Palladium-Assisted Carboacylation of Olefins

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Abstract: Olefins, including ethene, propene, 1-hexene, *cis*- and *trans*-2-butene, styrene, and *N*-vinylacetamide, were complexed to palladium(II), alkylated with the anions of diethyl methylmalonate or cyclohexanone, and then acylated by treatment with CO and methanol, resulting in overall difunctionalization of the olefin. With diethyl methylmalonate alkylation occurred primarily at the 2 position of terminal olefins, and acylation at the 1 position resulted. Cyclohexanone enolate alkylation occurred predominantly at the 2 position of propene and *N*-vinylacetamide, but at the 1 position of 1-hexene. With the protected cyanohydrin of benzaldehyde and ethene, the corresponding γ-keto ester was prepared. Glutamic acid could be prepared from diethyl acetamidomalonate, ethene, CO, and methanol.

Introduction

Nucleophilic attack on palladium-complexed olefins generates, at least transiently, σ-alkylpalladium complexes. Those stabilized by being part of a five-membered chelate ring (i.e., from amination[1] and methoxylation[2] of cyclooctadiene, and from methoxylation[3] and alkylation[4] of allylamines and sulfides) can often be isolated and fully characterized. When chelation of this type is absent, σ-alkylpalladium complexes normally cannot be isolated, but rather undergo spontaneous decomposition by β-hydride elimination. Regardless of stability, σ-alkylpalladium complexes generated in this fashion undergo facile insertion reactions with carbon monoxide to produce σ-acyl complexes. Again, those stabilized by chelation as part of a five-membered ring (i.e., from aminocarbonylation of cyclooctadiene[1] and terminal monoolefins[5]) can be isolated and characterized, while those lacking this type of chelate stabilization (from methoxycarbonylation of cyclooctadiene,[2] allylamines,[3] and monoolefins[6]) spontaneously decompose to give metal-free organic materials. The overall process, in all cases, is a difunctionalization of the olefinic substrate, resulting in the introduction of a nucleophile at one olefin terminus and acyl functionality (normally an ester group) at the other.

We have recently reported the palladium-assisted alkylation of olefins by carbanions,[7,8] a process which proceeds through unstable σ-alkylpalladium complex intermediates. Herein we report the successful coupling of this alkylation reaction with the insertion of carbon monoxide, resulting in the overall carboacylation of olefins of potential use in organic synthesis (eq 1).

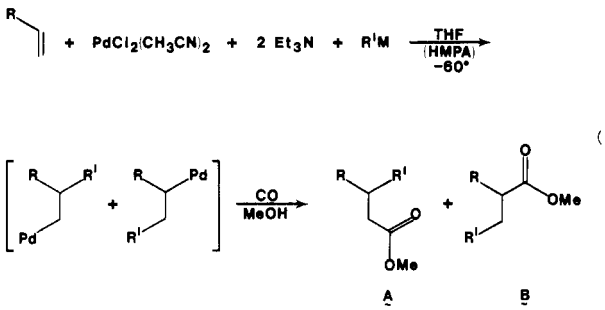
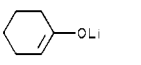
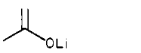


Table I. Palladium-Assisted Carboacylation of Olefins (Equation 1)

olefin	R'M	products, % yield[a]
ethene	$LiC(CH_3)(COOEt)_2$	R = H, A = B, 63
propene	$LiC(CH_3)(COOEt)_2$	R = Me, A, 84
1-hexene	$LiC(CH_3)(COOEt)_2$	R = *n*-Bu, A, 76; other isomers,[b] 10
N-vinylacetamide	$LiC(CH_3)(COOEt)_2$	R = NHAc, A, 61
styrene	$LiC(CH_3)(COOEt)_2$	R = Ph, A, 26
cis-2-butene	$LiC(CH_3)(COOEt)_2$	*b*, 36
trans-2-butene	$LiC(CH_3)(COOEt)_2$	*b*, 33
ethene	 i	R = H, A = B, 68
propene	i	R = Me, A, 70; B, 7
1-hexene	i	R = *n*-Bu, A, 10; B, 25; other isomers,[b] 18
N-vinylacetamide	i	R = NHAc, A, 46
styrene	i	R = Ph, A, 19; B, 12
cis-2-butene	i	*b*, 17
trans-2-butene	i	*b*, 17
propene		R = Me, A, 26; B, 14
ethene	$LiC(Ph)(CN)(OSiMe_3)$	$PhCOCH_2CH_2COOMe$, 50[c]
ethene	$NaC(NHAc)(COOEt)_2$	R = H, A = B, 56

[a] Yields of isolated, purified products, based on Pd. [b] Mixtures of positional isomers were obtained—see text. [c] After hydrolysis of the protected cyanohydrin.

