Rhodium-Catalyzed Asymmetric [4 + 2] Cycloisomerization Reactions

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The catalysis by transition metals of chemical transformations that do not readily take place is becoming an important tool in organic chemistry. The rhodium-catalyzed [4 + 2] cycloisomerization of unactivated trienes and dieneynes, a reaction that is the functional analogue of the Diels−Alder reaction, is an example of such a transformation (Figure 1). This transformation can be performed on substrates that do not readily undergo thermal or Lewis acid catalyzed Diels−Alder reactions. Although metal-catalyzed intramolecular [4 + 2] cycloisomerization reactions have been investigated by a number of workers, this transformation has not been developed into a generally useful asymmetric process.[1−7] Additionally, metals have been used to catalyze both [4 + 4] and [5 + 2] cycloisomerizations.[8−14] We recently reported an active catalyst for the [4 + 2] cycloisomerization of trienes and dieneynes.[15] The goal in the development of that system was to find a phosphine-based catalyst that was sufficiently active and general to allow for the discovery an asymmetric variant of the reaction. Livinghouse has reported the use of DIOP derivatives in the cyclization of both trienes and dieneynes, with one case giving 87% ee.[6] More recently, Livinghouse, as well as our group, reported the value of varying the counterion associated with the catalysts used in these reactions.[7,15] In their paper, they reported selectivities ranging from 61% to 79% ee for the cycloisomerization of a given triene substrate with a rhodium−DIOP system. We report here the inital results of a study in which both triene and dieneyne substrates were investigated with a number of chiral bisphosphine ligands. Selectivities of 98% ee for trienes and up to 95% ee for dieneynes are reported.

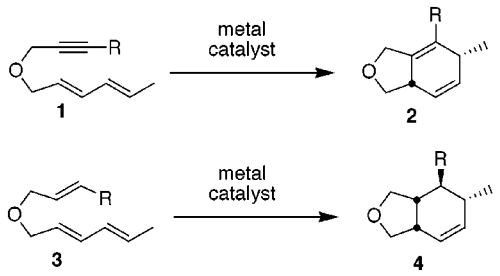

Figure 1.

Results and Discussion

A number of different chiral bisphosphine rhodium catalysts were used to catalyze the cycloisomerization of triene **5** (Table 1). The first ligand used, CHIRAPHOS, provided a 76% yield of the cycloisomerization product in 72% enantiomer excess. Encouraged by this result, a number of other ligands were investigated. DIOP, a ligand used by Livinghouse to perform this reaction, gives with our system a 42% yield in 77% ee when the reaction is run at 55 °C. When the reaction temperature is dropped to room temperature, the selectivity does not significantly improve and the reaction does not proceed to completion over 3 days. Reaction with a methyl DUPHOS based catalyst yields none of the cycloisomerization, with only vinyl ether **7** isolated.

The most selective ligand of those tested with triene **5** was BINAP (Table 1, entry 7). Our inital attempt with this system was disappointing. BINAP in dichloromethane provided only vinyl ether **7** and none of the cycloisomerization product (entry 6). However, examination of this catalyst in ethyl acetate gives the volatile cycloisomerization product as *essentially one enantiomer* in 64% isolated yield (Table 1, entry 7).

It was initially hoped that one catalyst system could be developed that would cycloisomerize both trienes and dieneynes with high selectivity. However, catalysis of the cycloisomerization of dieneyne **8** with (*S*)-BINAP in dichloromethane gave only a 37% yield in 3 h with low selectivity (Table 2, entry 1). The other appreciable product in this system was identified as an oligomer of the starting alkyne. Reaction with ethyl acetate as the solvent shuts down this pathway, giving a 79% yield of diene **11** but with low selectivity, 39% ee. Reaction using CHIRAPHOS or DIOP as the ligands again gives the desired products with low selectivity.

