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Novel Free Radical Ring-Expansion Reactions

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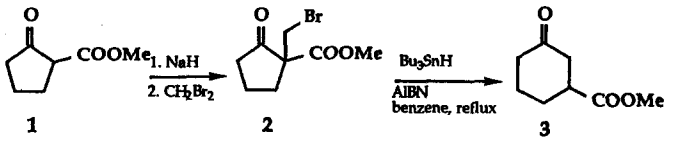
Abstract: *A novel free radical initiated ring expansion of haloalkyl β-keto esters is described. Following alkylation of the β-keto ester with the appropriate dihalide, the resulting halide is treated at reflux with tri-n-butyltin hydride. Rearrangement to the homologated γ-keto ester occurs smoothly. An oxy radical intermediate is proposed for the reaction.*

Introduction

Not as widely distributed as the five- and six-membered rings, the medium sized rings constitute, nonetheless, an important component of alicyclic organic chemistry. Considerable attention has been devoted to the synthesis of medium sized rings, yet the need continues for convenient new methods, particularly those tolerant of functional groups and those leading to rings bearing novel functionality. The free radical method described here provides a general new route to the medium sized rings.[1,2] The new method is, at this stage, most readily applied to β-keto esters and provides a direct link to the well established Dieckman and Claisen condensations.

Results and Discussion

The method is simple. The anion of the β-keto ester is alkylated with methylene dibromide. The bromomethyl substituted β-keto ester is then heated to reflux in benzene with tri-*n*-butyltin hydride[1-3] in the presence of AIBN. Ring expansion occurs smoothly yielding the γ-keto ester of the next higher ring size.[4] For example (eq. 1) methyl cyclopentanone-2-carboxylate (1) was alkylated with methylene dibromide yielding

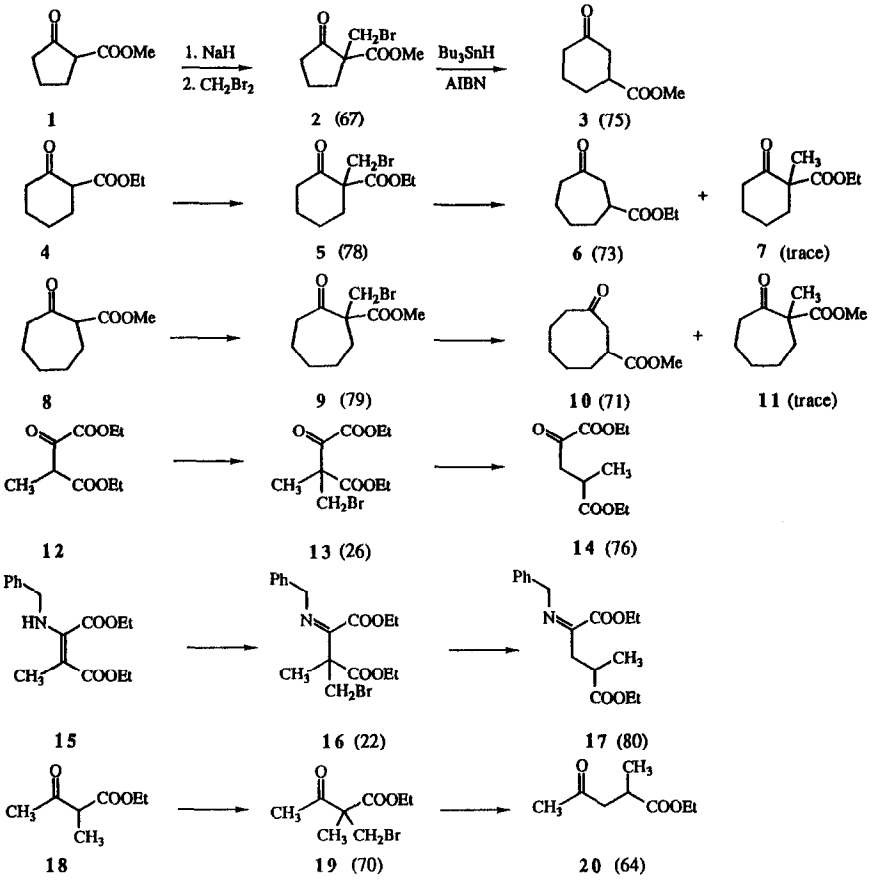


1 2 3 (1)

the bromomethyl adduct 2 (67%). Following isolation, 2 was treated with tri-*n*-butyltin hydride and a catalytic amount of AIBN in refluxing benzene.[5,6] Smooth rearrangement to the ring expanded product, methyl cyclohexanone-3-carboxylate (3), occurred in 75% yield. Further examples are collected in Table 1.

Table 1

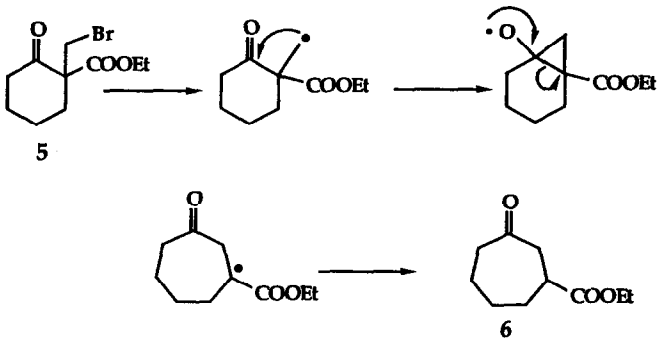
Free radical rearrangement of bromomethyl-substituted β-keto esters (% isolated yield)



The one-carbon ring-expansion reactions take place in uniformly high yield providing access to medium sized rings from readily available starting materials. The five-membered ring **2** expands readily under normal conditions of concentration, but the six- and seven-membered rings require syringe pump techniques in order to maximize the yield of rearrangement products **6** and **10** at the expense of the undesired direct reduction products **7** and **11** (Table 1). Using the syringe pump technique, the yields of ring expansion products **6** and **10** from the six- and seven-membered rings are quite acceptable, and only traces of direct reduction products **7** and **11** were observed.

Especially notable among the examples in Table 1 is the rearrangement of the Schiff base **16** to the Schiff base **17**. This (and the **13** ⟶ **14** rearrangement) may be regarded as a model for the coenzyme B_{12} dependent interconversion of β-methylaspartic acid with glutamic acid catalyzed by the enzyme glutamate mutase. In order that this be accepted as a model, it must be assumed that the enzyme functions through the agency of a Schiff base intermediate. There are serious questions surrounding this assumption,[7] and it is by no means established that this is the case.

The ring expansion reaction probably occurs (Scheme 1) by attack of the first-formed primary radical on



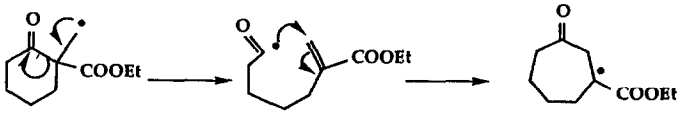
Scheme 1

the carbonyl carbon. The resulting oxy radical then forces the internal cyclopropane ring bond to cleave. The radical center is shifted to the carbon adjacent to the ester where it is stabilized through conjugation to the extent of approximately 5 kcal/mole.

In its ease of rearrangement, the cyclopentanone ester 2 is more reactive than its six-and seven-membered ring counterparts as judged by the negligible amount of direct reduction product formed from 2. This order of reactivity seems reasonable in light of the proposed cyclic mechanism. The transition state leading to the cyclopropyloxy intermediate in the rate determining step introduces substantial eclipsing interactions in the six- and seven-membered rings whereas the eclipsing interactions in the cyclopentanone derived cyclopropyloxy radical intermediate differ little from those of the starting ketone 2. The 3.6 kcal/mole[8] difference in strain energy between the bicyclo[3.1.0]hexane and bicyclo[4.1.0]heptane intermediate ring systems will favor the latter, depending upon the degree of strain conveyed to the transition state. However, in the six-membered ring intermediate substantial angle strain arises from going to the half-chair transition state.

The ester plays a critical role in the rearrangement.[9] It provides useful activation for the bromomethylation reaction. It also appears to activate the ketone toward attack by the nucleophilic methylene radical, and, once the bond to the carbonyl carbon is formed, the ester provides the driving force for cyclopropane ring cleavage leading to ring expansion.

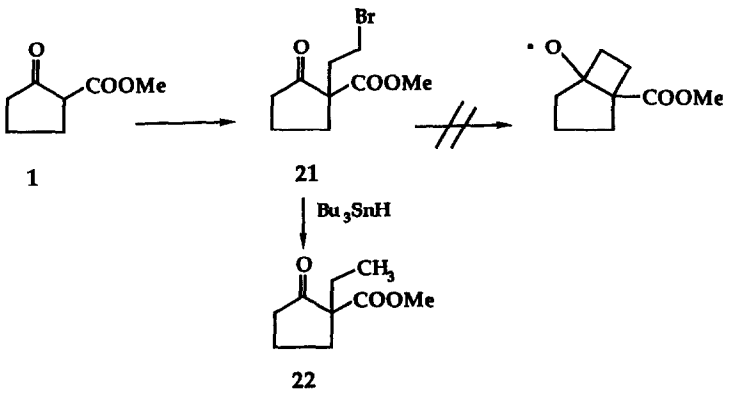
A fragmentation pathway (Scheme 2) provides a mechanistic alternative. Cleavage of the ring



Scheme 2

carbonyl-carbon bond would yield an acyl radical and an acrylate, which could recombine in the opposite sense, the acyl radical adding to the β-carbon of the acrylate. The same final radical intermediate as that in the cyclopropyloxy radical mechanism (Scheme 1) is obtained. There is no direct evidence to distinguish the mechanisms of Scheme 1 and Scheme 2. However, the cyclopropyloxy radical mechanism in Scheme 1 is favored on the basis of evidence obtained in experiments which extend the scope of the ring-expansion.

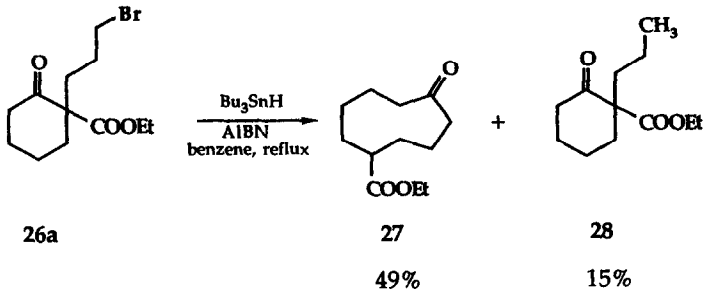
Ring Expansion by Three- and Four-Carbons. The ring expansion can be extended to include longer chain insertions. These experiments were begun by attaching a two-carbon bromoethyl unit to methyl cyclopentanone-2-carboxylate (1). The outlook for this experiment was not favorable. If the mechanism required formation of the intermediate four-membered ring oxy radical (Scheme 3), this would probably not



Scheme 3

compete favorably with chain transfer reduction of the initial primary radical. In fact, the only product isolated from this reaction was the reduction product 22.