Results and Discussion

Successful carboacylation of olefins requires that two successive palladium-assisted reactions proceed in reasonable yield. At the same time, a number of competing processes must be suppressed. Thus, alkylation of the olefin must be essentially complete *prior* to exposure to carbon monoxide since carbon monoxide will compete with olefin for a coordination site on palladium, lowering the yield of alkylation and generating side products resulting from nucleophilic attack on coordinated carbon monoxide. Next, carbon monoxide must insert into the palladium–carbon σ bond under conditions milder than those required for β-hydride elimination and a reagent to trap the unstable σ-acyl complex (in this case methanol) must be provided. Finally, there is a regiochemical complication, in that alkylation of unsymmetrical olefins often gives mixtures of primary and secondary σ-alkylpalladium complexes,[7,8] and secondary complexes insert carbon monoxide only slowly.[9]

With a variety of both stabilized and nonstabilized carbanions as nucleophiles, and terminal and internal olefins as substrates, all of these criteria can be met by careful control of experimental

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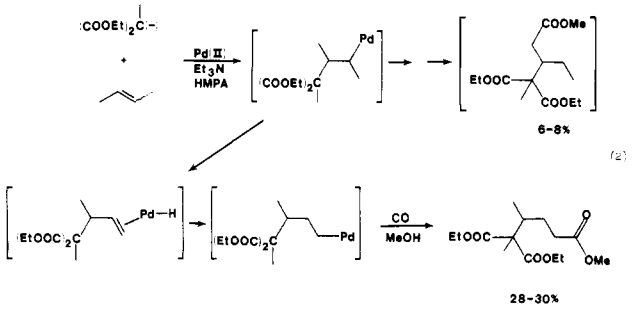
conditions. The results are summarized in Table I. The yields of carboacylation observed roughly parallel the yields of the alkylation reactions of the various carbanion–olefin combinations,[7,8] indicating that the carbonyl insertion reaction is quite efficient. Thus, with the stabilized carbanion of diethyl methylmalonate, and the olefins ethene, propene, and 1-hexene, high yields of carboacylation are obtained. With these olefins by far the major product is that resulting from alkylation at the 2 position and carbonylation at the 1 position (isomer A), with only traces of the other regioisomer (B) or further rearranged products being obtained. This reflects both the regioselectivity of the alkylation reaction (2-attack strongly favored)[7,8] and the facility of migratory insertion by primary alkylmetal complexes relative to secondary complexes.[9] While stabilized carbanions are known[7,8] to alkylate olefins in the absence of HMPA, it was observed that addition of HMPA resulted in higher yields of alkylation and higher regioselectivity for alkylation at the 2 position. HMPA similarly facilitates this carboacylation reaction, as exemplified by the reaction of 1-hexene with diethyl methylmalonate. In the absence of HMPA, only 44–46% of isomer A (alkylation at the 2 position, acylation at the 1 position) is obtained, together with 13–23% of mixed olefin isomers from alkylation at the 1 position followed by β-hydride elimination. In contrast, in the presence of HMPA, 70–75% of carboacylation product A is obtained, along with only minor (<10%) amounts of other regioisomers, and no β-elimination products. The electron-rich enamide *N*-vinylacetamide also reacts to produce the highly functionalized diester amide in good yield. In contrast, styrene reacts in only poor yield, undergoing exclusive alkylation at the benzylic position. (Simple alkylation of this olefin also occurs at the benzylic position in only poor yield.)

The carboacylation of both *cis*- and *trans*-2-butene by diethyl methylmalonate gives the same major product in modest yields (again, equivalent to the alkylation reaction itself). The product is that arising from acylation of the *terminal* carbon of the butenes, indicating that the initially formed secondary σ-alkylpalladium complex rearranges to a primary σ-alkyl complex prior to CO insertion (eq 2). Presumably the rearrangement occurs via a