Our attempt with DUPHOS (entry 5) as a ligand initially did not prove to be significantly better than previous examples. In dichloromethane, while the cycloisomerization product was obtained in good selectivity, 81% ee, the major product was found to be dimer **14**. When the reaction was run in the presence of ethyl acetate, high selectivity was found, but again the reaction was plagued by formation of dimer **14**. It was reasoned that decreasing the reactivity of the catalyst precursor may affect the distribution between products **11** and **14**. It was eventually discovered that, in the case of terminal alkynes, the best catalyst system was methyl DUPHOS without removal of the initially bound olefin by hydrogenation. The best conditions were found to be 3% catalyst with a mixture of CH_2Cl_2 and ethyl acetate as

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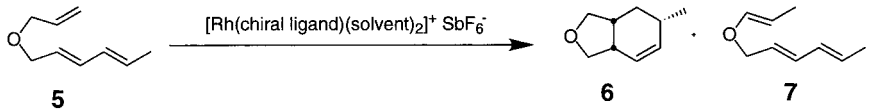
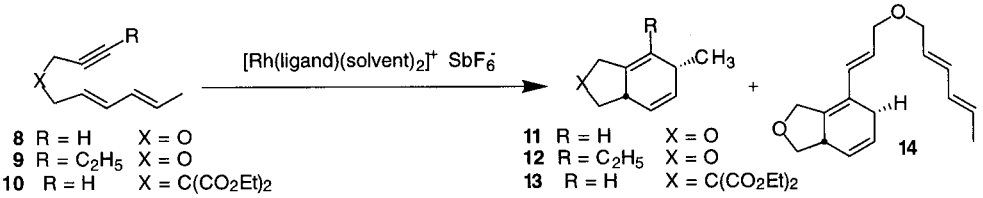
Table 1. Asymmetric Induction in Isomerization of 5[a]



entry	chiral ligand	conditions	yield **6** (%)	ee[b] **6** (%)	yield **7** (%)
1	(*S*,*S*)-CHIRAPHOS	CH_2Cl_2, 25 °C, 18 h	76	72	
2	(*S*,*S*)-DIOP	CH_2Cl_2, 55 °C, 24 h	42	77	
3	(*S*,*S*)-DIOP	CH_2Cl_2, 25 °C, 3 d	40[c]	78	
4	(*S*,*S*)-Me,Me-DUPHOS	acetone, 25 °C, 12 h	0	0	60
5	(*S*,*S*)-Me,Me-DUPHOS	CH_2Cl_2/EtOAc (6:1) 55 °C, 1 h	0	0	54
6	(S)-BINAP	CH_2Cl_2, 25 °C, 8 h	0	0	52
7	(S)-BINAP[d]	EtOAc, 55 °C, 72 h	64	>98	

[a] All reactions were carried out with 0.07−0.1 mmol substrate and 6 mol % chiral ligand unless otherwise specified. The catalyst was prepared by prehydrogenation of the phosphine rhodium olefin complex before addition of the substrate. [b] The selectivities were determined by capillary GC using a Chiraldex, Gamma-cyclodextrin trifluoroacetyl 30 m × 0.25 mm column. [c] 40% conversion of starting material. [d] Reaction was carried out using 10 mol % (*S*)-BINAP.

Table 2. Asymmetric Induction of Dieneynes[a]



entry	compd	chiral ligand	conditions	yield **11**−**13** (%)	ee[b] (%)	yield **14** (%)
1	**8**	(*S*)-BINAP[c]	CH_2Cl_2, 25 °C, 3 h	37	13	
2	**8**	(*S*)-BINAP[c]	EtOAc, 55 °C, 60 h	79	39	
3	**8**	(*S*,*S*)-CHIRAPHOS[c]	CH_2Cl_2, 25 °C, 24 h	70	9	
4	**8**	(*S*,*S*)-DIOP[c]	CH_2Cl_2, 25 °C, 24 h	70	43	
5	**8**	Me,Me-DUPHOS[c,d]	CH_2Cl_2, 25 °C, 2 h	15	81	60
6	**8**	Me,Me-DUPHOS[c,d,f]	CH_2Cl_2/EtOAc (6:1), 55 °C, 6 h	25	90	73
7	**8**	Me,Me-DUPHOS[d,e,f]	CH_2Cl_2, 25 °C, 4 h	54	93	28
8	**8**	Me,Me-DUPHOS[d,e,g]	CH_2Cl_2/EtOAc (6:1), 55 °C, 4 h	85	95	
9	**8**	Me,Me-DUPHOS[d,e,f]	TFE, 55 °C, 12h	75	91	
10	**9**	Me,Me-DUPHOS[c,d,f]	CH_2Cl_2, 25 °C, 4h	98	81	
11	**9**	Me,Me-DUPHOS[c,d,f]	CH_2Cl_2/EtOAc (6:1), 55 °C, 10 h	76	88	
12	**10**	Me,Me-DUPHOS[c,d,f]	CH_2Cl_2, 25 °C, 20h	64	72	
13	**10**	Me,Me-DUPHOS[c,d,f]	CH_2Cl_2/EtOAc (6:1), 55 °C, 11 h	78	91	