The three-carbon and four-carbon ring expansions proved to be more fruitful and interesting. Treatment of ethyl cyclohexanone-2-carboxylate (4) with 1,3-dibromopropane yielded the bromopropyl adduct 26a. When the latter was treated with tri-*n*-butyltin hydride and a catalytic amount of AIBN in refluxing



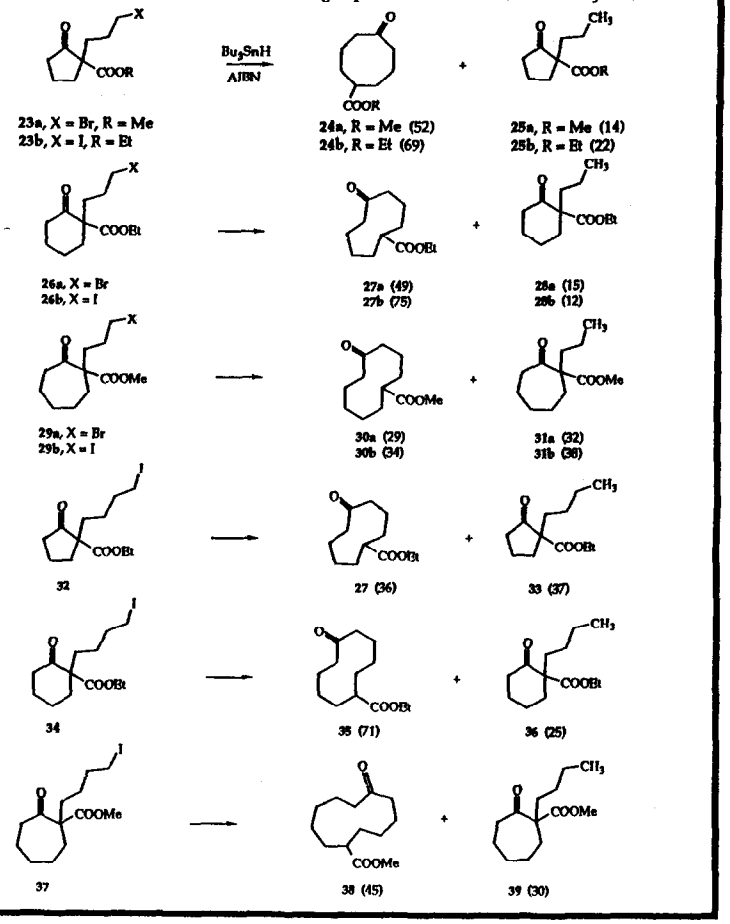
benzene, rearrangement yielded the nine-membered ring expanded product 27. In this reaction, even under conditions of high dilution, the direct reduction product ethyl 2-*n*-propylcyclohexanon-2-carboxylate (28) was produced. Fortunately, the ring expanded products and the direct reduction products in this series are readily separated by chromatographic means (see the Experimental Part).

Four-carbon ring expansion proceeds by the same sequence of steps starting with 1,4-iodo- or 1,4-dibromobutane and the appropriate β-keto ester. Examples of three- and four-carbon ring expansion reactions are collected in Table 2.

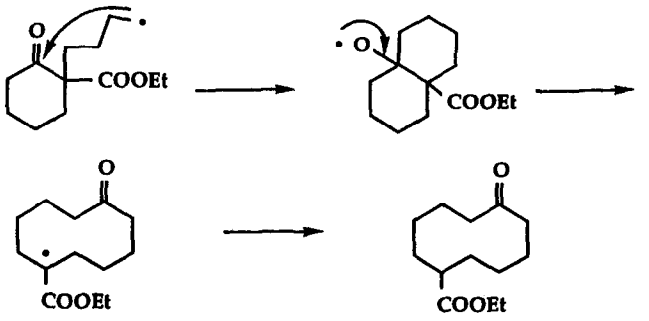
As anticipated, based on the recent findings of Porter,[10] the alkyl iodides often give significantly better yields as a consequence of improved chain transfer reaction.[10] Rearrangements of 23b and 26b in comparison with 23a and 26a (Table 2) are illustrative of the point. However, no difference was observed between 29a and 29b.

Table 2

Three- and Four-carbon Free Radical Ring Expansion Reactions (% isolated yield)



This series of experiments reinforces the postulate of preference for radical attack on the carbonyl carbon. It is not possible for the initial primary radical to unravel to an acyl radical-acrylate intermediate as it is in the one-carbon situation. The oxy radical (Scheme 4) resulting from attack of the primary radical on the carbonyl group is the most likely intermediate in this sequence.



Scheme 4

Experimental Section

General Alkylation Procedure. Methyl 1-Bromomethyl-2-oxocyclopentanoate (2). A solution of 0.43 g (3.0 mmoles) of methyl 2-oxocyclopentanoate (1) in 2 mL of dry THF was added slowly to a suspension of 0.127 g (3.6 mmoles, 67.6% suspension in mineral oil) of NaH in 5 mL of THF containing 0.645 g (3.6 mmoles) of hexamethylphosphoramide (HMPA) at room temperature under argon. The reaction mixture was stirred at room temperature for 1 hr, then treated with 2.6 g (15.0 mmoles) of dibromomethane. The reaction mixture was refluxed at 80° for 10 hr, then poured into a separatory funnel containing 100 mL of ether. The organic layer was washed with five 5-mL portions of water, dried over K_2CO_3, filtered and concentrated, affording 810 mg of a brown oil. Column chromatography on 8 g of silica gel (elution with 4:1 hexane-ethyl acetate) gave 435 mg (67%) of the desired bromide 2 as colorless oil, R_f 0.43 (3:1 hexane-ethyl acetate). The 300 MHz proton nmr spectrum ($CDCl_3$) showed a two-proton bromomethyl AB quartet (J = 10.5 Hz) at δ 3.75 and δ 3.6, a three-proton methyl singlet at δ 3.72 and a six-proton multiplet at δ 2.62-1.93. The ^{13}C nmr spectrum ($CDCl_3$) showed 8 lines at δ: 211.2 (s), 167.9 (s), 60.9 (s), 52.8 (q, J = 148.8 Hz), 38.08 (t, J = 130 Hz), 33.6 (t, J = 156.4 Hz), 32.2 (t, J = 132.2 Hz), and 19.2 (t, J = 131.8 Hz). The IR spectrum (neat) showed bands at: 2955 (m, CH), 1753 (vs, CO, 5-membered ketone), 1726 (vs, ester carbonyl), and 1435 cm^{-1} (m). The mass spectrum (70 eV) showed peaks at m/z (rel. int.): 205, 203 (2, M^+-OMe), 155 (37, M^+-Br), 123 (28, M^+-MeOH-Br), and 95 (30, M^+-Br-CO-MeOH). Exact mass calc'd for $C_7H_8{}^{79}BrO_2$: 202.9708. Found: 202.9708.

General Rearrangement Procedure. Rearrangement of Methyl 1-Bromomethyl-2-oxocyclopentanoate (2). To a 250-ml, round-bottomed flask fitted with a magnetic stirring bar and a reflux condenser were added methyl 1-bromomethyl-2-oxocyclopentanoate (2) (100 mg, 0.43 mmoles), dry benzene (80 mL), and tri-*n*-butyltin hydride (116 mg, 0.399 mmoles). AIBN (7 mg, 0.04 mmoles) was added, and the flask was heated for 24 hr at reflux. The reaction mixture was cooled to room temperature and evaporated on the rotary evaporator yielding an oil, which was dissolved in 30 ml of dichloromethane and washed with ten 1-mL portions of 10% potassium fluoride solution. The organic layer was dried over K_2CO_3, filtered and concentrated. The resulting oil was taken up in 30 mL of acetonitrile, washed with four 5-mL portions of hexane and concentrated. Column chromatography on 2 g of silica gel (elution with 2:1 hexane-ethyl acetate) gave 49.4 mg (75%) of the rearranged product, methyl 3-oxocyclohexanoate (3), a colorless oil, R_f 0.31 (2:1 hexane-ethyl acetate). The 300 MHz proton nmr spectrum ($CDCl_3$) showed a three-proton singlet at δ 3.7, a one-proton methine multiplet at δ 2.8, a two-proton methylene doublet (J = 7.8 Hz) at δ.2.55, a two-proton methylene multiplet at δ 2.43-2.26, a two-proton methylene multiplet at δ 2.11-1.97, and a two-proton methylene multiplet at δ 1.90-1.64. The ^{13}C nmr spectrum ($CDCl_3$) showed 8 lines at δ: 208.4 (s), 173.6 (s), 51.4 (q, J = 147.2 Hz), 42.4 (t, J = 129.8 Hz and d, J = 129.1 Hz overlapped), 40.3 (t, J = 129.0 Hz), 27.1 (t, J = 128 Hz), and 23.8 (t, J = 129.1 Hz). The IR spectrum (neat) showed bands at: 2953.4 (m, CH), 2870.4 (m, CH), 1732.3 (vs, CO, ester), 1715 (vs, CO, 6-membered ketone), and 2435 cm^{-1} (m). The mass spectrum (70 eV) showed peaks at m/z (rel. int.): 156 (3, M^+), 124 (8, M^+-OMe), and 97 (32, M^+-COOMe). Exact mass calc'd for $C_8H_{12}O_3$: 156.0786. Found: 156.0787.

Ethyl 1-Bromomethyl-2-oxocyclohexanoate (5). Following the general alkylation procedure, ethyl 2-oxocyclohexanoate (4) (0.504 g, 3.0 mmoles) was alkylated with dibromomethane (2.6 g, 15.0 mmoles) for 17 hr at reflux. Column chromatography on 8 g of silica gel (elution with 4:1 hexane-ethyl acetate) after standard aqueous workup gave 606 mg (78%) of the desired bromide 5 as a colorless oil, R_f 0.51 (5:1 hexane-ethyl acetate). The 300 MHz proton nmr spectrum ($CDCl_3$) of 5 showed a two-proton methylene multiplet at δ 4.22, a two-proton bromomethyl AB quartet (J = 10.5 Hz) at δ 3.83 and δ 3.5, a one-proton multiplet at δ 2.73-2.66, a two-proton multiplet at δ 2.46-2.41, a one-proton multiplet at δ 2.11-1.93, a four-proton multiplet at δ 1.52-1.88, and a three-proton methyl triplet (J = 7.2 Hz) at δ 1.27. The ^{13}C nmr spectrum ($CDCl_3$) showed 10 lines at δ: 205.09 (s), 168.5 (s), 61.6 (t, J = 148.6 Hz), 61.1 (s), 40.6 (t, J = 130 Hz), 35.2 (t, J = 157.5 Hz), 35.0 (t, J = 129.0 Hz), 27.06 (t, J = 130.0 Hz), 21.8 (t, J = 128.9 Hz), and 13.8 (q, J = 127.4 Hz). The IR spectrum (neat) showed bands at: 2942 (m, CH), 1732 (vs, CO, ester), 1713 (vs, CO, 6-membered ketone), and 1265 cm^{-1} (s). The mass spectrum (70 eV) showed peaks at m/z (rel. int.): 219, 217 (4, M^+-OEt), 183 (90, M^+-Br), 137 (60, M^+-EtOH-Br), and 109 (30, M^+-Br-CO-EtOH). Exact mass calc'd for $C_8H_{10}O_2{}^{79}Br$: 216.9864. Found: 216.9864.