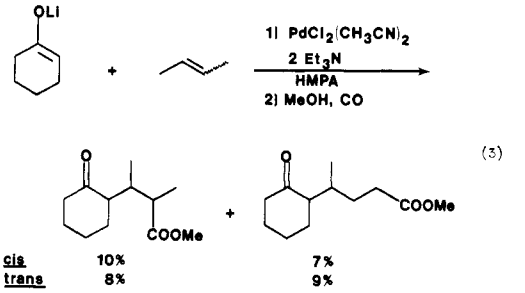


β-hydride elimination–readdition. The readdition is very efficient since no olefinic product was obtained. Since CO insertion into secondary alkyl complexes is slow and since a facile pathway to primary alkyl complexes exists, predominantly rearranged product is formed. Similar facile rearrangements have been observed in the palladium(II)-catalyzed carbonylation of olefins to diesters. In these cases also no olefinic products from β-hydride elimination were observed.[9]

Less stabilized carbanions such as simple ketone enolates are also efficient in this carboacylation of olefins. Thus the enolate of cyclohexanone reacts with ethene, propene, and *N*-vinylacetamide almost exclusively at the 2 position to produce the corresponding keto esters in moderate to high yield. In contrast, styrene alkylates at both the α and β positions (1.5:1) to produce the corresponding esters. In all these cases both the yields and the regioselectivity of carboacylation closely parallel those of the corresponding alkylation reactions.

The reactions of cyclohexanone enolate with 1-hexene and with internal olefins are somewhat more complex. The major product (25%) corresponds to alkylation at the 1 position and carbonylation at the 2 position (B). Since alkylation at the 1 position produces a secondary alkylpalladium complex which can migrate along the hexyl chain by successive β-hydride elimination–readdition processes, carbonylation at *each* carbon of the alkyl chain is possible. Indeed, an inseparable mixture of at least three other side chain ester isomers, with a combined yield of 18%, is also obtained. Finally, a small amount of regioisomer A (10%) is obtained.[10]

Migration of this type is also noted in the reactions of *cis*- and *trans*-2-butene, which give a 1:1 mixture of internal and terminal (from migration) esters (eq 3). (The low overall yields with these



olefins were due both to the problems in the separation of isomers and to the production of dialkylation products.[8]) This stands in contrast to the reaction of diethyl methylmalonate with these same olefins, in which the major product is that from acylation at the primary (terminal) position (eq 2). These differences reflect a difference in the relative rates of insertion and rearrangement between the different σ-alkylpalladium complexes.

Finally, this carboacylation reaction is not restricted to simple carbanions. The protected cyanohydrin of benzaldehyde (an acyl anion equivalent) reacts with ethylene and carbon monoxide to produce the corresponding γ-keto ester after hydrolysis. Similarly, sodium diethyl acetamidomalonate reacts with ethene and carbon monoxide to give the corresponding triester amide, which could be hydrolyzed and decarboxylated to glutamic acid. In contrast, lithium phenylacetylide fails to alkylate ethene, but rather undergoes direct carbonylation itself, producing methyl phenylpropiolate in moderate yield.

Structure Assignments. For many of the compounds listed in Table I, ^{1}H NMR data did not allow unequivocal assignment of structure and ^{13}C NMR was required. Structures were assigned by considering the parent compounds (those resulting from the reaction of the carbanion with ethylene and CO), and assigning the ^{13}C chemical shifts of each carbon using the data of James and Stille[11] and Batchelor et al.[12] For products resulting from reactions of substituted olefins, ^{13}C spectra for both possible regioisomers (A and B) were calculated using the data of Lindeman and Adams[13] and Wehrli and Wirthlin.[14] In all cases the structure which corresponded to the best fit calculated ^{13}C NMR spectrum was also consistent with the ^{1}H NMR spectrum, and with the regiochemistry observed in the simple alkylation of the particular olefin with the requisite carbanion. The ^{13}C data is available as supplementary material.

Summary

Olefins react with carbanions and carbon monoxide in the presence of Pd(II) and methanol to undergo a facile carboacylation process. When the alkylation step produces a primary σ-alkylpalladium complex, the overall reaction goes in good yield to produce a single product, and should be of use in organic synthesis. When the alkylation step produces a secondary σ-alkylpalladium complex having adjacent β hydrogens, extensive rearrangement occurs. In these cases mixtures of products are obtained, and the

(10) The structure of isomer A was assigned primarily by its ^{13}C NMR spectrum, which showed an ester carbonyl carbon at 173.29 ppm and a terminal CH_3 at 13.84 ppm. In all cases reported here and in ref 14, esters on primary carbons appeared upfield from 175 ppm, while those on secondary carbons appeared downfield from 175 ppm. Hence isomer A (R = *n*-Bu) is the only structure consistent with all of the data.

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process is of little synthetic utility.