[a] All reactions were carried out with 0.7−0.1 mmol substrate and 6 mol % chiral ligand unless otherwise specified. [b] The selectivities were determined by capillary GC using a Chiraldex, Gamma-cyclodextrin trifluoroacetyl 30 m × 0.25 mm column. [c] The catalyst was prepared by prehydrogenation of the phosphine rhodium olefin complex before addition of the substrate. [d] All examples with Me,Me-DUPHOS were carried out with the *S*,*S* enantiomer. [e] The complex, Rh(*S*,*S*-Me,Me-DUPHOS)(hepta-2,5-diene)$_2$Cl, was used to catalyze this reaction without hydrogenation. [f] The reaction was run in the presence of 2% excess ligand relative to the complex. [g] 3% catalyst with 1% excess ligand was used.

solvent and excess ligand present. Under these conditions, the product was obtained in good yield (85%) and high selectivity (95% ee) (Table 2, entry 8). A reaction was performed to determine if using trifluoroethanol (TFE) as solvent had an advantageous effect on the reaction, as it did in some of the original Livinghouse work (entry 9). In this system, with antimony hexafluoride as the counterion, there appears to be no clear advantage to the use of TFE as the reaction solvent.

With a set of optimized reaction conditions in hand, an internal alkyne was then evaluated. It was found that the best reaction conditions for the cycloisomerization with internal alkyne **9** were not those used for dieneyne **8** but rather methyl DUPHOS with the catalyst precursor first being pretreated with H_2 to remove the hepta-2,5-diene ligand (Table 2, entry 11). In the case of this substrate, methylene chloride can be used as the solvent without formation of the dimer or oligomer products. Apparently, the dimerization and oligomerization pathways are suppressed by the presence of a group other than H at the alkyne terminus.

A dieneyne with an entirely carbon tether was also examined. Cycloisomerization of **10** under the conditions found to be best for dieneynes with internal alkynes gave the desired product in good yield and selectivity (Table 2, entry 13).

The effect of adding ethyl acetate to the solvent system is quite pronounced. In general, there is a decrease in the overall rate of reaction when ethyl acetate is added to or used as the solvent. However, reaction systems with ethyl acetate added consistently gave the highest selectivities. This is both in an enantiomeric sense and in the provision of the cycloisomerization product as the major product. The exact role of ethyl acetate in these reactions is not clear. Presumably, coordination of ethyl acetate to an intermediate along the catalytic cycle alters the rate of both the desired and undesired pathways. An exhaustive investigation of different solvents has not been

undertaken. However, the use of THF or benzene as the solvents for these reactions gives results similar to those with pure dichloromethane.

Conclusion

Although we have yet to achieve our goal of finding a catalyst system that is general in the stereoselective cycloisomerization of trienes and dieneynes, we have found that these reactions can be done with high selectivity. The selectivities in this paper are *the highest reported for these reactions* and have begun to map out what types of catalytic conditions are necessary for selective asymmetric cycloisomerization reactions. We are currently investigating other catalyst systems, as well as substrates with nitrogen tethers.

Experimental Section

Representative Catalyst Synthesis. Under N_2, $[Rh(NBD)Cl]_2$ (305 mg, 0.6615 mmol) and 10 mL of acetone were placed into a 25 mL vial containing a stir bar. To this solution was added $AgSbF_6$ (455 mg, 1.323 mmol). Silver chloride precipitated immediately from the light orange solution. After 10 min of stirring, the heterogeneous solution was drawn up into a 10 mL syringe and filtered airless via syringe filter into another vial containing a stir bar, diphenylphosphinoethane (527 mg, 1.323 mmol), and 5 mL of acetone under N_2. An immediate color change from light orange to deep red was observed. This solution was stirred for 45 min, after which the volume of the reaction was reduced on a rotary evaporator until red crystals started to form. The solution was allowed to stand at room temperature under N_2 for 5 h. The dark red crystals were collected and washed with Et_2O. After drying in vacuo, 741 mg (67%) of product was obtained. The same procedure was used for all the chiral rhodium complexes used in this paper.