Rearrangement of Ethyl 1-Bromomethyl-2-oxocyclohexanoate (5).

(a) *Under Standard Conditions: 5 mM in n-Bu_3SnH.* Following the general rearrangement procedure, a solution of ethyl 1-bromomethyl-2-oxocyclohexanoate (5) (15 mg, 0.043 mmoles), tri-*n*-butyltin hydride (15.4 mg, 0.0532 mmoles) and AIBN (3.5 mg, 0.02 mmoles) in 11 mL of benzene was heated for 17 hr at reflux. After standard aqueous workup, column chromatography of the crude product on 2 g of silica gel (elution with 3:1 hexane-ethyl acetate) gave 3.7 mg (36%) of the rearranged product, ethyl 3-oxocycloheptanoate (6) as a colorless oil, and 4.2 mg (40%) of the reduced product, ethyl 1-methyl-2-oxocyclohexanoate (7), R_f 0.5 and R_f 0.6 (3:1 hexane-ethyl acetate) respectively.

The 300 MHz proton nmr spectrum ($CDCl_3$) of the rearranged product **6** showed a two-proton methylene quartet (J = 7.1 Hz) at δ 4.14, a one-proton quartet (J_{AB} = 15.5, J_{vic} = 10.8 Hz) at δ 2.8, a two proton multiplet at δ 2.72-2.65, a two-proton multiplet at δ 2.57-2.42, a six-proton multiplet at δ 2.13-1.44, and a three-proton methyl triplet (J = 7.1 Hz) at δ 1.25. The ^{13}C nmr spectrum ($CDCl_3$) showed 10 lines at δ: 211.9 (s), 174.3 (s), 60.6 (t, J = 148.1 Hz), 45.38 (t, J = 127.9 Hz), 43.75 (t, J = 126.6 Hz), 41.09 (d, J = 134.6 Hz), 33.08 (t, J = 128.6 Hz), 28.14 (t, J = 125.3 Hz), 23.78 (t, J = 126.2 Hz), and 14.03 (q, J = 126.5 Hz). The IR spectrum (neat) showed bands at: 2930.2 (m, CH), 2858.9 (m, CH), 1728.4 (vs, CO, ester), 1701 (vs, CO, 7-membered ketone), and 1246.2 cm^{-1} (m). The mass spectrum (70 eV) showed peaks at m/z (rel. int.): 184 (4, M^+), 139 (5, M^+-OEt), and 111 (20, M^+-COOEt). Exact mass calc'd for $C_{10}H_{16}O_3$: 184.1100. Found: 184.1100.

The 300 MHz proton nmr spectrum ($CDCl_3$) of the reduced product **7** showed a two-proton methylene multiplet at δ 4.15-4.21, a two-proton multiplet at δ 2.52-2.4, a one-proton multiplet at δ 2.04-2.02, a three-proton multiplet at δ 1.43-1.69, a three-proton methyl singlet at δ 1.28, and a three-proton methyl triplet (J = 7.1 Hz) at δ 1.25. The ^{13}C nmr spectrum ($CDCl_3$) showed 10 lines at δ: 207.3 (s), 172.4 (s), 60.6 (t, J = 147 Hz), 56.5 (s), 40.05 (t, J = 128 Hz), 37.8 (t, J = 132 Hz), 26.98 (t, J = 129 Hz), 22.14 (t, J = 131 Hz), 20.6 (q, J = 130.0 Hz), and 13.5 (q, J = 127 Hz). The IR spectrum (neat) showed bands at: 2938 (s, CH), 2867 (m, CH), 1718 (vs, CO, ketone and ester), and 1155 cm^{-1} (m). The mass spectrum (70 eV) showed peaks at m/z (rel. int.): 184 (36, M^+), 156 (53.7, M^+-C_2H_4), 141 (67, M^+-C_2H_4-Me), 139 (36, M^+-OEt), and 111 (72, M^+-COOEt). Exact mass calc'd for $C_{10}H_{16}O_3$: 184.1100. Found: 184.1100.

(b) Under Dilute Conditions: 1 mM in n-Bu_3SnH. Ethyl 1-bromomethyl-2-oxocyclohexanoate (**5**) (15 mg, 0.043 mmoles), dry benzene (55 mL), and tri-*n*-butyltin hydride (15.4 mg, 0.0532 mmoles) were added to a 100-mL, round-bottom flask fitted with a magnetic stirring bar and a reflux condenser. AIBN (3.5 mg, 0.02 mmoles) was added, and the flask was heated for 17 hr at reflux. The reaction mixture was worked up as described above to yield 7.6 mg (73%) of the rearranged product, ethyl 3-oxocycloheptanoate (**6**) as a colorless oil. A trace of the reduced product, ethyl 1-methyl-2-oxocyclohexanoate (**7**) was detected by TLC.

(c) Reaction using a Syringe Pump. A solution of tri-*n*-butyltin hydride (46 mg, 0.17 mmoles) in 4 mL of benzene was added over 10 hr to a stirring, refluxing solution of the bromide **5** (30 mg, 0.114 mmoles) in 7 mL of benzene. AIBN (ca. 1 mg) was added to the reaction mixture every four hours during the reaction. The reaction was worked up as described above and yielded 12.5 mg (70%) of the rearranged product **6** and the 3.9 mg (13%) of the starting material **5**. The reduced product **7** could not be detected by ^1H NMR or by TLC.

Methyl 1-Bromomethyl-2-oxocycloheptanoate (9). Following the general alkylation procedure, methyl 2-oxocycloheptanoate (**8**) (0.510 g, 3.0 moles) was alkylated with dibromomethane (2.6 g, 15.0 mmoles). Column chromatography on 8 g of silica gel (elution with 3:1 hexane-ethyl acetate) after standard aqueous workup gave 628 mg (80%) of the desired bromide **9** as a colorless oil, R_f 0.45 (3:1 hexane-ethyl acetate). The 300 MHz proton nmr spectrum ($CDCl_3$) showed a two-proton bromomethyl AB quartet (J = 10.4 Hz) at δ 4.01 and δ 3.5, a three-proton methyl singlet at δ 3.76, and a ten-proton multiplet at δ 2.75-1.24. The ^{13}C nmr spectrum ($CDCl_3$) showed 10 lines at δ: 206.4 (s), 169.4 (s), 64.06 (s), 52.5 (q, J = 148 Hz), 41.7 (t, J = 130.3 Hz), 35.7 (t, J = 156 Hz), 30.6 (t, J = 129.5 Hz), 29.5 (t, J = 127 Hz), 25.41 (t, J = 129.8 Hz), and 24.0 (t, J = 125.4 Hz). The IR spectrum (neat) showed bands at: 2930.2 (m, CH), 1738.1 (vs, CO, ester), 1705.3 (vs, CO, 7-membered ketone), and 1246 cm^{-1} (s). The mass spectrum (70 eV) showed peaks at m/z (rel. int.): 233, 231 (3, M^+-MeOH), 183 (80, M^+-Br), 151 (90, M^+-MeOH-Br), and 123 (68, M^+-Br-CO-MeOH). Exact mass calc'd for $C_9H_{12}O_2{}^{81}Br$: 233.000. Found: 233.000.

Rearrangement of Methyl 1-Bromomethyl-2-oxocycloheptanoate (9). Following the general rearrangement procedure, a solution of methyl 1-bromomethyl-2-oxocycloheptanoate (**9**) (100 mg, 0.38 mmoles), tri-*n*-butyltin hydride (110 mg, 0.382 mmoles), and AIBN (20 mg, 0.12 mmoles) in 350 mL of benzene was heated for 17 hr at reflux. After standard aqueous workup, column chromatography on 2 g of silica gel (elution with 3:1 hexane-ethyl acetate) gave 49.2 mg (71%) of the rearranged product, methyl 3-oxocyclooctanoate (**10**) as a colorless oil, R_f 0.45 (3:1 hexane-ethyl acetate). The 300 MHz proton nmr spectrum ($CDCl_3$) showed a three-proton methyl singlet at δ 3.69, a one proton multiplet at δ 2.93, a one-proton triplet (J = 12.9 Hz) at δ 2.79, a one-proton doublet of doublets (J_{AB} = 12.5, J_{vic} = 2.19 Hz) at δ 2.56, a two-proton multiplet at δ 2.42, and an eight-proton multiplet at δ 2.04-1.39. The ^{13}C nmr spectrum ($CDCl_3$) showed 10 lines at δ: 214.2 (s), 174.6 (s), 51.6 (q, J = 146.6 Hz), 42.6 (t, J = 124 Hz), 42.5 (d, J = 133 Hz), 42.4 (t, J = 124 Hz), 29.5 (t, J = 130.6 Hz), 26.95 (t, J = 124.2 Hz), 24.5 (t, J = 126.8 Hz), and 23.0 (t, J = 123.7 Hz). The IR spectrum (neat) showed bands at: 2938.0 (m, CH), 2860 (m, CH), 1734 (vs, CO, ester), 1701 (vs, CO, 8-membered ketone), and 1279 cm^{-1} (m). The mass spectrum (70 eV) showed peaks at m/z (rel. int.): 184 (9, M^+), 152 (5, M^+-MeOH), and 127 (16, M^+-CO-MeOH). Exact mass calc'd for $C_{10}H_{16}O_3$: 184.1099. Found: 184.1100.