Experimental Section

General and Materials. These are as described in a previous paper.[8]

General Reaction Procedure for the Carboacylation of Olefins by Lithium Diethyl Methylmalonate. In a 100-mL, two-necked, round-bottom flask fitted with a stopcock and a rubber serum cap, $PdCl_2(CH_3CN)_2$ (1.0 mmol) was degassed (by alternate evacuation and filling with argon) and dissolved in 22 mL of argon-saturated THF. Liquid olefins (2–5 mmol) were introduced via syringe, while gaseous olefins (excess) were introduced by attaching a balloon filled with the appropriate olefin to the flask's stopcock, purging the argon, and stirring the $PdCl_2(CH_3CN)_2$ under an olefin atmosphere for 0.5 h. HMPA (4 mL) was added to the resulting homogeneous, amber solution (with ethylene, propene, and *N*-vinylacetamide no HMPA was added), and after 0.1 h the solution was cooled to −78 °C. Triethylamine (2.0 mmol) was added dropwise over 0.2 h, the solution was warmed to −60 °C, and a precooled (−78 °C) THF solution of the carbanion (1.3 mmol in 8 mL of THF, prepared from LDA) was added over 0.2 h. This mixture was stirred at −60 °C for 0.75 h, methanol (15 mL precooled) was added, a CO-filled balloon was attached to the stopcock, and the solution was allowed to slowly warm to 25 °C. After stirring for 12 h at 25 °C, the black slurry was centrifuged to remove Pd metal, and the supernatant concentrated under vacuum to give the crude product. For the reactions involving HMPA, the concentrated solution was diluted with 150 mL of diethyl ether (from the washings of the Pd(0) precipitate) and 200 mL of petroleum ether. The ether solution was extracted with 2 × 70 mL of water and once with 70 mL of saturated sodium chloride solution and dried over anhydrous $MgSO_4$. Filtration and evaporation of the solvent under vacuum gave the crude product.

Reaction of Lithium Diethyl Methylmalonate. A. With Ethene. Purification by flash chromatography[15] (3 × 18 cm, silica gel, 4:1 hexane–ethyl acetate, R_f 0.31) gave 167 mg (63%) of pure 1-methyl-1,1,3-propanetricarboxylic acid 1,1-diethyl-3-methyl ester: NMR ($CDCl_3$) δ 1.24 (t, J = 7 Hz, 6, OCH_2CH_3), 1.39 (s, 3, CCH_3), 1.29–2.6 (m, 4, CH_2CH_2), 3.65 (s, 3, $COOCH_3$), 4.15 (q, J = 7 Hz, 4, OCH_2CH_3); IR (neat) 1735 (C=O) cm^{-1}. Anal. ($C_{12}H_{20}O_6$) C, H.

B. With Propene. Purification by preparative layer chromatography (SiO_2, 4:1 hexane–ether, twice, R_f 0.4) gave 0.23 g (84%) of 1,2-dimethyl-1,1,3-propanetricarboxylic acid 1,1-diethyl-3-methyl ester: NMR (CCl_4) δ 0.93 (d, J = 7 Hz, 3, $CHCH_3$), 1.26 (t, J = 7 Hz, 6, OCH_2CH_3), 1.33 (s, 3, CCH_3), 1.9–2.9 (m, ABC with C proton coupled to CH_3, δ_A = 2.1, δ_B = 2.5, δ_C = 2.7, J_{AB} = 16, J_{AC} = 11, J_{BC} = 3 Hz, 3, $-CH(CH_3)CH_2COOMe$), 3.66 (s, 3, $COOCH_3$), 4.16 (q, J = 7 Hz, 4, OCH_2CH_3); IR (neat) 1735 (C=O) cm^{-1}. Anal. ($C_{13}H_{22}O_6$) C, H.

C. With 1-Hexene. Purification by medium-pressure liquid chromatography (SiO_2, 30:1 hexane–ether) gave 250 mg (76%) of 1-methyl-2-*n*-butyl-1,1,3-propanetricarboxylic acid 1,1-diethyl-3-methyl ester: NMR ($CDCl_3$) δ 0.90 (m, 3, *n*-$BuCH_3$), 1.25 (t, J = 7 Hz, 6, OCH_2CH_3), 1.38 (s, 3, CCH_3), 1.2–1.45 (m, 6, $-(CH_2)_3-$), 2.0–2.5 (ABC system with C proton coupled to CH_2, δ_A = 2.20, δ_B = 2.54, δ_C = 2.73, J_{AB} = 16, J_{AC} = 7, J_{BC} = 4 Hz, 3, $CHCH_2COOMe$), 3.67 (s, 3, OCH_3), 4.16 (q, J = 7 Hz, 4, OCH_2CH_3); IR (neat) 1746 (C=O) cm^{-1}. Anal. ($C_{16}H_{28}O_6$) C, H.