General Catalysis Procedure. $[Rh(NBD)(diphosphine)]^+(SbF_6)^-$ (37 mg, 0.044 mmol) was placed in a Schlenk tube and dissolved in 6 mL of freshly distilled, deoxygenated solvent. H_2 gas was then bubbled through the solution for 2 min (solution color changed to dark red) followed by N_2 gas for 2 min. (This step is omitted for the reaction of dieneyne **8**.) The substrate (0.735 mmol) was added to the catalyst solution along with 1 mL of solvent. The Schlenk tube was then freeze−pump−thaw−degassed (3 cycles) and stirred under N_2 at ambient temperature. The course of the reaction was followed by TLC (5% ethyl acetate/hexane). After the reaction was deemed complete, the solvent was removed under reduced pressure. The products were purified by flash chromatography.

Evaluation of Selectivity. The selectivity for the reactions was determined by GC analysis of the crude reaction mixture, using a chiral capillary column (Chiraldex B-TA 10 m × 0.25 mm). The enantiomeric excesses are reported to ±0.5% with baseline resolution of enantiomers.

Assignment of Relative and Absolute Stereochemistry. The relative and absolute stereochemistry of compound **6** was assigned by correlation to a sample of the molecule synthesized by the method of Livinghouse.[6] The absolute stereochemistry of compound **11** was assigned by correlation to the product obtained from the reaction with (+)-DIOP.[16] The retention times of the remaining molecules are assumed to follow the same order.

Purity of Compounds. Compounds were judged to be at least 95% pure by NMR. All reported yields are isolated yields. Most of the products are quite volatile and consequently the actual yield of product produced is generally higher than the amount of material isolated.

4-Oxo-1,6(*E*),8(*E*)-decatriene (5). Into a 250 mL round-bottom flask equipped with a magnetic stir bar was placed NaH (1.1 g of a 60% dispersion in oil, 28.0 mmol). The dispersion was triturated with pentane (3 × 10 mL) to remove the oil. A rubber septum was fitted to the flask, and the air in the flask was replaced with N_2. To the flask was added 75 mL of THF. This heterogeneous solution was cooled to 0 °C. Then, 2,4-hexadiene-1-ol (2.5 g, 2.9 mL, 25.5 mmol) was added via syringe over 5 min. After the addition, the reaction was warmed slowly to room temperature and stirred for 45 min. The reaction was then cooled to 0 °C, and allyl bromide (3.3 g, 27.3 mmol) was added via syringe. The reaction was then warmed slowly to room temperature and stirred overnight. Ice water (100 mL) was added to quench the reaction, and the organic layer was separated. The aqueous layer was extracted with ethyl ether (3 × 50 mL). The organic layers were then combined, washed with dilute brine, dried over $MgSO_4$. The solvent was removed on a rotary evaporator, and the crude product was subjected to flash column chromatography over silica gel (5% ethyl acetate/hexane solvent system) yielding 2.25 g (64%) of **5** (R_f = 0.30): ^{1}H NMR (300 MHz, $CDCl_3$) δ = 6.21 (dd, J = 10.3 Hz, J = 15.1 Hz, 1 H), 6.06 (dd, J = 14.8 Hz, J = 14.8 Hz, 1 H), 5.86−5.97 (m, 1 H), 5.59−5.77 (m, 2 H), 5.28 (d, J = 12.3 Hz, 1 H), 5.18 (d, J = 10.4 Hz, 1 H), 1.76 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 134.8, 133.2, 130.8, 129.9, 126.6, 116.9, 70.9, 70.5, 18.1; IR (FT-IR, film) ν = 3018, 2933, 2853, 2915, 1662 cm^{-1}; LREI m/z (%) = $[M]^+$ 138 (44.6); HREI calcd for $C_9H_{14}O$ minus H, 137.0966; found, 137.0968.