Diethyl 3-Bromomethyl-3-methyl-2-ketosuccinate (13). Under an atmosphere of nitrogen, 4.088 g (0.036 moles) of potassium *t*-butoxide was placed in a three-necked, 250-mL, round-bottom flask. The flask was fitted with a reflux condenser and 250 mL of dry benzene was added. To this solution 6.624 g (0.032 moles) of diethyl oxalpropionate (**12**) was added at a rate of 0.13 mL/min. Dibromomethane (37.0 g, 0.21 moles) and 0.79 g (0.003

moles) of 18-crown-6 were added. The reaction mixture was allowed to reflux for 6 hr and, upon cooling to 5°, was poured into a separatory funnel which contained 150 mL of ether and 50 mL of ice cold 7% hydrochloric acid. The ether layer was washed once with 50 mL of ice cold 7% hydrochloric acid and with two 25-mL portions of water; then it was dried with sodium sulfate, filtered and concentrated in vacuo to 8.59 g of a dark brown oil. Column chromatography on 300 g of silica gel (elution with 75:25 hexane-ethyl acetate) afforded 2.514 g (26%) of the desired bromide **13**. The 300 MHz proton nmr spectrum ($CDCl_3$) showed two two-proton methylene quartets at δ 4.34 (J = 7.2 Hz) and at δ 4.23 (J = 7.1 Hz), a bromomethyl AB quartet (J = 10.7 Hz) at δ 4.0 and δ 3.7, a three-proton methyl singlet at δ 1.5, and two three-proton triplets (J = 7.1 Hz) at δ 1.2 and δ 1.1. The IR spectrum (neat) showed bands at: 2970 (w, CH), 1750 (m, CO), and 1725 cm^{-1} (s, CO). The mass spectrum (15 eV) showed peaks at m/z (rel. int.): 251, 249 (1, M^+-OEt), 223, 221 (75, M^+-COOEt), 195, 193 (25, M^+-COCOOEt), 115 (100, $C_6H_{11}O_2^+$). Exact mass calc'd for $C_8H_{10}O_4{}^{79}Br$; 248.9762. Found: 248.9762.

Rearrangement of Diethyl 3-Bromomethyl-3-methyl-2-ketosuccinate (13). Following the general rearrangement procedure, a solution of diethyl 3-bromomethyl-3-methyl-2-ketosuccinate (**13**) (10.2 mg, 0.033 mmoles), AIBN (3 mg, 0.018 mmoles) and tri-*n*-butyltin hydride (9.0 mg, 0.031 mmoles) in dry benzene (6.2 mL) was heated for 10 hr at reflux. After standard aqueous workup, column chromatography on 2 g of silica gel (elution with 3:1 hexane-ethyl acetate) provided 5.4 mg (76%) of the rearranged product **14**. Some starting material **13** (9%) was recovered as a colorless oil The 300 MHz proton nmr spectrum ($CDCl_3$) of the rearranged product **14** showed two two-proton methylene quartets (J = 7.1 Hz) at δ 4.3 and δ 4.1, a doubled AB quartet at δ 3.3 and 2.9 (J_{AB} = 18.3, J_{vic} = 8.3 and 5.1 Hz), a one-proton multiplet at δ 3.0, a three-proton methyl triplet at δ 1.4 (J = 7.1 Hz), a three-proton methyl triplet at δ 1.26 (J = 7.1 Hz), and a three-proton methyl doublet at δ 1.25 (J = 7.0 Hz). The IR spectrum (neat) showed bands at: 2920 (s, CH), 2849 (s,CH), and 1728 cm^{-1} (vs, CO). The mass spectrum (70 eV) showed peaks at m/z (rel. int.) : 216 (6, M^+), 171 (10, M^+-OEt), 143 (100, M^+-COOEt), 115 (58, M^+- COCOOEt). Exact mass calc'd for $C_{10}H_{16}O_5$: 216.0998. Found: 216.0994.

Ethyl 2-Benzylamino-3-carboethoxybut-2-enoate (15). A solution of diethyl oxalpropionate (**12**) (20 g, 99 mmoles), benzylamine (10.8 mL, 99 mmoles), and *p*-toluenesulfonic acid (0.8 g, 4.2 mmoles) in 250 mL of dry benzene was heated at reflux for 26 hr. Water was removed using a Soxhlet extractor containing calcium hydride. Upon cooling to room temperature, the reaction mixture was concentrated under reduced pressure yielding 36 g of a light yellow oil. Column chromatography on 250 g of silica gel (7:1 hexane-ethyl acetate containing 0.5% of Hunig's base) provided 8.9 g of the desired enamine **15** as a colorless oil. The 300 MHz proton nmr spectrum ($CDCl_3$) showed two three-proton methyl triplets at δ 1.25 (J = 7.0 Hz) and at δ 1.27 (J = 7.2 Hz), a three-proton methyl singlet at δ 1.7, two two-proton methylene quartets at δ 4.24 (J = 7.2) and at 4.15 (J = 7.0 Hz), a two-proton benzylic doublet (J = 5.8 Hz) at δ 4.27, and a five-proton aromatic multiplet at δ 7.29. The IR spectrum (neat) showed bands at: 3275 (w, NH), 2975 (m, CH), 1730 (s, CO), 1630 (s, C=C), and 1595 cm^{-1} (s). The mass spectrum (15 eV) showed peaks at m/z (rel. int.): 291 (100, M^+), 262 (17, M^+-Et), 246 (40, M^+-EtO), and 218 (53, M^+-COOEt). Exact mass calc'd for $C_{16}H_{21}NO_4$: 291.1471. Found: 291.1467.

Diethyl 2-Benzylimino-3-bromomethyl-3-methylsuccinate (16). Under an atmosphere of nitrogen, 1.3 g (11.6 mmoles) of potassium *t*-butoxide was placed in a 25-mL, round-bottom flask. The flask was fitted with a three-way stopcock with attached balloon, and 8 mL of dry benzene was added. A solution of 2.59 g (8.93 mmoles) of the enamine **15** and 3.1 g (11.6 mmoles) of 18-crown-6 in 7 mL of dry benzene was rapidly added to the slurry. The reaction mixture became dark red in ca. 30 sec, then dibromomethane (8.73 mL, 124.6 mmoles) was added rapidly. The reaction mixture was stirred for 20 hr at room temperature then poured into a separatory funnel with 180 mL of ethyl acetate. The organic layer was washed with four 10-mL portions of saturated potassium chloride solution, dried over sodium sulfate, filtered and concentrated to 3.548 g of a yellow oil. Column chromatography on 280 g of silica gel (elution with 7:1 hexane-ethyl acetate containing 0.5% of Hunig's base) provided 754 mg (22%) of the desired Schiff base **16**. The 300 MHz proton nmr spectrum ($CDCl_3$) showed two three-proton methyl triplets at δ 1.27 (J = 7.2 Hz) and δ 1.33 (J = 7.3 Hz) , a three-proton methyl singlet at δ 1.58, a bromomethyl AB quartet (J_{AB} = 10.3 Hz) at δ 4.04 and δ 3.71, a four proton methylene multiplet at δ 4.32-4.13, a two-proton benzylic singlet at δ 4.73 and a five-proton aromatic multiplet at δ 7.4-7.32. The ^{13}C nmr spectrum ($CDCl_3$) showed 15 lines at δ: 170.3 (s), 161.9 (s), 160.7 (s), 138.2 (s), 128.0 (d, J = 159.3 Hz), 127.2 (d, J = 158.5 Hz), 126.6 (d, J = 160.7 Hz), 61.42 (t, J = 148.6 Hz), 61.3 (t, J = 148.6 Hz), 57.3 (t, J = 135.7 Hz), 54.3 (s), 37.5 (t, J = 158.2 Hz), 20.1 (q, J = 131.0 Hz), 13.75 (q, J = 127.0 Hz), and 13.69 (q, J = 127.0 Hz). The IR spectrum ($CHCl_3$) showed bands at: 2955 (m, CH), 1715 (s, CO), and 1640 cm^{-1} (m, C=N). The mass spectrum (70 eV) showed peaks at m/z (rel. int.): 385, 383 (19, M^+), 356, 354 (5, M^+-Et), 312, 310 (59, M^+-COOEt), and 290 (65, M^+-$BrCH_2$). Exact mass calc'd for $C_{17}H_{22}NO_4{}^{81}Br$: 385.0712. Found: 385.0712.

Rearrangement of Diethyl 2-Benzylimino-3-bromomethyl-3-methylsuccinate (16). Following the general rearrangement procedure, a solution of diethyl 2-benzylimino-3-bromomethyl-3-methylsuccinate (**16**) (10 mg, 0.026 mmoles), AIBN (3 mg, 0.018 mmoles) and tri-*n*-butyltin hydride (9.0 mg, 0.026 mmoles) in dry benzene (5.5 mL) was heated for 19 hr at reflux. The rearranged Schiff base **17** (5.6 mg) was obtained as a colorless oil after standard

aqueous workup. The ^1H NMR of this substance was quite complex, probably as consequence of coexistence of the four possible diastereomers. However, it revealed the presence of neither the starting material **16** nor the rearranged-hydrolyzed product, diethyl 4-methyl-2-ketoglutarate **14**, which exhibits a characteristic one-proton AB quartet at δ 3.31. The IR spectrum (neat) showed bands at: 2980 (w, CH), 1730 (m, CO), 1650 (w), and 1454 cm^{-1} (w). The mass spectrum (70 eV) showed peaks at m/z (rel. int.): 305 (3.6, M^+), 260 (4.5, M^+-OEt), 232 (17, M^+-COOEt), 204 (25), and 91 (100, $PhCH_2^+$). Exact mass calc'd for $C_{17}H_{23}O_4N$; 305.1627. Found: 305.1627.

Column chromatography on 2 g of silica gel (elution with 80:20:0.1 hexane-ethyl acetate-Hunig's base) provided 4.5 mg (80%) of rearranged and hydrolyzed diethyl 4-methyl-2-ketoglutarate **14**, a colorless oil, whose nmr and IR spectra were identical to those of an authentic sample.

Ethyl 2-Bromomethyl-2-methylacetoacetate (19). Following the general alkylation procedure, ethyl 2-methylacetoacetate (**18**) (0.216 g, 1.5 mmoles) was alkylated with dibromomethane (1.3 g, 7.5 mmoles) for 29 h at reflux. Column chromatography on 8 g of silica gel (elution with 4:1 hexane-ethyl acetate) after standard aqueous workup gave 247 mg (70%) of the desired bromide **19** as a colorless oil, R_f 0.42 (4:1 hexane ethyl acetate). The 300 MHz proton nmr spectrum ($CDCl_3$) showed a two proton methylene multiplet at δ 4.2, a two-proton bromomethyl AB quartet (J = 10.6 Hz) at δ 3.8 and δ 3.67, two three-proton methyl singlets at δ 2.2 and at δ 1.52, and a three-proton methyl triplet (J = 7.2 Hz) at δ 1.28. The IR spectrum (neat) showed bands at: 2984.3 (m, CH), 1738.1 (vs, CO, ester), 1714.9 (vs, CO), and 1277 cm^{-1} (s). The mass spectrum (70 eV) showed peaks at m/z (rel. int.): 195, 193 (1.4, M^+-MeCO), 193, 191 (1.1, M^+-OEt), and 157 (12, M^+-Br). Exact mass calc'd for $C_6H_8O_2{}^{79}Br$: 190.9708. Found: 190.9708.