In addition a minor amount (10%) of another isomer (by ^{13}C NMR) of this material was isolated.

D. With *N*-Vinylacetamide. The reaction was run in the usual fashion, using a slight excess (1.2 mmol to 1 mmol of Pd) of the olefin. Purification by medium-pressure liquid chromatography (SiO_2, 4:1 ethyl acetate–hexane) gave 197 mg (61%) of a white solid (mp 94–95 °C from cyclohexane), 1-methyl-2-acetamido-1,1,3-propanetricarboxylic acid 1,1-diethyl-3-methyl ester: NMR ($CDCl_3$) δ 1.27, 1.30 (d of t, J = 7 Hz, 6, OCH_2CH_3), 1.50 (s, 3, CCH_3), 1.96 (s, 3, $NHCOCH_3$), 2.5–2.7 (AB of ABX system, δ_A = 2.6, δ_B = 2.7, J_{AB} = 6, J_{AX} = 9, J_{BX} = 5 Hz, 2, $COCH_2CNH$), 3.17 (s, 3, OCH_3), 4.17, 4.21 (d of q, J = 7 Hz, 4, OCH_2CH_3), 4.9–5.2 (m, X of ABX, coupled to NH, 1, $NHCHCH_2$), 6.79 (br d, J = 10 Hz, 1, NH); IR ($CHCl_3$) 1726 (ester C=O), 1675 (amide C=O) cm^{-1}. Anal. ($C_{14}H_{23}NO_6$) C, H, N.

E. With Styrene. Purification by medium-pressure liquid chromatography (20:1 hexane–ether) gave 90 mg (26%) of 1-methyl-2-phenyl-1,1,3-propanetricarboxylic acid 1,1-diethyl-3-methyl ester: NMR ($CDCl_3$) δ 1.20, 1.27 (d of t, J = 7 Hz, 6, OCH_2CH_3), 1.33 (s, 3, CCH_3), 3.03 (d, J = 8 Hz, 2, CH_2COOMe), 3.55 (s, 3, COOMe), 4.01 (t, J = 8 Hz, 1, PhCH), 4.14, 4.27 (d of q, J = 7 Hz, 4, OCH_2CH_3), 7.34 (s, 5, ArH); IR (neat) 1733 (C=O) cm^{-1}. Anal. ($C_{18}H_{24}O_6$) C, H.

F. With *cis*-2-Butene. Purification by flash chromatography[15] (SiO_2, 3 × 17 cm, 4:1 hexane–ethyl acetate, R_f 0.40) gave 109 mg (36%) of carboacylated product. VPC analysis (10 ft, 3% SE-30, Chromosorb W, 180 °C) showed the product to consist of 15% 1-methyl-2-ethyl-1,1,3-propanetricarboxylic acid 1,1-diethyl-3-methyl ester (7.0 min) and 85% 1,2-dimethyl-1,1,4-butanetricarboxylic acid 1,1-diethyl-4-methyl ester (9.5 min), identical in all respects with the products obtained from *trans*-2-butene.

G. With *trans*-2-Butene. Purification by medium-pressure liquid chromatography (SiO_2, 15:1 hexane–ether) gave 100 mg (33%) of carboacylated product. VPC analysis as in F showed the same two triesters in roughly the same proportions (19% to 81%): NMR (major isomer, $CDCl_3$) δ 0.91 (d, J = 7 Hz, 3, $CH(CH_3)$), 1.25 (t, J = 7 Hz, 6, OCH_2CH_3), 1.35 (s, 3, CCH_3), 1.4–2.5 (m, 5, CH_2CH_2CH), 3.67 (s, 3, $COOCH_3$), 4.16 (q, J = 7 Hz, 4, OCH_2CH_3); IR (neat) 1733 (C=O) cm^{-1}. Anal. ($C_{14}H_{24}O_6$) C, H. The minor isomer was identified by its ^{13}C NMR (see supplementary table).

General Reaction Procedure for the Carboacylation of Olefins by 2-Lithiocyclohexanone. The procedure described for use of malonate anion was used here, except that 1.6 mmol of carbanion (from LDA) was used.

