1H NMR (200 MHz) δ 7.22 (5 H, m), 3.63 (3 H, s), 3.47 and 2.91 (2 H, AB q, J = 13.9 Hz), 1.0–2.7 (12 H, m); IR (neat) 1740, 1710 cm^{-1}; m/e 274 (80), 215 (40), 214 (100); exact mass calcd for $C_{17}H_{22}O_3$ 274.1569, found 274.1569. Further elution yielded a mixture of two compounds. These were separated by MPLC (6% ethyl acetate/hexane) to afford 75 mg (38%) of one diastereoisomer of **2-(1-carbomethoxy-2-phenylethyl)cycloheptanone** (**33b**) as a light brown oil: ^1H NMR (200 MHz) δ 7.15 (5 H, m), 3.54 (3 H, s), 3.16 (1 H, m), 2.81 (3 H, m), 2.49 (2 H, m), 1.2–2.0 (8 H, m); ^{13}C NMR δ 213.8 (s), 174.5 (s), 138.9 (s), 128.8 (d), 128.4 (d), 126.4 (d), 53.2 (d), 51.4 (q), 49.4 (d), 43.8 (t), 36.4 (t), 29.0 (t), 28.6 (t), 23.8 (t); IR (neat) 1740, 1700 cm^{-1}. Anal. Calcd for $C_{17}H_{22}O_3$: C, 74.42; H, 8.08. Found: C, 74.58; H, 8.15. Further elution afforded 92 mg (47%) of the other diastereoisomer of **33b** as a light brown oil: ^1H NMR (200 MHz) δ 7.23 (5 H, m), 3.51 (3 H, s), 2.9 (4 H, m), 2.5 (2 H, s), 1.2–2.1 (8 H, m); ^{13}C NMR δ 214.4 (s), 138.8 (s), 129.0 (d), 128.3 (d), 126.4 (d), 52.6 (d), 51.4 (q), 48.9 (d), 43.5 (t), 35.5 (t), 29.2 (t), 29.0 (t), 28.4 (t), 23.7 (t); IR (neat) 1730, 1700 cm^{-1}. Anal. Calcd for $C_{17}H_{22}O_3$: C, 74.42; H, 8.08. Found: C, 74.42; H, 8.16.

Preparation of Authentic Samples of the α-Methylated Cyclic β-Keto Esters. The α-methylated cyclic β-keto esters corresponding to the compounds resulting from direct reduction by Bu_3SnH of the α-iodomethyl- or α-(phenylseleno)methyl keto esters were prepared by the general procedure for methylation of β-keto esters of Rhoads et al.[44] The spectral data for these compounds were as follows:

Ethyl 1-methyl-2-oxocyclopentane-1-carboxylate (**37a**): ^1H NMR (200 MHz) δ 4.14 (2 H, q, J = 7.4 Hz), 1.7–2.6 (6 H, m), 1.25 (3 H, s), 1.19 (3 H, t, J = 7.4 Hz); IR (neat) 1750, 1725 cm^{-1}; m/e 170 (2), 142 (73), 125 (29), 97 (45).

Methyl 1-methyl-2-oxocyclohexane-1-carboxylate (**37b**): ^1H NMR (200 MHz) δ 3.66 (3 H, s), 1.4–2.5 (8 H, m), 1.21 (3 H, s); ^{13}C NMR δ 207.8 (s), 173.2 (s), 56.9 (s), 52.3 (q), 40.5 (t), 38.1 (t), 27.4 (t), 22.5 (t), 21.3 (q); IR (neat) 1730, 1715 cm^{-1}; m/e 170 (22), 142 (17), 139 (12), 138 (14), 111 (20), 110 (19).

Methyl 1-methyl-2-oxocycloheptane-1-carboxylate (**37c**): ^1H NMR (200 MHz) δ 3.70 (3 H, s), 2.7 (1 H, m), 2.5 (1 H, m), 2.15 (1 H, m), 1.4–1.9 (7 H, m), 1.34 (3 H, s); ^{13}C NMR δ 210.2 (s), 173.8 (s), 58.6 (q), 52.2 (q), 41.8 (t), 35.3 (t), 30.1 (t), 25.8 (t), 24.7 (t), 21.4 (q); IR (neat) 1740, 1710 cm^{-1}; m/e 184 (7), 153 (2), 152 (60), 127 (24), 125 (32), 124 (33).

Methyl 1-methyl-2-oxocyclooctane-1-carboxylate (**37d**): ^1H NMR (200 MHz) δ 3.52 (3 H, s), 1.4–2.8 (12 H, m), 1.14 (3 H, s); ^{13}C NMR δ 212.5 (s), 173.0 (s), 58.0 (q), 52.1 (q), 38.3 (t), 31.4 (t), 29.2 (t), 25.4 (t), 23.9 (t), 23.3 (t), 17.6 (t); IR (neat), 1740, 1710 cm^{-1}; m/e 198 (8), 167 (22), 166 (100), 139 (17).

Ethyl 2-Oxo-1-((phenylseleno)methyl)cyclopentane-1-carboxylate (**34a**). A solution of ethyl 2-oxocyclopentane-1-carboxylate (520 mg, 3.3 mmol) and DBU (550 mg, 3.3 mmol) in DMF (10 mL) was stirred at room temperature for 10 min. Bromo(phenylseleno)methane (900 mg, 3.6 mmol) was added and the solution was stirred at 70 °C for 1 h. The reaction mixture was cooled to room temperature and was diluted with water (20 mL). The aqueous phase was extracted with ether (3 × 10 mL), and the combined extracts were washed with brine (3 × 10 mL). The residue after concentration under reduced pressure of the dried organic phase was purified by flash chromatography (5% ethyl acetate/hexane) to give 750 mg (70%) of **34a** as a clear oil: ^1H NMR (200 MHz) δ 7.54 (2 H, m), 7.28 (3 H, m), 4.12 (2 H, q, J = 7 Hz), 3.52, 3.09 (2 H, AB q, J = 12.5 Hz), 1.8–2.6 (6 H, m), 1.22 (3 H, t, J = 7 Hz); IR (neat), 3060, 1755, 1725 cm^{-1}; m/e 326 (44), 281 (18), 169 (100); exact mass calcd for $C_{15}H_{18}O_3{}^{80}Se$ 326.0421, found 326.0419.

Methyl 2-Oxo-1-((phenylseleno)methyl)cyclohexane-1-carboxylate (**34c**). Methyl 2-oxocyclohexane-1-carboxylate 310 mg, 2.0 mmol) was alkylated with bromo(phenylseleno)methane (550 mg, 2.2 mmol) using DBU (300 mg, 2.0 mmol) as base by following the alkylation procedure used to prepare **34a**. Purification of the crude reaction product by flash chromatography (10% ethyl acetate/hexane) afforded 340 mg (52%) of the alkylation product **34c** as a yellow oil: ^1H NMR (200 MHz) δ 7.5 (2 H, m), 7.2 (3 H, m), 3.59 (3 H, s), 3.42, 3.12 (2 H, AB q, J = 12.5 Hz), 1.4–2.7 (8 H, m); IR (neat) 3060, 1730, 1715, 1480 cm^{-1}; m/e 326 (10), 237 (13), 169 (71), 157 (68), 79 (100); exact mass calcd for $C_{15}H_{18}O_3{}^{80}Se$ 326.0421, found 326.0423.