Rearrangement of Ethyl 2-Bromomethyl-2-methylacetoacetate (19). Following the general rearrangement procedure, a solution of ethyl 1-bromomethyl-2-methylacetoacetate (**19**) (30 mg, 0.128 mmoles), tri-*n*-butyltin hydride (44 mg, 0.15 mmoles) and AIBN (10 mg, 0.06 mmoles) in dry benzene (30 mL). was heated for 24 hr at reflux. After standard aqueous workup, column chromatography on 2 g of silica gel (elution with 4:1 hexane-ethyl acetate) yielded 12.9 mg (64%) of the rearranged product, ethyl 2-methyl-3-oxopentanoate (**20**) as a colorless oil, R_f 0.38 (3:1 hexane ethyl acetate). The 300 MHz proton nmr spectrum ($CDCl_3$) showed a two-proton methylene quartet (J = 7.13 Hz) at δ 4.12, a two proton multiplet at δ 2.91, a one-proton doublet of doublets (J = 20.2, 7.79 Hz) at δ 2.46, a three-proton singlet at δ 2.15, a three-proton doublet (J = 6.86 Hz) at δ 1.39, and a three-proton triplet (J = 7.13 Hz) at δ 1.24. The IR spectrum (neat) showed bands at: 2980 (m, CH), 1732 (vs, CO, ester), 1709 (vs, CO, ketone), and 1163 cm^{-1} (m).

Methyl 1-Bromoethyl-2-oxocyclopentanoate (21). Following the general alkylation procedure, methyl 2-oxocyclopentanoate (**1**) (496 μL, 4.0 mmoles) was alkylated with 1,2-dibromoethane (5.23 g, 28 mmoles) at reflux for 8 hr. Column chromatography (3:2 n-hexane-ethyl acetate) of the crude product after standard aqueous workup gave 610 mg (61%) of the bromide **21**. The 300 MHz proton nmr spectrum ($CDCl_3$) showed a three-proton methyl singlet at δ 3.72, a two-proton bromomethyl multiplet at δ 3.55 - 3.32, and an eight-proton multiplet at δ 2.58 - 1.91. The ^{13}C nmr spectrum ($CDCl_3$) showed 9 lines at δ: 212.8 (s), 170.3 (s), 59.68 (s), 52.3 (q, J = 147.38 Hz), 36.65 (t, J = 134.3 Hz), 32.95 (t, J = 134.0 Hz), 29.56 (t, J = 120.5 Hz), 27.46 (t, J = 153.2 Hz), 19.3 (t, J = 133.05 Hz). The IR spectrum (neat) showed bands at: 2955.3 (w, CH), 1749.7 (vs, CO, ketone), 1726.5 (vs, CO, ester), 1435.2 (m), 1259.7 (m), and 1163.2 (m) cm^{-1}. The mass spectrum (70 eV) showed peaks at m/z (rel. int.): 250, 248 (0.8, M^+), 222, 220 (37.2, M^+-CH_2=CH_2), 119, 117 (17.1 M^+-OCH_3). Exact mass calc'd for $C_9H_{13}O_3{}^{79}Br$: 248.0048. Found: 248.0049.

Reaction of Methyl 1-Bromoethyl-2-oxocyclopentanoate (21) with Tri-*n*-butyltin hydride. A solution of tri-*n*-butyltin hydride (54 μL, and AIBN (3 mg) in 4 mL of benzene was added dropwise over 20 hr to a refluxing solution of the bromide **21** (33 mg, 0.134 mmoles) in 80 mL of benzene. Column chromatography (4:1 n-hexane - ethyl acetate) of the crude product, after standard aqueous workup, gave the reduced product **22** (16.2 mg, 71%) whose spectral data were identical to those of an authentic sample.

Authentic Methyl 1-Ethyl-2-oxocyclopentanoate (22). Following the general alkylation procedure, methyl 2-oxocyclopentanoate (**1**) (496 μL, 4.0 mmoles) was alkylated with ethyl iodide (1.27 g, 8.0 mmoles) at room temperature for 2 hr. Column chromatography (4:1 n-hexane-ethyl acetate) of the crude product after standard aqueous workup gave 476 mg (70%) of the product **22**.

The 300 MHz proton nmr spectrum ($CDCl_3$) showed a three-proton methyl singlet at δ 3.71, a two-proton multiplet at δ 2.6-2.2, a four-proton multiplet at δ 2.1-1.85, a two-proton multiplet at δ 1.7-1.55, and a three-proton methyl triplet (J = 7.49 Hz) at δ 0.89. The ^{13}C nmr spectrum ($CDCl_3$) showed 9 lines at δ: 214.5 (s), 171.4 (s), 60.5 (s), 52.02 (q, J = 147.4 Hz), 37.7 (t, J = 129.7 Hz), 31.8 (t, J = 133.0 Hz), 26.5 (t, 130.3 Hz), 19.2 (t, J = 132.18 Hz), 8.87 (q, J = 126.8 Hz). The IR spectrum (neat) showed bands at: 2968.8 (s, CH), 2883.9 (w, CH), 1750 (vs, CO, ketone), 1726.5 (vs, CO, ester), 1460.3 (m), 1435.2 (m), 1230.7 (vs), and 1147.8 (vs) cm^{-1}. The mass spectrum (70 eV) showed peaks at m/z (rel. int.): 170 (3.4, M^+), 142 (38, M^+-C_2H_4), 139 (12.7, M^+-OCH_3), 111 (13, M^+-$COOCH_3$). Exact mass calc'd for $C_9H_{14}O_3$: 170.0943. Found: 170.0943.

Methyl 1-Bromopropyl-2-oxocyclopentanoate (23a). Following the general alkylation procedure, methyl 2-oxocyclopentanoate (**1**) (0.568 g, 4.0 mmoles) was alkylated with 1,3-dibromopropane (1.21g, 6.0 mmoles) at

reflux for 21 hr. Column chromatography (elution with 4:1 n-hexane-ethyl acetate) of the crude product on 8 g of silica gel after aqueous workup afforded 628 mg (59%) of the bromide **23a** as a pale yellow oil. The 300 MHz proton nmr spectrum ($CDCl_3$) showed a three-proton singlet at δ 3.72, a two-proton bromomethyl multiplet at δ 3.39, a two-proton multiplet at δ 2.6-2.2, and a eight-proton multiplet at δ 2.1-1.6. The IR spectrum (neat) showed bands at: 2955.3 (m, CH), 1726.5 (vs, CO, ester and ketone), 1435 (m), 1236 (s). The ^{13}C nmr spectrum ($CDCl_3$) showed 10 lines at δ: 213.2 (s), 170.5 (s), 58.9 (s), 51.7 (q, J = 147.2 Hz), 37.03 (t, J = 129.5 Hz), 32.8 (t, J = 151.7 Hz), 32.38 (t, J = 132.7 Hz), 31.7 (t, J = 127.8 Hz), 27.5 (t, J = 125.2 Hz), 18.9 (t, J = 132.0 Hz). The mass spectrum (70 eV) showed peaks at m/z (rel. int.): 264, 262 (3.5, M^+), 236, 234 (65, M^+-C_2H_2), 183 (52, M^+-R_2). Exact mass calc'd for : 264.0184. Found: 264.0185.

Rearrangement of Methyl 1-Bromopropyl-2-oxocyclopentanoate (23a). A solution of tri-*n*-butyltin hydride (151.48 mg, 0.52 mmoles) and AIBN (12 mg, 0.07 mmoles) in 10 mL of benzene was added dropwise over 26 hr to a refluxing solution of the bromide **23a** (86.1 mg, 0.33 mmoles) in 160 mL of benzene, then the reaction was heated at reflux for an additional 3 hr. Column chromatography of this crude product on 2 g of silica gel (elution with 3:2 n-hexane-ethyl acetate) after standard aqueous workup afforded 31.3 mg (52 %) of the rearranged product **24a** as a colorless oil and 8.4 mg (14%) of the reduced product **25a**.

The 300 MHz proton nmr spectrum ($CDCl_3$) of the rearrangement product **24a** showed a three-proton singlet at δ 3.64, a four-proton multiplet at δ 2.67-2.26, a five-proton multiplet at δ 2.2-1.9, and a four-proton multiplet at δ 1.89-1.5. The ^{13}C nmr spectrum ($CDCl_3$) showed 7 lines at δ: 210.8 (s), 176.2 (s), 51.4 (q, J = 146.7 Hz), 41.77 (d, J = 126.7 Hz), 41.60 (t, J = 127.8 Hz), 29.8 (t, J = 127.44 Hz), 24.17 (t, J = 127.9 Hz). The IR spectrum (neat) showed bands at: 2951.5 (m,CH), 2862.7 (w, CH), 1734.2 (vs, CO, ester), 1699.5 (vs, CO, ketone), 1437.1 (m), and 1255.8 (m) cm^{-1}. The mass spectrum (70 eV) showed peaks at m/z (rel. int.): 184 (4.3, M^+), 153 (4.0, M^+-OCH_3), 125 (5.2, M^+-$COOCH_3$), 97 (9, M^+-$COOCH_3$-C_2H_4). Exact mass calc'd for $C_{10}H_{16}O_3$: 184.1099. Found: 184.1100.

The 300 MHz proton nmr spectrum ($CDCl_3$) of the reduced product **25a** showed a three-proton singlet at δ 3.70, a two-proton multiplet at δ 2.46-2.19, a three-proton multiplet at δ 2.03-1.84, a five-proton multiplet at δ 1.67-1.18, and a three-proton methyl triplet (J = 7.33 Hz) at δ 0.91. The IR spectrum (neat) showed bands at: 2959.2 (m, CH), 2894.3 (w, CH), 1732.3 (vs, CO, ester and ketone), 1435.2 (w), 1225.0 (m), and 1159.4 (m) cm^{-1}. The mass spectrum (70 eV) showed peaks at m/z (rel. int.): 184 (26, M^+), 153 (6.3, M^+-OCH_3), 142 (35, M^+-$CH_3CH{=}CH_2$), 125 (75, M^+-$COOCH_3$).