Reaction of 2-Lithiocyclohexanone. A. With Ethene. Purification by medium-pressure liquid chromatography gave 124 mg (68%) of methyl 2-oxocyclohexanepropanoate:[16] NMR ($CDCl_3$) δ 1.2–2.3 (m, 8, ring and chain CH_2), 2.3–2.6 (m, 5, CHC=O), 3.72 (s, 3, $COOCH_3$); IR (neat) 1734 (ester C=O), 1707 (ketone C=O). Anal. ($C_{10}H_{16}O_3$) C, H.

B. With Propene. Purification by medium-pressure liquid chromatography (SiO_2, 15:1 hexane–ether) gave 152 mg (77%) of carboacylated products. VPC analysis (10 ft, 3% SE-30, Chromosorb W, 140 °C) indicated that the product was 90% methyl β-methyl-2-oxocyclohexanepropanoate:[16] NMR ($CDCl_3$) δ 0.92, 0.97 (d of d, J = 6 Hz, 3, diastereomeric $CHCH_3$), 1.3–2.1 (m, 7, ring and chain CH_2), 2.1–2.7 (m, 5, CHC=O), 3.64 (s, 3, $COOCH_3$); IR (neat) 1734 (ester C=O), 1705 (ketone C=O) cm^{-1}. Anal. ($C_{11}H_{18}O_3$) C, H. A minor product (~10%, 11.8 min) was methyl α-methyl-2-oxocyclohexanepropanoate: NMR ($CDCl_3$) δ 1.14 (d, J = 7 Hz, 3, $CHCH_3$), 1.3–2.0 (m, 8, ring and chain CH_2), 2.0–2.7 (m, 6, CHCO), 3.65 (s, 3, $COOCH_3$); IR (neat) 1732 (ester C=O), 1703 (ketone C=O) cm^{-1}. Anal. ($C_{11}H_{18}O_3$) C, H.

C. With 1-Hexene. Purification by medium-pressure liquid chromatography (SiO_2, 12:1 hexane–ether) gave methyl β-*n*-butyl-2-oxocyclohexanepropanoate (25 mg, 10%): NMR ($CDCl_3$) δ 0.90 (m, 3, CH_2CH_3), 1.0–1.5 (m, 6, $(CH_2)_3$), 1.5–2.1 (m, 7, ring CH_2's, chain CH), 2.1–2.6 (m, 5, CHCO), 3.66 (s, 3, OCH_3); IR (neat) 1735 (ester C=O), 1710 (ketone C=O) cm^{-1}. Anal. ($C_{14}H_{24}O_3$) C, H.

In addition methyl α-*n*-butyl-2-oxocyclohexanepropanoate (59 mg, 25%) was obtained: NMR (CCl_4) δ 0.88 (t, J = 6 Hz, 3, CH_2CH_3), 1.1–1.6 (m, 6, CH_2), 2.1 (m, 8, ring and chain CH_2 β and γ to (C=O), 2.2–2.6 (m, 4, CHCO), 3.65 (s, 3, OCH_3); IR (neat) 1735 (ester C=O), 1710 (ketone C=O) cm^{-1}. Anal. ($C_{14}H_{24}O_3$) C, H. The differentiation between the α and β *n*-butyl isomers was made by ^{13}C NMR (see supplementary table). VPC analysis of the crude reaction mixture (10 ft, 3% SE-30, Chromosorb W, 170 °C, α isomer 5.0 min, β isomer 5.6 min) confirmed the isolated ratio of α and β isomers. In addition, three other minor isomers (6.2, 7.0, and 7.6 min, ≈6% each) were detected. While insufficient material was available for full characterization, IR spectra of these products showed both ester and ketone carbonyl bands.

D. With *N*-Vinylacetamide. Purification by medium-pressure liquid chromatography (SiO_2, 6:4 hexane–acetone) gave 112 mg (46%) of a white solid (mp 115–116 °C, cyclohexane) of methyl β-acetamido-2-oxocyclohexanepropanoate: NMR ($CDCl_3$) δ 1.6–2.4 (m, 6, ring CH_2), 1.96 (s, 3, $NHCOCH_3$), 2.40 (m, 2, CH_2CO), 2.66 (d, J = 5 Hz, 3, CHCO, CH_2COOMe), 3.68 (s, 3, OCH_3), 4.6 (m, 1, $AcNHCH$), 6.6 (m, 1, NH); IR ($CDCl_3$) 3200–3500 (NH), 1740 (ester C=O), 1712 (ketone C=O), 1661 (amide CO) cm^{-1}. Anal. ($C_{12}H_{19}NO_4$) C, H, N.