Methyl 2-Oxo-1-((phenylseleno)methyl)cyclooctane-1-carboxylate (**34f**). Methyl 2-oxocyclooctane-1-carboxylate (920 mg, 5 mmol) was taken up in methanol (3 mL), and a 2 M solution of sodium methoxide in methanol (2.6 mL, 5.2 mmol) was added dropwise. The solution was stirred at room temperature for 10 min. Chloro(phenylseleno)methane (1.13 g, 5.5 mmol) and a catalytic amount of sodium iodide (80 mg, 0.5

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mmol) were added, and the solution was heated under reflux for 3 h. The bulk of the solvent was removed under reduced pressure, and the residue was treated with ether (10 mL) and 10% aqueous hydrochloric acid (10 mL). The organic layer was isolated and the aqueous phase was extracted with ether (10 mL). The combined extracts were dried and were concentrated under reduced pressure. The residue was purified by flash chromatography (5% ethyl acetate/hexane) to give 1.05 g (59%) of the alkylation product **34f** as a clear oil: ^{1}H NMR (200 MHz) δ 7.5 (2 H, m), 7.2 (o H, m), 3.68, 3.08 (2 H, AB q, J = 12.5 Hz), 3.47 (3 H, s), 1.4–2.9 (12 H, m); IR (neat) 3030, 1730, 1705, 1480 cm^{-1}; m/e 354 (44), 352 (21), 197 (50); exact mass calcd for $C_{17}H_{22}O_3{}^{80}Se$ 354.0734, found 354.0735.

Standard Alkylation Procedure B for the Iodomethylation of β-Keto Esters. Methyl 1-(Iodomethyl)-2-oxocyclohexane-1-carboxylate (34d). Following the general procedure of Widdowson,[20m] NaH (1.3 g, 28 mmol) was washed with hexane (2 × 5 mL) and was suspended in DMSO (30 mL). A solution of methyl 2-oxocyclohexane-1-carboxylate (4.1 g, 26 mmol) in DMSO (10 mL) was added dropwise to the NaH suspension, and the reaction mixture was stirred until hydrogen evolution had ceased. The reaction mixture was cooled in an ice bath, and a solution of diiodomethane (4 mL, 50 mmol) in DMSO (10 mL) was added dropwise. The addition was accompanied by mild evolution of heat. The reaction mixture was stirred for 3 h at room temperature, and the resulting homogeneous solution was diluted with water (100 mL) and was extracted with 10% ether/hexane (3 × 100 m). The combined extracts were washed with brine (2 × 100 mL). The organic phase was dried and was concentrated under reduced pressure. The residue was purifed by flash chromatography (initial elution with 5% ethyl acetate/hexane increasing to 10% ethyl acetate/hexane) to give 5.6 g (73%) of the alkylation product **34d** as a clear oil: ^{1}H NMR (200 MHz) δ 3.78 (3 H, s), 3.63, 3.34 (2 H, AB q, J = 10.3 Hz), 1.3–2.8 (8 H, m); IR (neat) 1730, 1710 cm^{-1}; m/e 297 (85), 296 (1), 237 (15), 169 (100). Anal. Calcd for $C_9H_{13}O_3I$: C, 36.51; H, 4.43; I, 42.86. Found: C, 36.36; H, 4.36; I, 42.52.

Methyl 1-(Iodomethyl)-2-oxocycloheptane-1-carboxylate (34e). Following the general iodomethylation procedure B, methyl 2-oxocycloheptane-1-carboxylate (3.4 g, 20 mmol) was alkylated with diiodomethane (3 mL, 37 mmol) to afford 3.5 g (56%) of the iodomethylation product **34e** as a clear oil: ^{1}H NMR (300 MHz) δ 3.79, 3.31 (2 H, AB q, J = 10.5 Hz), 3.76 (3 H, s), 1.3–2.8 (10 H, m); IR (neat) 1740, 1710 cm^{-1}; m/e 310 (2), 183 (100). Anal. Calcd for $C_{10}H_{15}O_3I$: C, 38.73; H, 4.87; I, 40.92. Found: C, 38.85; H, 4.70; I, 40.83.

Methyl 1-(Iodomethyl)-2-oxocyclooctane-1-carboxylate (34g). Following the general iodomethylation procedure B, methyl 2-oxocyclooctane-1-carboxylate (4.0 g, 22 mmol) was iodomethylated with diiodomethane (4 mL, 50 mmol) to afford 5.5 g (78%) of **34g** as a waxy solid: ^{1}H NMR (200 MHz) δ 3.98, 3.29 (2 H, AB q, J = 10.8 Hz), 3.75 (3 H, s), 1.2–3.0 (12 H, m); IR ($CHCl_3$) 1740, 1705 cm^{-1}; m/e 324 (0.3), 197 (100); exact mass calcd for $C_{11}H_{17}O_3I$ 324.0222, found 324.0223.

Ethyl 1-(Iodomethyl)-2-oxocyclopentane-1-carboxylate (34b). Following general iodomethylation procedure B, ethyl 2-oxocyclopentane-1-carboxylate (3.9 g, 25 mmol) was iodomethylated with diiodomethane to afford 2.8 g (39%) of alkylation product **34b** as a clear oil: ^{1}H NMR (300 MHz) δ 4.2 (2 H, m), 3.60, 3.36 (2 H, AB q, J = 10.2 Hz), 1.6–2.8 (6 H, m), 1.25 (3 H, t, J = 7.0 Hz); IR (neat) 1755, 1725 cm^{-1}; m/e 297 (M^+ + 1,5), 251 (7), 223 (8), 169 (100); exact mass calcd for ($C_9H_{13}O_3I$ + 1) 296.9988, found 296.9941.

Methyl 2-(Iodomethyl)-2-methyl-3-oxobutanoate (40a). Following the general iodomethylation procedure B, β-keto ester **39a** (2.6 g, 20 mmol) was alkylated with diiodomethane (2.4 mL, 30 mmol). Workup afforded, after purification of the crude product by flash chromatography (10% ethyl acetate/hexane), 2.4 g (45%) of the alkylation product **40a** as a clear oil: ^{1}H NMR (200 MHz) δ 3.74 (3 H, s), 3.58, 3.43 (2 H, AB q, J = 10.4 Hz), 2.19 (3 H, s), 1.46 (3 H, s); IR (neat) 1740, 1715 cm^{-1}; m/e 270.9 (1.5), 296.9 (1), 101 (83). Anal. Calcd for $C_7H_{11}O_3I$: C, 31.13; H, 4.11; I, 46.99. Found: C, 31.48; H, 3.99; I, 46.63.

