Pergamon

Tetrahedron 54 (1998) 1095–1106

TETRAHEDRON

Catalytic Generation and Trapping of Acylmetals Containing Ni and Cu with Enolates†

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Received 4 August 1997; accepted 30 September 1997

Abstract: Carbonylative cyclization of iodoarenes and iodoalkenes containing a proximal enolate precursor can selectively provide either cyclic ketones or lactones in the presence of Ni or Cu catalysts *via* trapping of putative acylmetal derivatives with *C*- or *O*-enolates, respectively; the ring size and regioselectivity of the reaction may be predicted based on two generalizations derived from the recently developed corresponding Pd-catalyzed reaction.

INTRODUCTION

Migratory insertion of CO into carbon-metal bonds is a fundamentally important process for carbon-carbon bond formation which is known to occur with essentially all transition metals.[1,2] Since the process itself is stoichiometric in transition metals, their catalytic use requires trapping of acylmetals for their recycling, and a variety of nucleophiles[1,2] and electrophiles, in some cases,[3] have been employed for this purpose. For trapping acylpalladiums, for example, hydrides, such as $HCOONEt_3H$, *C*-nucleophiles, such as organometals including nitriles, alkenes, and alkynes, *N*-nucleophiles, such as amines, and *O*-nucleophiles, such as alcohols, have been employed.[4] We have recently discovered that *C*- and *O*-enolates, both internal and external, can serve as agents for trapping acylpalladiums.[5] In one of these studies,[5b] some preliminary results on the conversion of **1** to **2** *via* carbonylative cyclization, catalyzed by Ni and Cu complexes, such as $Cl_2Ni(PPh_3)_2$, $Ni(COD)_2$, and Li_2CuCl_4, were presented (*e.g.*, Scheme 1). Much less effective as catalysts were $CpCo(CO)_2$, $Fe(CO)_5$, $ClRh(PPh_3)_3$, and $Cl_2Ru(PPh_3)_2$. Although trapping of acylnickels with *O*-nucleophiles,[6] such as H_2O and alcohols, *N*-nucleophiles,[7] such as amines, and *C*-nucleophiles,[8] such as organomercuries and stannanes, are known, the use of enolates appears to be unprecedented. Since Ni is substantially less expensive than Pd and since Ni complexes are known to be generally more reactive than the corresponding Pd compounds towards organic halides,[9] we have further delineated the scope and limitations of the Ni-catalyzed carbonylative cyclization of ω-haloesters and ω-haloketones which is thought to proceed *via* migratory insertion of CO and trapping of putative acylnickels with

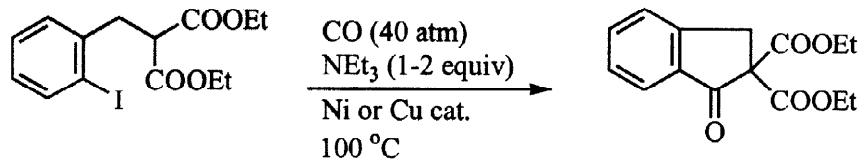
† This paper is dedicated to Professor Shun-Ichi Murahasi of Osaka University on the occasion of his 60th birthday.

‡ Postdoctoral Fellow on funds provided by Japan Society for Promotion of Science for Research Abroad (1997-99).

0040-4020/98/$19.00
PII: S0040-4020(97)10210-1

C- or *O*-enolates to produce ketones or enol esters, respectively. This paper mainly discusses the results obtained with Ni catalysts along with some related results obtained with Cu catalysts.

Scheme 1



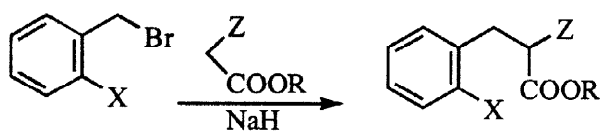
1 **2**

Ni or Cu catalysts: $Cl_2Ni(PPh_3)_2$, $Ni(COD)_2$, or Li_2CuCl_4

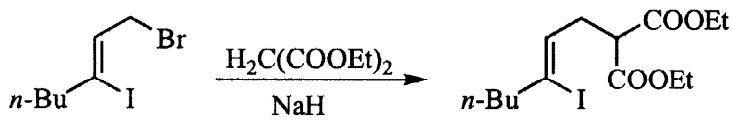
RESULTS AND DISCUSSION

Preparation of Carbonylative Cyclization Precursors. ω-Halogen-substituted malonate ester **1** and related derivatives **3-6**, which can serve as precursors to extra stabilized enolates, were prepared by base-promoted benzylation and allylation of the parent esters, as shown in Scheme 2.

Scheme 2



X	Z	R	Product	Yield (%)
I	COOEt	Et	**1a**	91
Br	COOEt	Et	**1b**	83
I	COMe	Et	**3**	91
I	SO_2Ph	Me	**4a**	88
Br	SO_2Ph	Me	**4b**	89
I	CN	Et	**5**	44

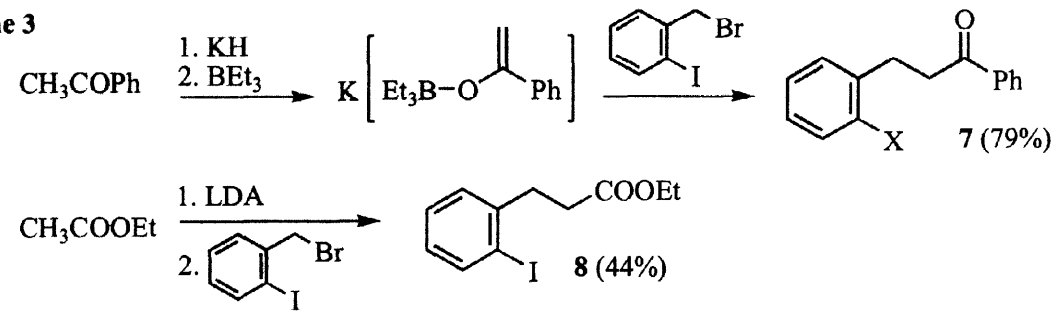


6 (84%)