E. With Styrene. Purification by medium-pressure liquid chromatography (SiO_2, 20:1 CH_2Cl_2–ether) gave two products. Methyl β-phenyl-2-oxocyclohexanepropanoate[17] (50 mg, 19%): NMR ($CDCl_3$) δ 1.1–2.1 (m, 6, ring CH_2), 2.4–3.0 (m, 5, CHCO, CH_2CO), 3.6 (m, 1, PhCH), 3.50 (s, 3, OCH_3), 7.28 (br s, 5, ArH); IR (neat) 1720 (ester C=O), 1700 (ketone C=O) cm^{-1}. Anal. ($C_{16}H_{20}O_3$) C, H.

Methyl α-phenyl-2-oxocyclohexanepropanoate[18] (31 mg, 12%): NMR ($CDCl_3$) δ 1.3–2.0 (m, 6, ring CH_2), 2.0–2.5 (m, 5, $CH_2COCHCH_2$), 3.6 (m, 1, PhCH), 3.63 (s, 3, OCH_3), 7.31 (br s, 5, ArH); IR (neat) 1734 (ester C=O), 1708 (ketone C=O) cm^{-1}. Anal. ($C_{16}H_{20}O_3$) C, H.

F. With *cis*-2-Butene. VPC analysis of the crude material (10 ft, 3% SE-30, Chromosorb W, 160 °C) showed two major ester products, t_R 9.5 (58%) and 13.3 min (42%). Separation by medium-pressure liquid chromatography (SiO_2, 20:1 CH_2Cl_2–ether) gave methyl α,β-dimethyl-2-oxocyclohexanepropanoate (22 mg, 10%, t_R 9.5 min): NMR ($CDCl_3$)

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δ 0.7–1.0 (m, 3, diastereomeric $CHCH_3$), 1.05 (d, J = 6 Hz, 3, $CH_3CHCOOMe$), 1.3–2.1 (m, 7, ring CH_2, chain CH), 2.1–2.5 (m, 4, $CHC{=}O$, $CH_2C{=}O$), 3.66 (s, 3, OCH_3); IR (neat) 1733 (ester C=O), 1708 (ketone C=O) cm^{-1}. Anal. ($C_{12}H_{20}O_3$) C, H.

In addition, methyl γ-methyl-2-oxocyclohexanebutanoate (16 mg, 8%, t_R 13.3 min) was obtained: NMR ($CDCl_3$) δ 0.86 (br d, J = 6 Hz, 3, $CHCH_3$), 1.0–2.0 (m, 9, ring and chain CH's), 2.0–2.5 (m, 5, $CH_2C{=}O$), 3.64 (s, 3, OCH_3); IR (neat) 1738 (ester C=O), 1709 (ketone C=O) cm^{-1}. Anal. ($C_{12}H_{20}O_3$) C, H.

G. With *trans*-2-Butene. VPC analysis as above showed the crude material to be a 45:55 mixture of propanoic and butanoic esters as in F. Isolation as above gave 17 mg (8%) of methyl α,β-dimethyl-2-oxocyclohexanepropanoate and 19 mg (9%) of methyl γ-methyl-2-oxocyclohexanebutanoate, identical with the samples reported in F.

Reaction of 2-Lithioacetone with Propene. Purification by evaporative distillation (1 Torr, 100 °C) gave 65 mg (40%) of an inseparable mixture of methyl 3-methyl-5-oxohexanoate[19] (65%) and methyl 2-methyl-5-oxohexanoate (35%).[20] For the 3-methyl compound (isomer A): NMR ($CDCl_3$) δ 0.95 (d, J = 6 Hz, 3, $CHCH_3$), 2.09 (s, 3, CH_3CO), 2.16–2.7 (m, 5, $COCH_2CH(CH_3)CH_2COOMe$), 3.61 (s, 3, OCH_3). For the 2-methyl compound (isomer B): NMR ($CDCl_3$) δ 1.12 (d, J = 7 Hz, 3, $CH_3CHCOOMe$), 1.6-1.9 (m, 6 lines, 2, $CH_2CH(CH_3)COOMe$), 2.09 (s, 3, CH_3CO), 2.16–2.7 (m, 3, CHCO), 3.61 (s, 3, OCH_3). For the mixture: IR (neat) 1736 (ester C=O), 1715 (ketone C=O) cm^{-1}. Anal. ($C_8H_{14}O_3$) C, H.