General Procedure C for the Rearrangement of the Iodomethylated or (Phenylseleno)methylated β-Keto Esters with Bu_3SnH. Rearrangement of Methyl 1-(Iodomethyl)-2-oxocyclohexane-1-carboxylate (34d). The iodide **34d** (300 mg, 1.0 mmol) was taken up in benzene (10 mL), and the solution was deoxygenated by passing nitrogen through it for 10 min. A separate solution of Bu_3SnH (320 μL, 1.1 mmol) and AIBN (16 mg, 0.1 mmol) in benzene (5 mL) was also deoxygenated. The substrate solution was heated under reflux, and the solution of Bu_3SnH and initiator was added by means of a syringe pump over 3 h. The reaction mixture was heated at reflux for a further 30 min. The solution was cooled to room temperature and was concentrated under reduced pressure. The residue was taken up in ether (10 mL) and was stirred with a 10% aqueous solution of potassium fluoride (5 mL) for 10 min. The organic layer was isolated from the white precipitate of polymeric tin residues, and the ether layer was dried and was concentrated under reduced pressure. GLC analysis (column B, 240 °C) of the reaction mixture showed the presence of two compounds in the ratio 18:82. The minor product corresponded with the direct reduction product **37b**. The residual oil was purified by flash chromatography (20% ethyl acetate/hexane) to give initially 26 mg (15%) of a clear oil which was identical with an authentic sample of **37b**. Further elution afforded 129 mg (76%) of **methyl 3-oxocycloheptane-1-carboxylate (38b)** as a clear oil: ^{1}H NMR (200 MHz) δ 3.67 (3 H, s), 2.5–3.0 (5 H, m), 1.4–2.1 (6 H, m); ^{13}C NMR δ 211.8 (s), 174.8 (s), 52.0 (q), 45.4 (t), 43.8 (t), 41.1 (d), 33.1 (t), 28.2 (t), 23.9 (t); IR (neat) 1740, 1705 cm^{-1}; m/e 171 (100), 170 (52), 111 (49); exact mass calcd for $C_9H_{14}O_3$ 170.0943, found 170.0943.

Rearrangement of Ethyl 1-(Iodomethyl)-2-oxocyclopentane-1-carboxylate. Following the general procedure C, iodide **34b** (300 mg, 1.0 mmol) was treated with Bu_3SnH (320 μL, 1.1 mmol) and AIBN (16 mg, 0.1 mmol). The residue isolated after workup was purified by flash chromatography (20% ethyl acetate/hexane) to give 140 mg (82%) of **ethyl 3-oxocyclohexane-1-carboxylate (38a)** as a clear oil: ^{1}H NMR (200 MHz) δ 4.14 (2 H, q, J = 7 Hz), 1.6–2.85 (9 H, m). 1.25 (3 H, t, J = 7 Hz); ^{13}C NMR δ 209.1 (s), 173.5 (s), 60.8 (t), 43.1 (t), 43.1 (d), 40.1 (t), 27.7 (t), 24.4 (t), 13.9 (q); IR (neat) 1730 cm^{-1} (broad); m/e 170 (9), 142 (5), 125 (12), 97 (100); exact mass calcd for $C_9H_{14}O_3$ 170.0943, found 170.0943.

Rearrangement of Methyl 1-(Iodomethyl)-2-oxocycloheptane-1-carboxylate. Following the general procedure C, iodide **34e** (340 mg, 1.1 mmol) was treated with Bu_3SnH (320 μL, 1.1 mmol) and AIBN (16 mg, 0.1 mmol). GLC analysis (column B, 240 °C) of the reaction mixture showed the presence of two compounds in the ratio 7:93. The minor product corresponded with the direct reduction product **37c**. The residue after workup was purified by flash chromatography (20% ethyl acetate/hexane) to give initially 10 mg (5%) of a clear oil which was identical with an authentic sample of **37c**. Further elution afforded 180 mg (90%) of **methyl 3-oxocyclooctane-1-carboxylate (38c)** as a clear oil: ^{1}H NMR (200 MHz) δ 3.67 (3 H, s), 1.2–3.0 (13 H, m); ^{13}C NMR δ 214.6 (s), 174.9 (s), 51.9 (q), 42.8 (d), 42.8 (t), 42.7 (t), 29.7 (t), 27.2 (t), 24.7 (t), 23.3 (t); IR (neat) 1740, 1705 cm^{-1}; m/e 175 (36), 184 (32), 153 (63), 152 (45), 125 (33), 124 (34); exact mass calcd for $C_{10}H_{16}O_3$ 184.1099, found 184.1100.

Rearrangement of Methyl 1-(Iodomethyl)-2-oxocyclooctane-1-carboxylate. Following the general procedure C, iodide **34g** (190 mg, 0.59 mmol) was treated with Bu_3SnH (190 μL, 0.65 mmol) and AIBN (9 mg, 0.05 mmol). GLC analysis (column B, 240 °C) of the reaction mixture showed the presence of two compounds in the ratio 17:83. The minor component corresponded with the direct reduction product **37d**. The crude residue isolated after workup was purified by flash chromatography. Initial elution with 10% ethyl acetate/hexane afforded 12 mg (10%) of a clear oil which was identical with an authentic sample of **37d**. Further elution (20% ethyl acetate/hexane) afforded 87 mg (75%) of **methyl 3-oxocyclononane-1-carboxylate (38d)** as a clear oil: ^{1}H NMR (200 MHz) δ 3.68 (3 H, s), 2.4–3.1 (5 H, m), 1.2–2.0 (10 H, m); ^{13}C NMR δ 214.9 s), 175.6 (s), 52.1 (q), 44.4 (t), 43.8 (t), 41.3 (d), 29.4 (t), 25.6 (2 × t), 24.3 (t), 23.0 (t); IR (neat) 1740, 1705 cm^{-1}; m/e 198 (24), 167 (67), 166 (90), 98 (100), 88 (99); exact mass calcd for $C_{11}H_{18}O_3$ 198.1256, found 198.1256.

Rearrangement of Ethyl 2-Oxo-1-((phenylseleno)methyl)cyclopentane-1-carboxylate. Following the general procedure C, phenyl selenide **34a** (160 mg, 0.5 mmol) was treated with Bu_3SnH (150 μL, 0.55 mmol) and AIBN (9 mg, 0.05 mmol). GLC analysis (column B, 240 °C) of the reaction mixture showed the presence of two new compounds in the ratio 2:98. The minor component corresponded with an authentic sample of the direct reduction product **37a**. The residue isolated after workup was purified by flash chromatography (20% ethyl acetate/hexane) to afford 75 mg (88%) of the major reaction product, **38a**, as a clear oil: spectral data for **38a** given previously.