Ethyl 1-Iodopropyl-2-oxocyclopentanoate (23b). Following the general alkylation procedure, ethyl 2-oxocyclopentanoate (780 mg, 5 mmoles) was alkylated with 1,3-diiodopropane (861 μL, 7.5 mmoles) for 10 hr at reflux. Column chromatography (elution with 5:1 n-hexane-ethyl acetate) of the crude product after standard workup afforded 39.4 mg (24%) of the iodide **23b**. The 300 MHz proton nmr spectrum ($CDCl_3$) showed a two-proton methylene quartet (J = 7.0 Hz) at δ 4.17, a two-proton iodomethyl multiplet at δ 3.15, a ten-proton multiplet at δ 2.2-1.6, and a three-proton methyl triplet (J = 7.0 Hz) at δ 1.25. The ^{13}C nmr spectrum ($CDCl_3$) showed 11 lines at δ: 213.8 (s), 170.3 (s), 61.01 (t, J = 150.14 Hz), 59.19 (s), 37.3 (t, J = 129.4 Hz), 34.1 (t, J = 126.0 Hz), 32.7 (t, J = 133.2 Hz), 28.5 (t, J = 125.2 Hz), 19.2 (t, J = 131.1 Hz), 13.8 (q, J = 127.1 Hz), 6.0 (t, J = 152.0 Hz). The IR spectrum (neat) showed bands at: 2985 (w, CH), 1749.7 (vs, CO,ester), 1722.6 (vs, CO, ketone), 1448.7 (w), and 1225 (m) cm^{-1}. The mass spectrum (70 eV) showed peaks at m/z (rel. int.): 324 (0.44, M^+), 296 (7.6, M^+-C_2H_4), 279 (18, M^+-OEt), 251 (11, M^+-COOEt), 197 (100, M^+-I). Exact mass calc'd for $C_{11}H_{17}O_3I$: 324.0222. Found: 324.0223.

Rearrangement of Ethyl 1-Iodopropyl-2-oxocyclopentanoate (23b). A solution of tri-*n*-butyltin hydride (103 mg, 0.36 mmoles) and AIBN (9 mg, 0.05 mmoles) in 5 mL of benzene was added dropwise over 20 hr to a refluxing solution of the iodide **23b** (97.2 mg, 0.3 mmoles) in 80 mL of benzene. After refluxing for an additional 24 hr, the reaction was cooled to room temperature and concentrated. Column chromatography (elution with 5:1 n-hexane ethyl acetate) of the crude product after standard workup afforded 41 mg (69%) of the rearrangement product **24b** as a colorless oil and 13.5 mg of the reduced product **25b**.

The 300 MHz proton nmr spectrum ($CDCl_3$) of the rearrangement product **24b** showed a two-proton methylene quartet (J = 7.1 Hz) at δ 4.09, a two-proton multiplet at δ 2.65-2.56, a two-proton multiplet at δ 2.35-2.26, a nine-proton mutiplet at δ 2.15-1.58, and a three-proton methyl triplet (J = 7.1 Hz) at δ 1.22. The ^{13}C nmr spectrum ($CDCl_3$) showed 8 lines at δ: 216.3 (s), 178.3 (s), 60.0 (t, J = 146.5 Hz), 41.8 (d, J = 126.6 Hz), 41.57 (t, J = 129.6 Hz), 29.7 (t, J = 129.0 Hz), 24.1 (t, J = 127.4 Hz), 13.8 (q, J = 126.8 Hz). The IR spectrum (neat) showed bands at: 2938.0 (m, CH), 1730.4 (vs, CO, ester), 1699.5 (vs, CO, ketone), 1468.1 (w), and 1176.7 (s) cm^{-1}. The mass spectrum (70 eV) showed peaks at m/z (rel. int.): 198 (30, M^+), 153 (43, M^+-OEt), 125 (50, M^+-COOEt). Exact mass calc'd for $C_{11}H_{18}O_3$: 198.1256. Found: 198.1256.

The 300 MHz proton nmr spectrum ($CDCl_3$) of the reduced product **25b** showed a two-proton methylene multiplet at δ 4.15, a three-proton multiplet at δ 2.55-2.18, a four-proton multiplet at δ 2.06-1.84, a three-proton multiplet at δ 1.70-1.30, a three-proton methyl triplet (J = 7.09 Hz) at δ 1.24, and a three-proton methyl triplet (J = 7.4 Hz) at δ 0.91. The IR spectrum (neat) showed bands at: 2961 (m, CH), 1751.6 (s, CO, ketone), 1728.4 (vs, CO,

ester), 1456 (w), 123 (m), and 1159.1 (m) cm^{-1}. The mass spectrum (70 eV) showed peaks at m/z (rel. int.): 198 (1.6, M^+), 170 (20, M^+-C_2H_4), 156 (100, M^+-$CH_3CH{=}CH_2$), 125 (29, M^+-COOEt). Exact mass calc'd for $C_{11}H_{18}O_3$: 198.1256. Found: 198.1257.

Ethyl 1-Bromopropyl-2-oxocyclohexanoate (26a). Following the general alkylation procedure, ethyl 1-oxocyclohexanoate (4) (680 mg, 4.0 mmoles) was alkylated with 1,3-dibromopropane (1.2 g, 6.0 mmoles) for 12 hr at reflux. Flash column chromatography (elution with 5:1 n-hexane-ethyl acetate) of the crude product after standard aqueous workup afforded 418 mg (36%) of the bromide **26a**.

The 300 MHz proton nmr spectrum ($CDCl_3$) showed a two-proton methylene quartet (J = 7.12 Hz) at δ 4.21, a two-proton bromomethyl multiplet at δ 3.39, a four-proton multiplet at δ 2.53-2.01, an eight-proton multiplet at δ 1.9-1.44, and a three-proton methyl triplet (J = 7.12 Hz) at δ 1.27. The ^{13}C nmr spectrum ($CDCl_3$) showed 12 lines at δ: 206.7 (s), 171.16 (s), 60.78 (t, J = 146.7 Hz), 59.8 (s), 40.5 (t, J = 130.0 Hz), 35.8 (t, J = 131.8 Hz), 33.3 (t, J = 151.3 Hz), 32.99 (t, J = 133.1 Hz), 27.4 (t, J = 132.4 Hz), 27.1 (t, J = 131.5 Hz), 22.11 (t, J = 127.8 Hz), 13.7 (q, J = 127.1 Hz). The IR spectrum (neat) showed bands at: 2941.8 (m, CH), 2866.6 (w, CH), 1714.9 (vs, CO, ester and ketone overlapped), 1448.7 (m), 1242.3 (s), and 1174.8 (m) cm^{-1}. The mass spectrum (70 eV) showed peaks at m/z (rel. int.): 292, 290 (0.2, M^+), 247, 245 (8, M^+-OEt), 219, 217 (6, M^+-COOEt), 211 (100, M^+-Br). Exact mass calc'd for $C_{10}H_{14}O_2{}^{81}Br$: 247.0157. Found: 247.0156.

Rearrangement of Ethyl 1-Bromopropyl-2-oxocyclohexanoate (26a). A solution of tri-*n*-butyltin hydride (120 μL, 0.45 mmoles) and AIBN (12 mg, 0.067 mmoles) in benzene (10 mL) was added dropwise over 24 hr to a refluxing solution of the bromide **26a** (87 mg, 0.3 mmoles) in 160 mL of benzene. Column chromatography (elution with 40:1 methylene chloride-acetonitrile) of the crude product after standard aqueous workup afforded 31.7 mg (49%) of the rearrangement product **27** and 9.6 mg (15%) of the reduced product **28**.

The 300 MHz proton nmr spectrum ($CDCl_3$) of the rearrangement product **27** showed a two-proton methylene quartet (J = 7.13 Hz) at δ 4.1, a four-proton multiplet at δ 2.52-2.34, an eleven-proton multiplet at δ 2.04-1.54, and a three-proton methyl triplet (J = 7.13 Hz) at δ 1.24. The ^{13}C nmr spectrum ($CDCl_3$) showed 11 lines at δ: 216.7 (s), 175.4 (s), 59.7 (t, J = 147.9 Hz), 42.4 (t, J = 127 Hz), 41.2 (d, J = 127.4 Hz), 27.9 (t, J = 125.6 Hz), 26.4 (t, J = 123.03 Hz), 24.0 (t, J = 119.2 Hz), 23.5 (t, J = 126.6 Hz), 22.4 (t, J = 127.6 Hz), 13.8 (q, J = 126.8 Hz). The IR spectrum (neat) showed bands at: 2938.0 (m, CH), 1728.4 (vs, CO, ester), 1701.4 (vs, CO, ketone), 1446.8 (m), and 1180.67 (m) cm^{-1}. The mass spectrum (70 eV) showed peaks at m/z (rel. int.): 212 (8.1, M^+), 184 (2.5, M^+-C_2H_4), 166 (25, M^+-EtOH), 156 (31.2, M^+-C_2H_4-CO), 138 (32, M^+-EtOH-CO). Exact mass calc'd for $C_{12}H_{20}O_3$: 212.1412. Found: 212.1413.

The 300 MHz proton nmr spectrum ($CDCl_3$) of the reduced product **28** showed a two-proton methylene quartet (J = 7.1 Hz) at δ 4.20, a four-proton mutiplet at δ 2.65-2.25, an eight-proton mutiplet at δ 2.1-1.15, a three-proton methyl triplet (J = 7.1 Hz) at δ 1.26, and a three-proton methyl triplet at δ 0.90 (J = 7.28 Hz). The IR spectrum (neat) showed bands at: 2939.9 (m, CH), 2870.4 (w, CH), 1714.9 (vs, CO, ester and ketone), 1450.7 (w), 1145.9 (m), and 1203.7 (vs) cm^{-1}. The mass spectrum (70 eV) showed peaks at m/z (rel. int.): 212 (1.2, M^+), 184 (1, M^+-C_2H_4), 170 (100, M^+-$CH_3CH = CH_2$).

Ethyl 1-Iodopropyl-2-oxocyclohexanoate (26b). Following the general alkylation procedure, ethyl 2-oxocyclohexanoate (4) (680 mg, 4.0 mmoles) was alkylated with 1,3-diiodopropane (1.8 g, 6 mmoles) for 17 hr at reflux. Flash column chromatography (elution with 250:2 methylene dichloride-acetonitrile) of the crude product after standard aqueous workup afforded 296 mg (22%) of the iodide **26b**.

The 300 MHz proton nmr spectrum ($CDCl_3$) showed a two-proton methylene quartet (J = 7.17 Hz) at δ 4.20, a two-proton iodomethyl multiplet at δ 3.15, a four-proton multiplet at δ 2.45, an eleven-proton multiplet at δ 1.9 - 1.39, and a three-proton methyl triplet at δ 1.27 (J = 7.17). The ^{13}C nmr spectrum ($CDCl_3$) showed 12 lines at δ: 206.94 (s), 171.2 (s), 60.9 (t, J = 150.9 Hz), 59.8 (s), 40.6 (t, J = 132.8 Hz), 35.9 (t, 131.6), 35.3 (t, J = 133.4 Hz), 28.2 (t, J = 125.6 Hz), 27.2 (t, J = 133.0 Hz), 22.2 (t, J = 128.2 Hz), 13.9 (q, J = 126.7 Hz), 6.31 (t, J = 148.3 Hz). The IR spectrum (neat) showed bands at: 2939.9 (m, CH), 2864.6 (w, CH), 1714.9 (vs, CO, ester and ketone overlapped), 1448.7 (m), and 1205.7 (m) cm^{-1}. The mass spectrum (70 eV) showed peaks at m/z (rel. int.): 338 (0.2, M^+), 293 (8, M^+-OEt), 265 (9.5, M^+-COOEt), 211 (100, M^+-I). Exact mass calc'd for $C_{10}H_{14}O_2I$: 293.0039. Found: 293.0040.