Reaction of the Lithium Salt of Me_3Si-Protected Benzaldehyde Cyanohydrin with Ethene. The crude reaction solution (THF) was stirred with 30 mL of 2 N HCl for 0.75 h at 25 °C and extracted with ether (3 × 75 mL), and the combined extracts were washed with 2 N HCl (3 × 30 mL) and water (30 mL). Ice was added to the organic phase and the mixture was shaken with dilute NaOH (70 mL) for 0.1 h. (Care must be taken to avoid overhydrolysis to the carboxylic acid.) After washing with water and drying over anhydrous $MgSO_4$ the organic phase was concentrated under vacuum. Purification by medium-pressure liquid chromatography (SiO_2, 30:1 hexane–ether) gave 288 mg (50%) of methyl 3-benzoylpropionate:[21] NMR (CCl_4) δ A_2B_2 system δ_A = 2.55, δ_B = 3.16 (m, 4, $COCH_2CH_2COOMe$), 3.60 (s, 3, OCH_3), 7.4 (m, 3, ArH), 7.9 (m, 2, ArH); IR (CCl_4) 1740 (ester C=O), 1690 (Ar C=O), 1600 (Ar C=C) cm^{-1}. Anal. ($C_{11}H_{12}O_3$) C, H.

Reaction of Sodium Diethyl Acetamidomalonate with Ethene. The reaction was run in the usual fashion (Et_3N, HMPA) using carbanion prepared with LDA and 10% HMPA. Purification of the crude reaction mixture by medium-pressure liquid chromatography (SiO_2, 7:3 ethyl acetate–hexane) gave 240 mg of material. NMR ($CDCl_3$) showed this to be a 7:3 mixture of the desired product, 1-acetamidopropanetricarboxylic acid 1,1-diethyl-3-methyl esters (56%), identical in all respects with authentic material prepared by an alternate route,[22] and diethyl acetamidomalonate. This mixture resisted separation.

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Supplementary Material Available: ^{13}C NMR data (Table II) (8 pages). Ordering information is given on any current masthead page.

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Bimanes. 5. Synthesis and Properties of *syn*- and *anti*-1,5-Diazabicyclo[3.3.0]octadienediones (9,10-Dioxabimanes)

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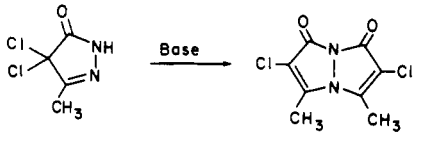
Abstract: A simple three-step synthesis of two essentially new classes of bicyclic heterocyclic compounds, the *syn*- and *anti*-1,5-diazabicyclo[3.3.0]octadienediones, from β-keto esters via the pyrazolinone and halopyrazolinone is described. The syn compounds (-3,6-diene-2,8-diones) are usually strongly fluorescent; the anti derivatives (-3,7-diene-2,6-diones) are normally nonfluorescent and very phosphorescent. A short form name, 9,10-dioxabimanes, is introduced (*bi*, two, and *manus*, hand), with substituents adjacent to the carbonyl designated R_1 (or α) and substituents at the second carbon being labeled R_2 (or β). "9,10-Dioxabimanes" may be described as *syn*-(or *anti*-)(R_2,R_1)B. 9,10-Dioxabimanes are relatively high-melting, sublimable, stable molecules with simple NMR and fairly characteristic IR spectra. The (R_2,Cl)B derivatives can be hydrogenated to (R_2,H)B compounds. Bromination of (CH_3,R_1)B produces useful monobromo and dibromo compounds. A plausible mechanism for the formation of both classes of 9,10-dioxabimanes is presented. The formation of mixed 9,10-dioxabimanes (e.g., (R_2,R_1)(R_2',R_1')B) from mixtures of halopyrazolinones is readily accounted for. The 9,10-dioxabimane rings are hydrogenated with some difficulty to a mixture of products, including some in which the N–N bond has been cleaved. *syn*-(CH_3,CH_3)B resists oxidation by a variety of agents but can be converted to an α-acetoxy derivative with ceric ion.

Introduction

In the course of attempts to prepare 2-octadecynoic acid via the treatment of the appropriate 4,4-dichloro-3-pyrazolin-5-one (the Carpino procedure[1c]) we noted the formation of a highly fluorescent compound in ca. 0.1% yield. The precursor for 2-butynoic acid yielded a similar fluorescent compound in 0.03% yield, and spectroscopic and analytical data suggested the possibility that the fluorescent compounds were derivatives of 1,5-diazabicyclo[3.3.0]octadienedione (eq 1).



(1)

Reasonably efficient and fairly general syntheses for the fluorescent compounds and the nonfluorescent isomers were de-

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