Rearrangement of Methyl 2-Oxo-1-((phenylseleno)methyl)cyclohexane-1-carboxylate. Following the general procedure C, phenyl selenide **34c** (220 mg, 0.67 mmol) was treated with Bu_3SnH (185 μL, 0.68 mmol) and AIBN (11 mg, 0.07 mmol). GLC analysis (column B, 240 °C) of the reaction mixture showed the formation of two new compounds in the ratio 15:85 as well as the presence of unreacted starting material. The minor component corresponded with an authentic sample of the direct reduction product **37b**. The residue isolated after workup was purified by flash chromatography. Initial elution with 5% ethyl acetate/hexane afforded 5 mg (5%) of the direct reduction product **37b**. Further elution with 10% ethyl acetate/hexane afforded 55 mg of unreacted starting material. Further elution gave 55 mg (48%) of the ring-expanded product **38b** as a clear oil: spectral data for **38b** given previously.

Rearrangement of Methyl 2-Oxo-1-((phenylseleno)methyl)cyclooctane-1-carboxylate. Following the general procedure C, phenyl selenide

34f (270 mg, 0.76 mmol) was treated with Bu_3SnH (210 μL, 0.77 mmol) and AIBN (13 mg, 0.08 mmol). GLC analysis (column B, 240 °C) of the reaction mixture showed the formation of the direct reduction product and of the rearranged product in the ratio 22:78. The residue isolated after workup was purified by flash chromatography (20% ethyl acetate/hexane) to give initially 24 mg (16%) of a clear oil which was identical with an authentic sample of the direct reduction product **37d**. Further elution afforded 110 mg (73%) of the ring-expanded product **38d** as a clear oil: spectral data for **38d** given previously.

Methyl 2-Methyl-4-oxopentanoate (41a). An authentic sample of the title compound was prepared from methyl levulinate by the method of Scarpati:[45] ^1H NMR (200 MHz) δ 3.76 (3 H, s), 2.95 (2 H, m), 2.55 (1 H, m), 2.20 (3 H, s), 1.27 (3 H, d, J = 7.2 Hz); ^{13}C NMR δ 206.2 (s), 175.8 (s), 51.4 (q), 46.4 (t), 34.4 (d), 29.8 (q), 16.9 (q); IR (neat) 1740, 1720 cm^{-1}; m/e 144 (16), 129 (27), 113 (72), 112 (62), 87 (100); exact mass calcd for $C_7H_{12}O_3$ 144.0786, found 144.0786.

Rearrangement of Methyl 2-(Iodomethyl)-2-methyl-3-oxobutanoate. Following the general procedure C, iodide **40a** (200 mg, 0.74 mmol) was treated with Bu_3SnH (215 μL, 0.8 mmol) and AIBN (5 mg, 0.035 mmol). GLC analysis (column B, 140 °C) showed the formation of two new compounds in the ratio 14:86. The residual oil isolated after workup was purified by flash chromatography. Initial elution with 10% ethyl acetate/hexane afforded 9 mg (9%) of a clear oil which was identical with an authentic sample of **42a**. Further elution with 20% ethyl acetate/hexane gave 59 mg (55%) of methyl 2-methyl-4-oxopentanoate (**41a**) as a clear oil: spectral data for **4a** given previously.

Reaction of Methyl 1-(Iodomethyl)-2-oxocyclohexane-1-carboxylate with Bu_3SnH under "Standard" Conditions. The iodomethyl keto ester **34d** (150 mg, 0.5 mmol) and AIBN (5 mg, 0.03 mmol) were taken up in benzene (5 mL), and the solution was degassed under nitrogen. The deoxygenated solution was heated under reflux and Bu_3SnH (165 μL, 0.6 mmol) was added ($[Bu_3SnH]_0$ = 0.11 M). The reaction mixture was heated at reflux for 90 min. GLC analysis (column B, 240 °C) of the reaction mixture showed the presence of two compounds in the ratio 85:15. The **major** component corresponded to the direct reduction product **37b** and the **minor** component corresponded to the rearrangement product **38b**.

Kinetic Study of the Rearrangement of 34d. A solution of the iodide **34d** (66.1 mg, 0.22 mmol) in benzene containing biphenyl (26.4 mg, 0.171 mmol) as an internal GLC standard was used as a stock solution. For the stock solution (solution I), $[38]_0$ = 0.055 M. A 250-μL aliquot of the stock solution was withdrawn and placed in a 1-mL volumetric flask. AIBN (3 mg) and Bu_3SnH (1 molar equiv) were added, and the solution was made up to the mark (solution II, $[38]_0$ = 0.028 M). A 125-μL aliquot of the stock solution was placed in a separate 1-mL volumetric flask, AIBN and Bu_3SnH (1 molar equiv) were added as before, and the solution was made up to the mark (solution III, $[38]_0$ = 0.014 M). An aliquot of solution I (1 mL) was transferred to a glass ampule, and AIBN (3 mg) and Bu_3SnH (1 molar equiv) were added. The solution was deoxygenated by three cycles of freeze/pump/thaw and the ampule was sealed under vacuum. In a similar manner solutions II and III were transferred into ampules, deoxygenated, and sealed under vacuum. The ampules were heated in a constant-temperature bath set at 80 ± 0.1 °C for 12 h. The reaction mixtures were analyzed by GLC (column B, 210 °C for 3 min, 20 °C/min to 280 °C). The final concentration of cyclized products were determined from the GLC results, and the values of k_c/k_H were obtained from the appropriate integrated rate equation by an iterative technique as previously described.[31] Values of k_H were determined from the appropriate Arrhenius equation[22] and were used to determine k_c. The results obtained and the values of k_c/k_H calculated for each solution were as follows (initial stannane concentration, ratio of yields of rearranged and unrearranged products, k_c/k_H): solution I, 0.055, 6.3×10^{-3}, 1.8×10^{-3}; solution II, 0.028, 6.95×10^{-3}, 2.9×10^{-3}; solution III, 0.014, 5.0×10^{-3}, 2.8×10^{-3}.

2-((Phenylseleno)methyl)cyclohexanone (45). A solution of 1-((trimethylsilyl)oxy)cyclohexene (340 mg, 2.0 mmol) and chloro(phenylseleno)methane (500 mg, 2.5 mmol) in dichloromethane (2 mL) was cooled to −20 °C. A solution of titanium tetrachloride (240 μL, 2.2 mmol) in dichloromethane (2 mL) was added dropwise to the stirred solution. The reaction mixture was stirred at −20 °C for 1 h and allowed to gradually warm to room temperature for a further hour. The reaction mixture was quenched by the addition of saturated aqueous sodium bicarbonate (5 mL) and was extracted with ether (3 × 5 mL). The combined extracts were dried and were concentrated under reduced pressure. The residue was initially purified by flash chromatography (10% ethyl acetate/hexane) to give an impure sample of the required product. Further purification by MPLC (10% ethyl acetate/hexane) resulted in partial but incomplete removal of the impurity to give 100 mg (19%) of the alkylation product **45** as a yellow oil: ^1H NMR (200 MHz) [in part] δ 7.4 (2 H, **m**), 7.15 (3 H, m), 1.4–3.2 (11 H, m); IR (neat) 3070, 1740, 1480 cm^{-1}; m/e 268 (34), 111 (100); exact mass calcd for $C_{13}H_{16}O^{80}Se$ 268.0366, found 268.0367.