Rearrangement of Ethyl 1-Iodopropyl-2-oxocyclohexanoate (26b). A solution of tri-*n*-butylgermanium hydride (73 μL, 0.3 mmoles) and AIBN (3 mg, 0.017 mmoles) in benzene (5 mL) was added dropwise over 12 hr to a refluxing solution of the iodide **26b** (67.6 mg, 0.2 mmoles) in 80 mL of benzene. Column chromatography (elution with 5:1 hexane–ethyl acetate) of the crude product after standard aqueous workup afforded 32 mg (75%) of the rearrangement product **27** and 5 mg (12%) of the reduced product **28**.

The spectral data for the rearrangement product **27** and the reduced product **28** were identical to those of the products from the rearrangement of the corresponding bromide **26a**.

Methyl 1-Bromopropyl-2-oxocycloheptanoate (29a). Following the general alkylation procedure, methyl 2-oxocycloheptanoate (8) (680 mg, 4 mmoles) was alkylated with 1,3-dibromopropane (606 μL, 6.0 mmoles) for 24 hr

at reflux. Column chromatography (elution with 50:1 dichloromethane-acetonitrile) of the crude product after standard aqueous workup afforded 457 mg (39%) of the bromide **29a**.

The 300 MHz proton nmr spectrum ($CDCl_3$) of **29a** showed a three-proton methyl singlet at δ 3.72, a two-proton bromomethyl multiplet at δ 3.38, and a fourteen-proton multiplet at δ 2.8-1.4. The IR spectrum (neat) showed bands at: 2932.2 (m, CH), 2858.2 (w, CH), 1738.1 (vs, CO, ester), 1711.1 (vs, CO, ketone), 1446.8 (w), 1228.8 (m), and 1178.7 (m) cm^{-1}. The ^{13}C nmr spectrum ($CDCl_3$) showed 12 lines at δ: 208.8 (s), 172.4 (s), 62.04 (s), 51.99 (q, J = 147.1 Hz), 41.76 (t, J = 148.8 Hz), 33.8 (t), 33.4 (t), 32.8 (t), 29.58 (t), 27.8 (t), 25.32 (t, J = 129.4 Hz), 24.60 (t, J = 126.2 Hz). The mass spectrum (70 eV) showed peaks at m/z (rel. int.): 292, 290 (0.3, M^+), 260, 258 (7, M^+-CH_3OH), 233, 231 (6, M^+-$COOCH_3$), 211 (65, M^+-Br). Exact mass calc'd for $C_{11}H_{15}O_2{}^{79}Br$: 258.0255. Found: 258.0256.

Rearrangement of Methyl 1-Bromopropyl-2-oxocycloheptanoate (29a). A solution of tri-*n*-butyltin hydride (120 μL, 0.45 mmoles) and AIBN (12 mg, 0.007 mmoles) in benzene (10 mL) was added dropwise over 24 hr to a refluxing solution of the bromide **29a** (87 mg, 0.3 mmoles) in 80 mL of benzene. Column chromatography (elution with 5:1 n-hexane-ethyl acetate) of the crude product after standard workup afforded 18.6 mg (29%) of the rearrangement product **30** and 20.4 mg (32%) of the reduced product **31**.

The 300 MHz proton nmr spectrum ($CDCl_3$) of the rearrangement product **30** showed a three-proton methyl singlet at δ 3.65, a five-proton multiplet at δ 2.73-2.28, a twelve-proton multiplet at δ 2.1-1.2. The ^{13}C nmr spectrum ($CDCl_3$) showed 11 lines at δ: 214.1 (s), 176.7 (s), 51.6 (q, J = 147.4 Hz), 42.9 (t, J = 133.8 Hz), 41.9 (d, J = 129.4 Hz), 41.1 (t, J = 120.0 Hz), 27.8 (t, J = 126.6 Hz), 27.3 (t, J = 131.8 Hz), 25.4 (t), 23.5 (t), and 21.9 (t, J = 122.3 Hz). The IR spectrum (neat) showed bands at: 2934.1 (m, CH), 2870.4 (w, CH), 1734.2 (vs, CO, ester), 1699.5 (vs, CO, ketone), 1435.2 (m), 1699.5 (m), 1435.2 (m), and 1169.0 (m) cm^{-1}. The mass spectrum (70 eV) showed peaks at m/z (rel. int.): 212 (5, M^+), 180 (25, M^+-CH_3OH), 153 (23.5, M^+-$COOCH_3$). Exact mass calc'd for $C_{12}H_{20}O_3$: 212.1412. Found: 212.1413.

The 300 MHz proton nmr spectrum ($CDCl_3$) of the reduced product **31** showed a three-proton methyl singlet at δ 3.67, a four-proton multiplet at δ 2.9-2.2, a ten-proton multiplet at δ 2.1-1.2, and a three-proton methyl triplet (J = 7.3 Hz) at δ 0.89. The IR spectrum (neat) showed bands at: 2953.4 (w, CH), 2970.4 (w, CH), 1734.2 (vs, CO, ester), 1711.1 (vs, CO, ketone), and 1167.1 (m) cm^{-1}. The mass spectrum showed peaks at m/z (rel. int.): 212 (4, M^+), 181 (8.1, M^+-OCH_3), 170 (2.0, M^+-$CH_3CH{=}CH_2$), and 153 (6, M^+-$COOCH_3$). Exact mass calc'd for $C_{12}H_{20}O_3$: 212.1412. Found: 212.1413.

Methyl 1-Iodopropyl-2-oxocycloheptanoate (29b). Following the general alkylation procedure, methyl 2-oxocycloheptanoate (**8**) (680 mg, 4 mmoles) was alkylated with 1,3-diiodopropane (596 μL, 5.2 mmoles) for 2 hr at room temperature. Flash column chromatography (elution with 125:1 dichloromethane-acetonitrile) of the crude product after standard aqueous workup afforded 561 mg (41%) of the iodide **29b**.

The 300 MHz proton nmr spectrum ($CDCl_3$) showed a three-proton methyl singlet at δ 3.73, a two-proton iodomethyl multiplet at δ 3.15, a two-proton multiplet at δ 2.68-2.45, a two-proton multiplet at δ 2.18-2.00, and a ten-proton multiplet δ 1.83-1.62. The ^{13}C nmr spectrum ($CDCl_3$) showed 12 lines at δ: 208.8 (s), 172.4 (s), 62.0 (s), 52.05 (q, J = 147.1 Hz), 41.7 (t, J = 129.04 Hz), 36.12 (t, J = 127.7 Hz), 32.8 (t, J = 122.7 Hz), 29.6 (t), 28.6 (t), 25.32 (t, J = 130.18 Hz), 24.62 (t, J = 127.0 Hz), and 6.25 (t, J = 150.7 Hz). The IR spectrum (neat) showed bands at: 2932.2 (m, CH), 2858.9 (w, CH), 1736.2 (vs, CO, ester), 1709.1 (vs, CO, ketone), 1444.9 (m), 1225.0 (s), and 1153.6 (m) cm^{-1}. The mass spectrum (70 eV) showed peaks at m/z (rel. int.): 338 (1, M^+), 307 (3.8, M^+-OCH_3), 279 (7, M^+-$COOCH_3$), and 211 (100, M^+-I). Exact mass calc'd for $C_{12}H_{19}O_3I$: 338.0379. Found: 338.0380.

Rearrangement of Methyl 1-Iodopropyl-2-oxocycloheptanoate (29b). A solution of tri-*n*-butyltin hydride (70 μL, 0.27 mmoles) and AIBN (6 mg, 0.034 mmoles) in benzene (5 mL) was added dropwise over 20 hr to a refluxing solution of the iodide **29b** (58 mg, 0.1717 mmoles) in 80 mL of benzene. Column chromatography (elution with 5:1 n-hexane-ethyl acetate) of the crude product after standard aqueous workup afforded 12.7 mg (34 %) of the rearrangement product **30** and 13.7 mg (38%) of the reduced product **31**. The spectral data of both products were identical to those obtained from the corresponding bromide **29a**.

Ethyl 1-Iodobutyl-2-oxocyclopentanoate (32). Following the general alkylation procedure, ethyl 2-oxocyclopentanoate (653 mg, 4.1 mmoles) was alkylated with 1,4-diiodobutane (1.07 mL, 8.25 mmoles) for 24 hr at reflux. Flash column chromatography (6:1 n-hexane-ethyl acetate) of the crude product after standard aqueous workup afforded 798 mg (58%) of the iodide **32**.

The 300 MHz proton nmr spectrum ($CDCl_3$) showed a two-proton methylene quartet (J = 7.15 Hz) at δ 4.15, a two-proton iodomethyl triplet (J = 6.81 Hz) at δ 3.18, a four-proton multiplet at δ 2.6-2.2, an eight-proton multiplet at δ 2.1-1.27, and a three-proton methyl triplet (J = 7.15 Hz) at δ 1.26. The ^{13}C nmr spectrum ($CDCl_3$) showed 12 lines at δ: 214.5 (s), 170.7 (s), 61.2 (t, J = 150.1 Hz), 60.1 (s), 37.8 (t, J = 129.3 Hz), 33.4 (t, J = 128.6 Hz), 32.6 (t, J = 128.5 Hz), 32.4 (t, J = 132.7 Hz), 25.6 (t, J = 126.9 Hz), 19.5 (t, J = 132.5 Hz), 14.04 (q, J = 126.9 Hz), 6.3 (t, J = 150.9 Hz). The IR spectrum (neat) showed bands at: 2957 (m, CH), 1749.7 (vs, CO, ketone), 1722.6 (vs, CO, ester), 1454.5 (m), and 1174.8 (s) cm^{-1}. The mass spectrum showed peaks at m/z (rel. int.): 310 (3, M^+-C_2H_4), 293 (10, M^+-

OEt), 265 (5, M^+-COOEt), 211 (40, M^+-I), 183 (16, M^+-I-C_2H_8). Exact mass calc'd for $C_{11}H_9O_2I$: 310.0430. Found: 310.0430.

Rearrangement of Ethyl 1-Iodobutyl-2-oxocyclopentanoate (32). A solution of tri-*n*-butyltin hydride (121 μL, 0.40 mmoles) and AIBN (9 mg, 0.05 mmoles) in 6 mL of benzene was added dropwise over 12 hr to a refluxing solution of the iodide **32** (130 mg, 0.38 mmoles) in 80 mL of benzene. Column chromatography (100:1 methylene chloride-acetonitrile) of the crude product after standard aqueous workup afforded 29 mg (36%) of the rearrangement product **27** and 29.8 mg (37%) of the reduced product **33**.