4-Oxo-6(*E*),8(*E*)-decadien-1-yne (8). The procedure for the synthesis of **5** was followed. Reagents and amounts used were 2,4-hexadien-1-ol (3.6 mL, 0.041 mol), propargyl bromide (4.8 mL of an 80 wt % solution in toluene, 0.043 mol), and sodium NaH (1.82 g of a 60% dispersion in oil, 0.046 mol). Column chromatography on silica gel (5% ethyl acetate/hexane) of the crude product yielded 4.46 g (79%) of **8** (R_f = 0.28): ^{1}H NMR (300 MHz, $CDCl_3$) δ = 6.23 (dd, J = 10.4 Hz, J = 15.2 Hz, 1 H), 6.05 (dd, J = 15.0 Hz, J = 15.0 Hz, 1 H), 5.72 (dq, J = 14.9 Hz, J = 6.7 Hz, 1 H), 5.59 (dt, J = 15.3 Hz, J = 6.5 Hz, 1 H), 4.12 (s, 2 H), 4.07 (d, J = 6.6 Hz, 2 H), 2.41 (s, 1 H), 1.75 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 134.2, 130.6, 130.5, 125.5, 74.3, 70.0, 56.7, 18.1; IR (FT-IR, film) ν = 3296, 3021, 2854 cm^{-1}; LREI m/z (%) = $[M]^+$ 136 (9); HREI calcd for $C_9H_{12}O$, 136.0888; found, 136.0887.

6-Oxo-8(*E*),10(*E*)-dodecadien-3-yne (9). The dieneyne **8** (812 mg, 5.9 mmol) was placed in a 50 mL round-bottom flask equipped with a magnetic stir bar in 20 mL of THF under a N_2 atmosphere. The solution was cooled to 0 °C. To this solution was added ^{n}BuLi (2.4 mL of a 2.5 M solution in hexanes, 5.97 mmol) over 5 min. The solution became dark brown. The solution was stirred for 25 min, and then ethyl iodide (0.48 mL, 5.971 mmol) was delivered via syringe. The reaction was warmed to room temperature and stirred overnight. The reaction was quenched with 10 mL of distilled water, and the organic layer was separated. The aqueous layer was extracted with ethyl ether (2 × 20 mL), and the combined organic layers were dried over $MgSO_4$. The volatiles were removed on a rotary evaporator. The crude product was purified by passage through a plug of silica gel (5% ethyl acetate/hexane solvent system), yielding, after evaporation of the volatile components, 850 mg (87%) of **9** (R_f = 0.30): ^{1}H NMR (300 MHz, $CDCl_3$) δ = 6.19 (dd, J = 10.8 Hz, J = 15.1 Hz, 1 H), 6.02 (dd, J = 14.8 Hz, J = 14.8 Hz, 1 H), 5.53−5.74 (m, 2 H), 4.06−4.10 (m, 2 H), 4.02 (d, J = 6.5 Hz, 2 H), 2.20 (q, J = 7.6 Hz, 2 H), 1.72 (d, J = 6.6 Hz, 3 H), 1.11 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 133.8, 130.7, 130.2, 125.9, 88.2, 75.2, 69.8, 57.4, 18.1, 13.8, 12.4; IR (FT-IR, film) ν = 2977, 2937, 2917, 2852, 1456, 1447, 1356, 1319, 1136, 1110, 1079, 1059, 989 cm^{-1}; LREI (m/z (%) $[M - 29]^+$ 135 (100); HREI calcd for $[C_{11}H_{16}O - 29]^+$, 135.0810; found, 135.0810.

7,7-Bis(carboethoxy)-2(*E*),4(*E*)-heptadiene. To a 500 mL round-bottom flask equipped with a magnetic stir bar was added diethyl malonate (6.3 mL, 0.041 mol) dissolved in 175 mL of THF under N_2. The solution was cooled to 0 °C, and ^{n}BuLi (16.6 mL, 2.5 M solution in hexanes, 0.0414 mol) was added slowly via syringe. The solution was stirred for 40 min at 0 °C. To this solution was added 1-bromo-2,4-hexadiene (8 g, 0.050 mol) with 40 mL THF via syringe over 5−10 min. The reaction was warmed to room temperature and stirred. After 15 h, the reaction was quenched with 50 mL of distilled water. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate (3 × 150 mL). The organic layers were combined, washed with dilute brine, and dried over $MgSO_4$, and then the volatiles were removed on a rotary evaporator. TLC (5% ethyl acetate/hexane) showed that there were two products present.

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Flash chromatography over silica gel (5% ethyl acetate/hexane solvent system) yielded 4.31 g/43% (R_f = 0.15): ^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.59 (dq, J = 14.4 Hz, J = 7.2 Hz, 1 H), 5.45 (dt, J = 14.7 Hz, J = 7.2 Hz, 1 H), 4.17 (q, J = 7.2 Hz, 4 H), 3.36 (t, 7.6 Hz, 1 H), 2.62 (dd, J = 7.4 Hz, J = 7.6 Hz, 2 H), 1.70 (d, 6.6 Hz, 3 H), 1.24 (t, 7.1 Hz, 6 H) ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.9, 133.3, 131.0, 128.7, 126.1, 61.4, 52.1, 31.8, 18.0, 14.1.