Reaction of 45 with Bu_3SnH. A solution of phenyl selenide **45** (27 mg, 0.1 mmol) in benzene (2 mL) was thoroughly degassed with nitrogen and was heated under reflux. A degassed solution of Bu_3SnH (37 μL, 0.14 mmol) and AIBN (5 mg 0.03 mmol) in benzene (1 mL) was introduced by means of syringe pump addition over 1 h to the heated substrate solution. The solution was heated at reflux for a further hour. GLC analysis (column B, 80 °C for 4 min, 30 °C/min to 260 °C) of the reaction mixture showed only one new product, corresponding to 2-methylcyclohexanone. There was no trace of cycloheptanone in the reaction mixture.

***O*-Methyl *S*-Ethyl 2-Methylmonothiomalonate (39b).** A solution of methyl propionate (3.3 g, 37.5 mmol) in THF (30 mL) was added dropwise to a cooled (−60 °C) solution of LDA (80 mmol) in THF (100 mL) at sufficient rate such that the temperature of the solution was maintained below −50 °C. The solution was stirred for 10 min at −60 °C, and a solution of ethyl chlorothioformate (4 mL, 38 mmol) in THF (20 mL) was added to the reaction mixture over 30 min. The reaction mixture was allowed to slowly warm to room temperature. The reaction mixture was stirred for 3 h at room temperature and the solution was quenched with glacial acetic acid (5 mL) and THF (10 mL). The bulk of the solvent was removed under reduced pressure, and the residue was treated with water (50 mL) and was extracted with ether (3 × 50 mL). The combined extracts were washed successively with water (50 mL), saturated aqueous sodium hydrogen carbonate (50 mL), and brine (50 mL). The organic phase was dried and was concentrated under reduced pressure. The residue was purified by bulb-to-bulb distillation (110 °C at 20 mmHg) to give 4.9 g (74%) of the monothiomalonate **39b** as a clear oil: ^1H NMR (300 MHz) δ 3.72 (3 H, s), 3.62 (1 H, q, J = 7.2 Hz), 2.90 (2 H, q, J = 7.5 Hz), 1.42 (3 H, d, J = 7.2 Hz), 1.24 (3 H, t, J = 7.5 Hz); IR (neat) 1745, 1690 cm^{-1}; m/e 176 (13), 115 (100), 89 (32), 87 (25). Anal. Calcd for $C_7H_{12}O_3S$: C, 47.71; H, 6.86; S, 18.19. Found: C, 47.87; H, 6.88; S, 18.11.

***O*-Methyl *S*-Ethyl 2-(Iodomethyl)-2-methylmonothiomalonate (40c).** Following the general procedure B for the iodomethylation of β-keto esters, the monothiomalonate **39b** (2.4 g, 10.6 mmol) was alkylated with diiodomethane (1.6 mL, 20 mmol) to give, after workup and purification of the crude residue by flash chromatography (5% ethyl acetate/hexane), 2.9 g (67%) of the iodomethylation product **40c** as a clear oil: ^1H NMR (300 MHz) δ 3.79 (3 H, s), 3.73, 3.50 (2 H, AB q, J = 10.2 Hz), 2.95 (2 H, q, J = 7.4 Hz), 1.63 (3 H, s), 1.29 (3 H, t, J = 7.4 Hz); IR (neat) 1745, 1675 cm^{-1}; m/e 316 (5), 277 (11), 189 (6), 129 (13); exact mass calcd for $C_8H_{13}O_2IS$ 315.9630, found 315.9630.

***O*-Methyl *S*-Ethyl 2,2-Dimethylmonothiomalonate (42b).** NaH dispersion (330 mg, 7 mmol) was washed with hexane (2 × 5 mL) and was suspended in benzene (5 mL). A solution of the monothiomalonate **39b** (1.15 g, 6.5 mmol) in benzene (5 mL) was added dropwise, and the reaction mixture was stirred at room temperature until hydrogen evolution had ceased. A solution of iodomethane (470 μL, 7.5 mmol) in benzene (5 mL) was added over 15 min and the reaction mixture was stirred at room temperature for 40 h. The mixture was acidified with 10% aqueous acetic acid (20 mL), and the organic layer was isolated. The organic phase was washed with saturated aqueous sodium bicarbonate (10 mL) and with brine (10 mL). The organic phase was dried and was concentrated under reduced pressure. The residue was purified by bulb-to-bulb distillation (110 °C at 22 mmHg) to give 1.0 g (81%) of the dimethylated product **42b** as a clear oil: ^1H NMR (300 MHz) δ 3.76 (3 H, s), 2.92 (2 H, q, J = 7.5 Hz), 1.50 (6 H, s), 0.81 (3 H, t, J = 7.5 Hz); IR (neat) 1740, 1680 cm^{-1}; m/e 190 (42), 159 (13), 129 (93), 115 (51); exact mass calcd for $C_8H_{14}O_3S$ 190.0664, found 190.0707.

Reaction of 40c with Bu_3SnH. Following the standard high-dilution procedure C, the thioester **40c** (160 mg, 0.51 mmol) was treated with Bu_3SnH (160 μL, 0.6 mmol) and AIBN (9 mg, 0.05 mmol). GLC analysis (column B, 200 °C for 4 min, 20 °C/min to 280 °C) of the reaction mixture showed primarily (97%) formation of a product that corresponded with the direct reduction product **42b**. A small peak corresponding to an authentic sample of ***O*-methyl *S*-ethyl 3-methylmonothiosuccinate (41b)**, comprising 3% of the reaction products, was also observed. Standard workup followed by purification of the crude residue by column chromatography (10% ethyl acetate/hexane) afforded 88 mg (91%) of the dimethyl monothiomalonate **42b** as a clear oil: spectral data for **42b** given previously.

The reaction was repeated on the same scale, but the period of addition of the Bu_3SnH solution was increased to 8 h. GLC analysis now indicated the formation of **42b** and **41b** in the ratio 92:8.

Methyl 1-(3-Chloropropyl)-2-oxocyclopentane-1-carboxylate (48a). NaH (1.9 g, 40 mmol) was washed with hexane (2 × 10 mL) and was suspended in DMSO (30 mL). A solution of methyl 2-oxocyclo-

pentane-1-carboxylate (5.7 g, 40 mmol) in DMSO (10 mL) was added dropwise, and the reaction mixture was stirred until hydrogen evolution had ceased. A solution of 1-bromo-3-chloropropane (4.9 mL, 50 mmol) in DMSO (10 mL) was added over 15 min and the reaction mixture was stirred overnight at room temperature. The solution was treated with water (100 mL) and was extracted with 10% ether/hexane (3 × 50 mL). The combined extracts were washed with brine (3 × 50 mL) and were dried. The residue after removal of the solvent under reduced pressure was purified by column chromatography. Initial elution with 10% ethyl acetate/hexane, increasing to 20% ethyl acetate/hexane, afforded 3.9 g (45%) of the alkylation product **48a** as a clear oil: ^{1}H NMR (300 MHz) δ 3.60 (3 H, s), 3.42 (2 H, m), 1.4–2.6 (10 H, m); IR (neat) 1750, 1730 cm^{-1}; *m/e* 219 (4), 218 (3), 187 (6), 183 (3), 159 (4). Further elution afforded 2 g of a mixture of C- and O-alkylated material.