The 300 MHz proton nmr spectrum of the reduced product **33** showed a two-proton methylene multiplet at δ 4.16, a two-proton multiplet at δ 2.58-2.17, a ten-proton multiplet at δ 2.06-1.1, and a three-proton methyl triplet (J = 7.0 Hz) at δ 0.9. The IR spectrum (neat) showed bands at: 2959.2 (s, CH), 2860.8 (s, CH), 1751.67 (vs, CO, ketone), 1724.6 (vs, CO, ester), 1464.2 (m), and 1223.0 (s) cm^{-1}. The mass spectrum (70 eV) showed peaks at m/z (rel. int.): 212 (0.4, M^+), 184 (4.3, M^+-C_2H_4), 167 (12.4, M^+-OEt), 156 (100, M^+-$CH_3CH_2CH = CH_2$), 139 (15, M^+-COOEt). Exact mass calc'd for $C_{12}H_{20}O_3$: 212.1412. Found: 212.1412.

Ethyl 1-Iodobutyl-2-oxocyclohexanoate (34). Following the general alkylation procedure, ethyl 2-oxocyclohexanecarboxylate (**4**) (680 mg, 4.0 mmoles) was alkylated with of 1,4-diiodobutane (1.8 g, 5.8 mmoles) for 6 hr at room temperature. Flash chromatography (elution with 9:1 hexane-ethyl acetate) of the crude product after standard aqueous workup gave 1.03 g (73%) of the iodide **34** as a colorless oil. The 300 MHz proton nmr spectrum ($CDCl_3$) showed a two-proton methylene quartet at δ 4.21 (J = 7.1 Hz), a two-proton iodomethyl triplet (J = 7.0 Hz) at δ 3.17, a three-proton multiplet at δ 2.54-2.01, an eleven-proton multiplet at δ 1.91-1.29, and a three-proton methyl triplet at δ 1.27 (J = 7.1 Hz). The IR spectrum (neat) showed bands at: 2938 (m, CH), 2604 (w, CH), 1713 (vs, CO, ester and ketone). The ^{13}C nmr spectrum ($CDCl_3$) showed 13 lines at δ: 207.4 (s), 171.5 (s), 60.9 (t, J = 150 Hz), 60.3 (s), 40.8 (t, J = 131 Hz), 35.8 (t, J = 131 Hz), 33.4 (t, J = 128 Hz), 33.2 (t, J = 127 Hz), 27.3 (t, J = 131 Hz), 24.9 (t, J = 128 Hz), 22.3 (t, 127 Hz), 13.9 (q, J = 127 Hz), 6.15 (t, J = 149 Hz). The mass spectrum (70 eV) showed peaks at m/z (rel. int.): 307 (3.4, M^+-OEt), 279 (4.2, M^+-COOEt), 225 (13, M^+-I), and 170 (100). Exact mass calc'd for $C_{11}H_{16}O_2I$: 307.0195. Found: 307.0195.

Rearrangement of Ethyl 1-Iodobutyl-2-oxocyclohexanoate (34). A solution of tri-*n*-butyltin hydride (90 μL, 0.36 mmoles) and AIBN (10 mg, 0.061 mmoles) in benzene (5 mL) was added over 24 hr to a refluxing solution of the iodide **34** (105.6 mg, 0.3 mmoles) in 80 mL of benzene. The reaction mixture was heated to reflux for an additional 24 hr. Column chromatography on 2 g of silica gel (elution with 5:1 n-hexane-ethyl acetate) of the crude product after standard aqueous workup afforded 47.8 mg (71%) of the rearrangement product **35** and 16.9 mg (25%) of the reduced product **36**.

The 300 MHz proton nmr spectrum ($CDCl_3$) of the rearrangement product **35** showed a two-proton methylene quartet (J = 7.1 Hz) at δ 4.11, a two-proton multiplet at δ 2.75-2.66, a three-proton multiplet at δ 2.47-2.31, a twelve-proton multiplet at δ 1.98-1.42, and a three-proton methyl triplet (J = 7.1 Hz) at δ 1.24. The ^{13}C nmr spectrum ($CDCl_3$) showed 9 lines at δ: 214.08 (s), 176.10 (s), 60.03 (t, J = 147 Hz), 41.67 (t, J = 124.9 Hz), 41.47 (d, J = 126.2 Hz), 27.43 (t, J = 128.9 Hz), 23.6 (t, J = 124.8 Hz), 22.9 (t, J = 127.8 Hz), 14.1 (q, J = 126.6 Hz). The IR spectrum (neat) showed bands at: 2932 (m, CH), 2872 (w, CH), 1730 (vs, CO, ester), 1703 (vs, CO, ketone), and 1462 (m) cm^{-1}. The mass spectrum showed peaks at m/z (rel. int.): 226 (4.3, M^+), 181 (15, M^+-OEt), 170 (60), 153 (20, M^+-COOEt). Exact mass for $C_{13}H_{22}O_3$: 226.1569. Found: 226.1570.

The 300 MHz proton nmr spectrum ($CDCl_3$) of the reduced product **36** showed a two-proton methylene quartet (J = 7.13 Hz) at δ 4.19, a seventeen-proton multiplet at δ 2.52-1.16, and a three-proton methyl triplet (J = 7.13 Hz) at δ 0.88. The IR spectrum (neat) showed bands at: 2936 (m, CH), 2864 (w, CH), 1728 (s, CO, ester), and 1715 (vs, CO, ketone) cm^{-1}. The mass spectrum showed peaks at m/z (rel. int.): 226 (0.7, M^+), 181 (3.5, 14^+-OEt), 170 (25, M^+-CO-CH_2CH_2), 153 (7, M^+-COOEt). Exact mass calc'd for $C_{13}H_{22}O_3$: 226.1569. Found: 226.1570.

Methyl 1-Iodobutyl-2-oxocycloheptanoate (37). Following the general alkylation procedure, methyl 2-oxocycloheptanoate (**8**) (680 mg, 4 mmoles) was alkylated with 1,4-diiodobutane (1.5 g, 4.8 mmoles) at room temperature for 1 hr. Flash column chromatography (elution with 150:1 dichloromethane-acetonitrile) of the crude product after standard aqueous workup afforded 585 mg (41%) of **37**. The 300 MHz proton nmr spectrum ($CDCl_3$) showed a three-proton methyl singlet at δ 3.74, a two-proton iodomethyl triplet (J = 7.1 Hz) at δ 3.19 , a two-proton multiplet at δ 2.7-2.43, and a fourteen-proton multiplet at δ 2.2-1.23. The ^{13}C nmr spectrum ($CDCl_3$) showed 12 lines at δ: 209.2 (s), 172.8 (s), 62.6 (s), 52.2 (q, J = 150.0 Hz), 41.9 (t, J = 131.0 Hz), 34.0 (t, J = 129.0 Hz), 33.8 (t, J = 132.0 Hz), 32.5 (t, J = 127.5 Hz), 29.8 (t, J = 134.2 Hz), 25.6 (t, J = 134.2 Hz), 24.9 (t, J = 135.0 Hz), 6.3 (t, J = 156.7 Hz). The IR spectrum (neat) showed bands at: 2932.2 (m, CH), 2858.2 (w, CH), 1734.2 (vs, CO, ester), 1699.5 (vs, CO, ketone), 1456.4 (w), 1228.8 (m), and 1151.6 (m) cm^{-1}. The mass spectrum (70 eV) showed peaks at m/z (rel. int.): 352 (0.23, M^+), 321 (1.4, M^+-OCH_3), 293 (4.7, M^+-$COOCH_3$), 225 (7, M^+-I), 170 (100, M^+-$ICH_2CH_2CH{=}CH_2$). Exact mass calc'd for $C_{12}H_{18}O_2I$: 321.0352. Found: 321.0351.

Rearrangement of Methyl 1-Iodobutyl-2-oxocycloheptanoate (37). A solution of tri-*n*-butyltin hydride (80 μL, 0.297 mmoles) and AIBN (9 mg, 0.05 mmoles) in benzene (5 mL) was added over 20 hr to a refluxing solution of

the iodide **37** (69.8 mg, 0.198 mmoles) in 80 mL of benzene. Column chromatography (elution with 5:1 n-hexane-ethyl acetate) of the crude product following standard aqueous workup afforded 20.1 mg (45 %) of the rearranged product **38** and 13.4 mg (30%) of the reduced product **39**.

The 300 MHz proton nmr spectrum ($CDCl_3$) of the rearrangement product **38** showed a three-proton methyl singlet at δ 3.59, a five-proton multiplet at δ 2.6-2.20, a fourteen-proton multiplet at δ 1.93-1.2. The ^{13}C nmr spectrum ($CDCl_3$) showed 13 lines at δ: 214.1 (s), 176.6 (s), 51.4 (q, J = 146.6 Hz), 41.95 (t, J = 124.5 Hz), 41.66 (d, J = 125.8 Hz), 41.56 (d, J = 123.4 Hz), 27.59 (t), 26.23 (t), 26.14 (t), 24.00 (t), 22.71 (t), 22.32 (t), 22.16 (t). The IR spectrum (neat) showed bands at: 2943.7 (m, CH), 2872.4 (w, CH), 1734.2 (vs, CO, ester), 1705.3 (vs, CO, ketone), 1456.4 (w), and 1165.1 (w) cm^{-1}. The mass spectrum (70 eV) showed peaks at m/z (rel. int.): 226 (5.1, M^+), 194 (28.1, M^+-CH_3OH), 166 (18, M^+-CH_3OH-CO). Exact mass calc'd for $C_{13}H_{22}O_3$: 226.1569. Found: 226.1569.

The 300 MHz proton nmr spectrum ($CDCl_3$) of the reduced product **39** showed a three-proton methyl singlet at δ 3.71, a two-proton multiplet at δ 2.61-2.48, a two-proton multiplet at δ 2.18-1.91, a twelve-proton multiplet at δ 1.79-1.13, and a three-proton methyl triplet (J = 7.1 Hz) at δ 0.88. The IR spectrum (neat) showed bands at: 2932.2 (vs, CH), 2860.8 (m, CH), 1735.2 (vs, CO, ester), 1711.1 (vs, CO, ketone), 1456.4 (m), 1207.6 (s), 1147.8 (s). The mass spectrum (70 eV) showed peaks at m/z (rel. int.): 226 (0.66, M^+), 195 (4.3, M^+-OCH_3), 194 (5, M^+-CH_3OH), 170 (100, M^+-$CH_3CH_2CH{=}CH_2$). Exact mass calc'd for $C_{13}H_{22}O_3$: 226.1568. Found: 226.1568.

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