4,4-Bis(carboethoxy)-6(*E*),8(*E*)-decadiene-1-yne (10). To a 100 mL round-bottom flask equipped with a magnetic stir bar was added 7,7-bis(carboethoxy)-2(*E*),4(*E*)-heptadiene) (2.00 g, 8.33 mmol) dissolved in 50 mL of THF under N_2. The solution was cooled to 0 °C, and ^{n}BuLi (3.33 mL, 2.5 M solution in hexanes, 8.33 mmol) was added slowly via syringe. The solution was stirred for 40 min at 0 °C. To this solution was added propargyl bromide (0.97 mL of an 80 wt % solution in toluene, 8.75 mmol) over 5 min. The reaction was warmed to room temperature and stirred. After 15 h, the reaction was quenched with 25 mL of distilled water. The organic layer was separated, and the aqueous layer was extracted with 3 × 150 mL of ethyl acetate. The organic layers were combined, washed with dilute brine, and dried over $MgSO_4$, and the volatiles were removed on a rotary evaporator. Flash chromatography over silica gel (5% ethyl acetate/hexane solvent system) yielded 1.18 g (51%) of **10** (R_f = 0.30): ^{1}H NMR (300 MHz, $CDCl_3$) δ = 6.09 (dd, J = 10.4 Hz, J = 15.0 Hz, 1 H), 5.96 (dd, J = 15.6 Hz, J = 15.6 Hz, 1 H), 5.61 (dq, J = 14.7 Hz, J = 6.7 Hz, 1 H), 5.29 (dt, J = 15.2 Hz, J = 7.7 Hz, 1 H), 4.18 (q, J = 7.1 Hz, 4 H), 2.76−2.79 (m, 4 H), 2.00 (m, 1 H), 1.71 (d, J = 6.6 Hz, 3 H), 1.23 (t, J = 7.1 Hz, 6 H), ^{13}C NMR (75 MHz, $CDCl_3$) δ = 171.3, 136.7, 132.6, 130.6, 125.1, 80.6, 72.9, 63.2, 58.5, 36.8, 24.1, 19.6, 15.7; IR (FT-IR, film) ν = 3294, 2936, 2983, 1737 cm^{-1}; LRFAB [M + H]$^+$ 279.1; HRFAB calcd for [$C_{16}H_{22}O_4$ + H]$^+$, 279.1596; found, 279.1596.

Spectral Data for 5-Methyl-1,3,3aβ,4,5β,7aβ-hexahydroisobenzofuran (6): ^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.60 (m, 2 H), 4.00 (dd, J = 7.6 Hz, J = 7.6 Hz, 2 H), 3.59 (dd, J = 8.5 Hz, J = 2.1 Hz, 1 H), 3.36 (dd, J = 9.7 Hz, J = 1.8 Hz, 1 H), 2.63 (m, 1 H), 2.30 (m, 1 H), 2.16 (m, 1 H), 1.65 (m, 1 H), 1.01−1.14 (m, 1 H), 0.985 (d, J = 7.1, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 135.3, 124.6, 74.7, 72.6, 39.0, 37.3, 34.4, 30.0, 21.5; IR (FT-IR, film); ν = 2955, 2926, 2871, 2855 cm^{-1}; LREI m/z (%) = [M]$^+$ 138.1 (20.2); HREI calcd for $C_9H_{14}O$, 138.1045; found, 138.1030.

Spectral Data for 6-Methyl-1,3,3aβ,6β-tetrahydroisobenzofuran (11): ^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.69 (bs, 2 H), 5.40 (bs, 1 H), 4.39 (d, J = 12.1 Hz, 1 H), 4.24 (d, J = 12.2 Hz, 1 H), 4.18 (dd, J = 7.6 Hz, J = 7.6 Hz, 1 H), 3.23 (dd, J = 11.1 Hz, J = 7.4 Hz, 1 H), 3.03 (dd, J = 13.0 Hz, J = 9.3 Hz, 1 H), 2.83 (m, 1 H), 1.13 (d, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 137.9, 133.8, 122.0, 121.0, 72.2, 69.3, 39.4, 31.3, 21.7; IR (FT-IR, film) ν = 3023, 2961, 2929, 2854, 1454, 1368 cm^{-1}; LREI m/z (%) = [M]$^+$ 136 (14.8); HREI calcd for $C_9H_{12}O$, 136.0888; found, 136.0885.