Methyl 1-(3-Iodopropyl)-2-oxocyclopentane-1-carboxylate (48b). The chloride **48a** (1.2 g, 5.5 mmol) was taken up in acetone (50 mL), and sodium iodide (4 g, 27 mmol) was added. The reaction mixture was heated at 50 °C for 12 h. The bulk of the solvent was removed under reduced pressure, and the residue was treated with water (50 mL) and was extracted with ether (50 mL, 2 × 25 mL). The combined extracts were washed with brine (2 × 30 mL) and were dried. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography (10% ethyl acetate/hexane) to give 1.1 g (65%) of the iodide **48b** as a clear oil: ^{1}H NMR (300 MHz) δ 3.66 (3 H, s), 3.10 (2 H, m), 1.5–2.6 (10 H, m); IR (neat) 1750, 1730 cm^{-1}; *m/e* 311 (8), 310 (1), 279 (22), 183 (90).

General Procedure D for the Alkylation of Methyl 2-Oxocyclopentane-1-carboxylate in DMF. Methyl 2-Oxo-1-propylcyclopentane-1-carboxylate (48c). NaH (1.0 g, 21 mmol) was washed with hexane (2 × 5 mL) and was suspended in DMF (10 mL). A solution of methyl 2-oxocyclopentane-1-carboxylate (2.8 g, 20 mmol) in DMF (5 mL) was added dropwise to the suspension, and the reaction mixture was stirred until hydrogen evolution had ceased. A solution of 1-bromopropane (2.3 mL, 25 mmol) in DMF (5 mL) was added, and the reaction mixture was stirred at room temperature for 3 h. The resulting homogeneous solution was diluted with water (50 mL) and was extracted with ether (3 × 30 mL). The combined organic extracts were washed with brine (3 × 30 mL). The organic phase was dried and was concentrated under reduced pressure. The residue was purified by column chromatography (10% ethyl acetate/hexane increasing to 20% ethyl acetate/hexane) to give 1.8 g (49%) of the alkylation product **48c** as a clear oil: ^{1}H NMR (300 MHz) δ 3.67 (3 H, s), 1.1–2.6 (10 H, m), 0.88 (3 H, t, J = 7 Hz); ^{13}C NMR δ 214.8, 171.4, 60.5, 52.3, 37.9, 36.1, 32.6, 19.5, 18.2, 14.2; IR (neat) 1755, 1730 cm^{-1}; *m/e* 185 (6), 184 (1), 153 (10), 125 (16).

Reaction of 48b with Bu_3SnH. Following the standard procedure C, a solution of the iodide **48b** (400 mg, 1.3 mmol) was treated with Bu_3SnH (100 μL, 1.5 mmol) and AIBN (20 mg, 0.12 mmol). GLC analysis (column B, 240 °C) of the reaction mixture showed the formation of two products in the ratio 45:55. The minor component corresponded with an authentic sample of the direct reduction product **48c**. The crude residue isolated after standard workup of the reaction mixture was purified by flash chromatography. Elution with 20% ethyl acetate/hexane afforded 52 mg (28%) of a clear oil which was identical with an authentic sample of **48c**. Further elution afforded 56 mg (31%) of the ring-enlarged product, **methyl 5-oxocyclooctane-1-carboxylate (49a)**, as a clear oil: ^{1}H NMR (300 MHz) δ 3.55 (3 H, s), 2.55 (2 H, m), 1.5–2.3 (11 H, m); ^{13}C NMR δ 216.7 (s), 176.6 (s), 52.0 (q), 42.4 (d), 42.2 (2 × t), 30.4 (2 × t), 24.8 (2 × t); IR (neat) 1735, 1700 cm^{-1}; *m/e* 184 (8), 153 (9), 152 (11), 125 (16), 124 (19); exact mass calcd for $C_{10}H_{16}O_3$ 184.1099, found 184.1067.

Methyl 1-(4-Bromobutyl)-2-oxocyclopentane-1-carboxylate (48d). Following the general alkylation procedure D, a suspension of NaH (1.0 g, 20 mmol) in DMF (10 mL) was treated with a solution of methyl 2-oxocyclopentane-1-carboxylate (2.8 g, 20 mmol) in DMF (10 mL), and the resulting dark red solution was treated with a solution of 1,4-dibromobutane (4.8 mL, 40 mmol) in DMF (10 mL). The reaction mixture was stirred at room temperature for 14 h. The crude residue isolated after workup was purified by column chromatography. Initial elution with 10% ethyl acetate/hexane afforded a mixture of 1,4-dibromobutane and an unidentified byproduct. Further elution with 15% ethyl acetate/hexane gave 2.5 g (39%) of the bromide **48d** as a clear oil: ^{1}H NMR (300 MHz) δ 3.64 (3 H, s), 3.33 (2 H, t, J = 6.7 Hz), 1.3–2.6 (12 H, m); ^{13}C NMR δ 214.5 (s), 171.2 (s), 60.2 (s), 52.4 (q), 37.8 (t), 33.1 (t), 32.8 (t), 32.6 (t), 23.3 (t), 19.5 (t); IR (neat) 1750, 1725 cm^{-1}; *m/e* 277 (M^+ + 1, 60), 276 (1), 245 (41), 217 (14), 197 (14). Further elution afforded 1.1 g of a mixture of **4d**, the corresponding *O*-alkylation product, and unreacted starting material.

Methyl 1-Butyl-2-oxocyclopentane-1-carboxylate (48e). Following the general alkylation procedure D, a suspension of NaH (1.0 g, 20 mmol) in DMF (20 mL) was treated with methyl 2-oxocyclopentane-1-carboxylate (2.8 g, 20 mmol) in DMF (10 mL), and the resulting solution was treated with a solution of 1-bromobutane (3.2 mL, 30 mmol) in DMF (10 mL). The crude product after the standard workup was purified by bulb-to-bulb distillation to give 2.8 g (70%) of the alkylation product **48e** as a clear oil: ^{1}H NMR (300 MHz) δ 3.64 (3 H, s), 1.1–2.5 (12 H, m), 0.82 (3 H, t, J = 7.1 Hz); ^{13}C NMR δ 214.8, 171.4, 60.5, 52.3, 37.9, 33.6, 32.5, 26.9, 22.9, 19.5, 13.7; IR (neat) 1750, 1730 cm^{-1}; *m/e* 198 (0.4), 167 (6), 166 (2), 142 (100), 139 (10), 138 (14).

Reaction of 48d with Bu_3SnH. (i) At 80 °C: Following the standard high-dilution procedure C, the bromide **48d** (280 mg, 1.0 mmol) was treated with Bu_3SnH (300 μL, 1.1 mmol) and AIBN (16 mg, 0.1 mmol). GLC analysis (column B, 240 °C) of the reaction mixture showed the formation of two new products in the ratio 95:5. The major component corresponded with the direct reaction product **48e**. The reaction mixture was worked up in the usual manner, and the crude residue isolated after workup was purified by flash chromatography. Elution with 10% ethyl acetate/hexane afforded initially 155 mg (78%) of a clear oil which was identical with an authentic sample of the direct reduction product **48e**. Further elution afforded 6 mg (3%) of **methyl 5-oxocyclononane-1-carboxylate (49b)** as a clear oil: ^{1}H NMR (300 MHz) δ 3.65 (3 H, s), 2.3–2.6 (5 H, m), 1.5–2.1 (10 H, m); ^{13}C NMR δ 217.6 (s), 176.6 (s), 51.9 (q), 43.3 (t), 43.2 (t), 41.9 (d), 28.7 (t), 27.2 (t), 24.8 (t), 24.2 (t), 23.2 (t); IR (neat) 1735, 1700 cm^{-1}; *m/e* 198 (3), 167 (4), 166 (11), 139 (9), 138 (17); exact mass calcd for $C_{11}H_{18}O_3$ 198.1256, found 198.1247.

(ii) At 130 °C: The reaction was repeated as described above, except that *tert*-butylbenzene was used as the reaction solvent and the substrate solution was heated at 130 °C during the course of the addition of Bu_3SnH. GLC analysis of the reaction mixture showed the ratio of **49b**:**48e** had increased from 5:95 to 20:80. The reaction mixture was worked up and purified as outlined previously to afford 35 mg (18%) of the cyclononanone **49b** and 90 mg (47%) of the direct reduction product **48e**.

Methyl 1-((*E* or *Z*)-3-Bromo-2-propenyl)-2-oxocyclopentane-1-carboxylate (50a). Following the general alkylation procedure D, a suspension of NaH (1.25 g, 26 mmol) was suspended in DMF (10 mL) and was treated with a solution of methyl 2-oxocyclopentane-1-carboxylate (3.55 g, 25 mmol) in DMF (5 mL). A solution of (*E* or *Z*)-1,3-dibromopropene (3.0 mL, 30 mmol) in DMF (5 mL) was added to the red reaction mixture. The crude residue isolated after workup was purified by column chromatography. Initial elution with 10% ethyl acetate/hexane removed unreacted 1,3-dibromopropene. Gradual increase of the solvent polarity to 20% ethyl acetate/hexane afforded the crude product, which was further purified by bulb-to-bulb distillation (140 °C at 1 mmHg) to give 4.4 g (67%) of **50a** as a clear oil: ^{1}H NMR (300 MHz) δ 6.0–6.4 (2 H, m), 3.75 (3 H, s), 1.6–2.9 (8 H, m); IR (neat) 3080, 1750, 1730, 1620 cm^{-1}; *m/e* 261 (1), 230 (1), 202 (6), 181 (100). Anal. Calcd for $C_{10}H_{13}O_3Br$: C, 46.00; H, 5.02; Br, 30.60. Found: C, 46.31; H, 4.95; Br, 30.49.

Methyl 1-Allyl-2-oxocyclopentane-1-carboxylate (50b). Following the general procedure D, a suspension of NaH (770 mg, 16 mmol) in DMF (10 mL) was treated with a solution of methyl 2-oxocyclopentane-1-carboxylate (2.1 g, 15 mmol) in DMF (10 mL), and the resulting dark red solution was treated with a solution of allyl bromide (1.7 mL, 20 mmol) in DMF (10 mL). The crude product isolated after workup was purified by flash chromatography (10% ethyl acetate/hexane) to give 1.6 g (59%) of the allylated keto ester **50b** as a clear oil: ^{1}H NMR (300 MHz) δ 5.6 (1 H, m), 5.0 (2 H, m), 3.67 (3 H, s), 1.5–2.7 (8 H, m); ^{13}C NMR δ 214.4, 171.3, 132.9, 119.1, 59.9, 52.5, 38.0, 37.8, 32.0, 19.4; IR (neat) 3080, 1750, 1730, 1640 cm^{-1}; *m/e* 182 (4), 151 (13), 150 (9), 123 (29), 122 (31).

Reaction of 50a with Bu_3SnH. Following the standard high-dilution procedure C, the vinyl bromide **50a** (390 mg, 1.5 mmol) was treated with Bu_3SnH (460 μL, 1.7 mmol) and AIBN (20 mg, 0.12 mmol), with the addition taking place over 4 h. GLC analysis (column B, 240 °C) of the reaction mixture showed the formation of three new products, in the ratio 63:5:31, along with some unreacted starting material. The major component corresponded with an authentic sample of the direct reduction product **50b**. The residue after workup was purified by flash chromatography. Initial elution with 20% ethyl acetate/hexane afforded 100 mg (37%) of a clear oil which was identical with an authentic sample of the direct reduction product **50b**. Further elution afforded 40 mg of a mixture of the two other reaction products. The major component of this mixture was **methyl 5-oxo-3-cyclooctene-1-carboxylate (51)**: ^{1}H NMR (300 MHz) [in part] δ 6.42 (1 H, dt, J = 12, 7 Hz), 6.14 (1 H, broad d, J = 12 Hz), 3.68 (3 H, s), 1.3–2.9 (9 H, m); IR ($CHCl_3$) 1730, 1700, 1660 cm^{-1}; *m/e* 182 (7), 151 (13), 123 (29), 122 (28); exact mass calcd for $C_{10}H_{14}O_3$ 182.0945, found 182.0939.

Ethyl (*E* or *Z*)-2-Cyano-5-bromo-4-pentenoate (52) was prepared by alkylation of ethyl cyanoacetate with (*E* or *Z*)-1,3-dibromopropene by the general procedure of von Auwers[38] to give the title compound as a

clear oil: ^{1}H NMR (200 MHz) δ 6.2–6.5 (2 H, m), 4.25 (2 H, q, J = 7 Hz), 3.68 (0.6 H, t, J = 6.9 Hz), 3.62 (0.4 H, t, J = 7 Hz), 2.91 (0.6 H, m), 2.70 (0.4 H, m), 1.26 (3 H, t, J = 7 Hz); IR (neat) 3080, 2260, 1745, 1645 cm^{-1}.