Spectral Data for 4-Ethyl-5-methyl-1,3β,5,7aβ-tetrahydroisobenzofuran-4-yl (12): ^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.65−5.67 (bs, 2 H), 4.35 (s, 2 H), 4.12 (dd, J = 7.2 Hz, J = 7.2 Hz, 1 H), 3.20 (dd, J = 7.1 Hz, J = 11.3 Hz, 1 H), 3.01−3.10 (m, 1 H), 2.86−2.91 (m, 1 H), 2.14 (m, 1H) 1.93 (m, 1 H), 1.13 (d, J = 7.3 Hz, 3 H), 0.97 (t, J = 7.6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 134.6, 131.5, 131.3, 121.6, 71.9, 67.8, 40.8, 32.1, 23.5, 19.2, 12.7; IR (FT-IR, film) ν = 2964, 2934, 2873, 2851 cm^{-1}; LREI m/z (%) = [M]$^+$ 164 (4.9); HREI calcd for $C_{11}H_{16}O$, 164.1201; found, 164.1203.

Spectral Data for 3$\alpha\beta$,6,7,7aβ-Tetrahydro-2,2-bis(carboethoxy)-5-methyl-indane (13): ^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.70 (d, J = 7.6 Hz, 1 H), 5.55 (d, J = 7.8 Hz, 1 H), 5.29 (bs, 1 H), 4.19 (q, J = 7.2 Hz, 2 H), 4.15 (q, J = 7.0 Hz, 2 H), 2.56−2.95 (m, 4 H), 2.59 (dd, J = 12.3, J = 7.1, 1 H), 1.74 (dd, J = 12.3 Hz, J = 12.3 Hz, 1 H), 1.24 (t, J = 7.1 Hz, 3 H), 1.22 (t, J = 6.9 Hz, 3 H), 1.05 (d, J = 7.3 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 172.4, 171.8, 137.9, 131.9, 125.2, 122.3, 61.5, 61.4, 57.7, 39.8, 38.6, 37.8, 31.3, 21.9, 14.0; IR (FT-IR, film) ν = 2979, 1731 cm^{-1}; LRFAB [M + H]$^+$ 279.1; HRFAB calcd for [$C_{16}H_{23}O_4$ + H], 279.1596; found, 279.1596.

Spectral Data for 14: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.98−6.19 (m, 2 H), 5.51−5.73 (m, 4 H), 5.40 (d, J = 6.6 Hz, 1 H), 5.03 (dd, J = 10.0 Hz, J = 5.9 Hz, 1 H), 4.42 (d, J = 13.7 Hz, 1 H), 4.30 (d, J = 13.7 Hz, 1 H), 4.07−4.20 (m, 2 H), 3.90 (d, J = 6.1 Hz, 2 H), 3.73−3.85 (m, 3 H), 3.62 (dd, J = 7.8 Hz, J = 7.8 Hz, 1 H), 1.73 (d, J = 7.1 Hz, 3 H), 1.07 (d, J = 6.7 Hz, 3 H); ^{13}C NMR (300 MHz, CDCl3) δ = 149.1, 136.9, 136.8, 133.3, 130.9, 130.8, 129.9, 126.7, 120.8, 117.1, 76.5, 75.2, 74.0, 70.0, 42.4, 32.4, 20.2, 18.1; FT-IR (thin film) ν = 2852.6, 2868.0, 2914.3, 2929.7, 2959.6, 2998.2, 3015.5, 2338.6, 2361.7, 1362.6, 1374.2, 1436.9, 1457.1, 1652.9, 1662.5, 1669.3, 1675.1, 1684.7, 1690.5, 1695.3, 1700.2, 1717.5, 1733.9, MS (EI) m/z (%) = [M]$^+$ 272 (4), 174.1 (30), 159.1 (8), 145.1 (21), 133.1 (29), 105.1 (55), 91.1 (57), 81.1 (100), 65.1 (17), 53.1 (28).

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Supporting Information Available: ^{1}H and ^{13}C spectra for new compounds (16 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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