Reaction of 52 with Bu_3SnH. Following the general high-dilution reaction procedure C, bromide **52a** (230 mg, 1.0 mmol) was treated with Bu_3SnH (270 μL, 1.0 mmol) and AIBN (8 mg, 0.05 mmol). The crude residue isolated after workup was purified by flash chromatography. Initial elution with 10% ethyl acetate/hexane afforded 49 mg (32%) of a 1:1 mixture of **ethyl (*E* or *Z*)-5-cyano-4-pentenoate (53)** as a clear oil: ^{1}H NMR (300 MHz) δ 6.70 (0.5 H, dt, J = 16, 7 Hz), 6.51 (0.5 H, dt, J = 10.5, 7.5 Hz), 5.4 (1 H, m), 4.13 (2 H, broad q, J = 7 Hz), 2.4–2.8 (4 H, m), 1.25 (3 H, t, J = 7 Hz); ^{13}C NMR δ 171.6 (2 × s), 153.4 (d), 152.6 (d), 118.7 (s), 100.9 (d), 100.7 (d), 60.8 (t), 60.7 (t), 32.5 (t), 31.9 (t), 28.2 (t), 26.9 (t), 14.1 (2 × q); IR (neat) 3060, 2220, 1730, 1640 cm^{-1}; m/e 153 (5), 108 (63), 107 (48), 80 (88). Further elution afforded 54 mg (23%) of recovered starting material.

Registry No. 14, 107408-19-5; **18**, 620-79-1; **20**, 112818-02-7; **21**, 59803-41-7; **24**, 112818-03-8; **25a**, 112818-04-9; **25b**, 112211-71-9; **25c**, 112211-69-5; **29a**, 50984-08-2; **29b**, 112211-72-0; **29c**, 112818-05-0; **30a**, 112818-06-1; **30b**, 112211-73-1; **33a** (isomer 1), 112818-07-2; **33a** (isomer 2), 112818-08-3; **33b** (isomer 1), 112818-09-4; **33b** (isomer 2), 112818-10-7; **34a**, 112818-11-8; **34b**, 2900-10-9; **34c**, 112211-75-3; **34d**, 112818-12-9; **34e**, 112818-13-0; **34f**, 112211-76-4; **34g**, 112818-14-1; **37a**, 5453-88-3; **37b**, 7500-91-6; **37c**, 68081-50-5; **37d**, 112818-15-2; **38a**, 33668-25-6; **38b**, 37746-13-7; **38c**, 17606-96-1; **38d**, 112211-77-5; **39a**, 17094-21-2; **39b**, 82072-34-2; **40a**, 112818-16-3; **40c**, 112818-17-4; **41a**, 32811-25-9; **41b**, 112818-18-5; **42a**, 112818-16-3; **42b**, 77216-64-9; **45**, 74023-52-2; **48a**, 112818-19-6; **48b**, 110528-50-2; **48c**, 110528-54-6; **48d**, 61114-31-6; **48e**, 61777-25-1; **49a**, 2616-94-6; **49b**, 112818-20-9; **50a**, 112818-21-0; **50b**, 74036-93-4; **51**, 112818-22-1; **52**, 112818-23-2; **53**, 112818-24-3; $AcCH_2CO_2Et$, 141-97-9; *o*-$BrC_6H_4CH_2Br$, 3433-80-5; $NCCH_2CO_2Et$, 105-56-6; $BrCH_2SePH$, 60466-50-4; $ClCH_2SePh$, 83442-19-7; ICH_2I, 83442-19-7; $EtCO_2Me$, 554-12-1; ClCOSEt, 2941-64-2; $Br(CH_2)_2Me$, 106-94-5; $Br(CH_2)_4Br$, 110-52-1; BrBu, 109-65-9; $BrCH{=}CHCH_2Br$, 627-15-6; $BrCH_2CH{=}CH_2$, 106-95-6; ethyl 2-oxocyclopentane-1-carboxylate, 611-10-9; methyl 2-oxocyclohexane-1-carboxylate, 41302-34-5; methyl 2-oxocyclooctane-1-carboxylate, 5452-73-3; methyl 2-oxocycloheptane-1-carboxylate, 52784-32-4; 1-(trimethylsilyl)oxy)cyclohexene, 6651-36-1; 2-methylcyclohexanone, 583-60-8; methyl 2-oxocyclopentane-1-carboxylate, 10472-24-9.

A General Method for the Preparation of Carbonyl Compounds and Butenolides from Organomanganese Pentacarbonyl Complexes†[1]

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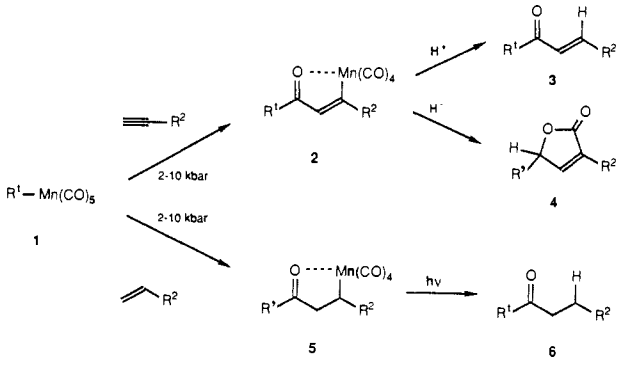
Abstract: Sequential insertion of carbon monoxide and either alkenes or alkynes into alkylmanganese pentacarbonyl complexes at high pressures (2–10 kbar) provided acyl-coordinated manganese complexes (manganacycles) in good yields. Unsymmetrical alkenes and alkynes displayed high regioselectivity in the insertion reaction. The resulting manganese complexes are valuable intermediates in the preparation of organic compounds. For instance, the adducts obtained from alkynes were demetalated under acidic conditions to give *E*-enones. Alternatively, hydride reduction of these adducts afforded butenolides by an intramolecular Reppe reaction. Photochemical demetalation of the alkene-derived manganacycles provided ketones. X-ray and chemical evidence is presented which demonstrates that the manganacycles derived from alkyne insertion are aromatic and should be depicted as metallafuran derivatives.

The insertion of transition metal–carbon bonds into carbon–carbon or carbon–oxygen multiple bonds is a key reaction in many heterogeneous and homogeneous transition metal catalyzed processes.[2-4] Migratory insertion of alkylmanganese pentacarbonyl complexes (**1**) is an excellent model for insertion of carbon monoxide into transition metal–alkyl bonds and this process has been investigated by Calderazzo,[5] Casey,[6] Flood,[7] and others.[8,9] As part of these studies, Pruett et al. demonstrated that electron-withdrawing substituents attached to the alkyl residue retarded the rate of migratory insertion in the manganese complexes.[8h] For instance, methyl manganese pentacarbonyl (**1**: R = Me) underwent facile migratory insertion while the benzyl analogue (**1**: R = CH_2Ph) was reluctant to form the corresponding acyl complex.

In a related series of experiments, Booth and co-workers demonstrated that methyl and phenylmanganese pentacarbonyl complexes (**1**: R^1 = Me or Ph), reactive manganese complexes with regard to migratory insertion, also underwent sequential insertion of carbon monoxide and an alkyne to produce manganacycles **2** (Scheme I) in good yields.[9] However, these authors did not report sequential insertion reactions with less reactive manganese com-

Scheme I



† Dedicated to Lloyd M. Jackman on the occasion of his 60th birthday.
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