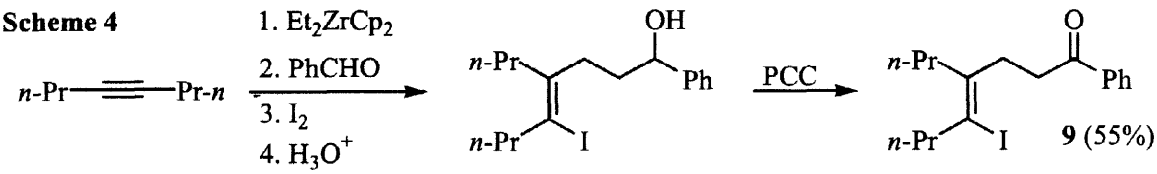
3-(*o*-Iodophenyl)-1-phenyl-1-propanone (**7**) was prepared in 79% yield by the reaction of *o*-iodobenyzl bromide with a potassium enoxyborate reagent generated *in situ* by successive treatment of acetophenone with KH suspended in THF and BEt_3[10] (Scheme 3). A more conventional procedure involving treatment of acetophenone with LDA in THF followed by addition of *o*-iodobenzyl bromide led to a rather messy mixture of products including **7** and the dibenzylated product. On the other hand, 3-(*o*-iodophenyl)propionic acid ethyl ester **8** was

prepared in 44% yield by the conventional method involving benyzlation of lithiated ethylacetate using LDA as a base (Scheme 3). In this case, no attempts were made to optimize the product yield, as the applicability of the borate procedure[10] has not yet been extended to the cases of ester alkylation. The $ZrCp_2$-promoted three-component coupling[11] using 4-octyne, benzaldehyde, and EtMgBr as three carbon sources gave the desired iodoalcohol which was oxidized with PCC to give **9** in 55% overall yield (Scheme 4). Malonate derivative **10** for the synthesis of a six-membered ketone was prepared by alkylation of diethyl malonate with the corresponding homobenzyl bromide, which, in turn, was prepared from 3,4-(methylenedioxy)phenylacetic acid (Aldrich) in 3 steps by (1) reduction with $LiAlH_4$, (2) bromination with CBr_4 and PPh_3, and (3) selective *ortho* iodination with I_2 and AgOTf[12] (Scheme 5). The preparation of **11** by benyzlation of ethoxyethyl-protected α-hydroxyphenylacetonitrile was achieved in 74% yield, as described previously,[13] while treatment of *o*-iodobenzyaldehyde with EtMgBr followed by oxidation with PCC provided **12** in 83% yield (Scheme 6).

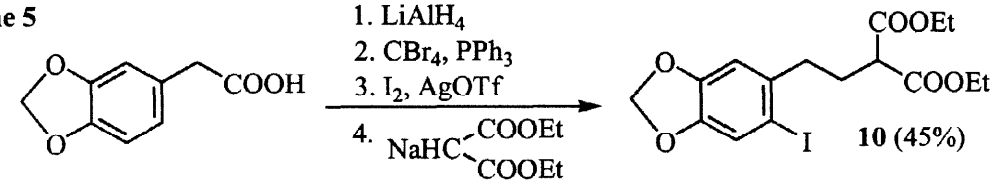
Scheme 3



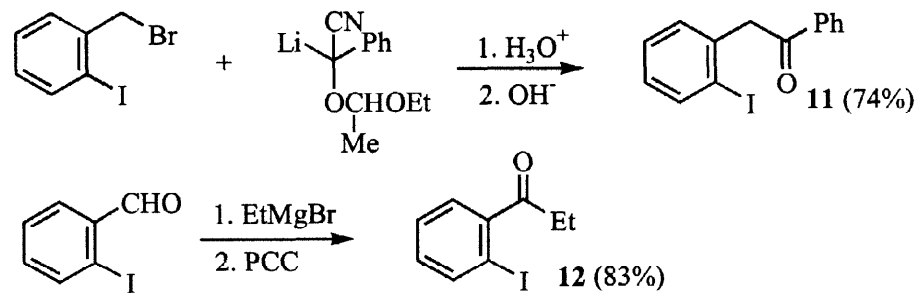
Scheme 4



Scheme 5



Scheme 6



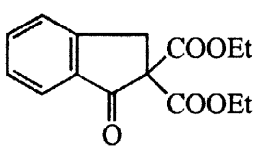
5-*C*-*exo* and 6-*C*-exo Carbonylative Cyclization Processes. As proposed previously, the *n*-*C*-*exo* process may be defined as the carbonylative formation of an *n*-membered ring *via* trapping of acylmetals with *C*-enolates such that the carbonyl group of the enolate precursor ends up exocyclic. On the basis of our previous study with Pd catalysts,[5e] cyclization of **1** and **3-8** was expected to proceed by the 5-*C*-*exo* process rather than the 7-*O*-*endo* or 7-*C*-*endo* process, the latter of which is possible only with **3**. Carbonylation of **1a**, **3**, **4a**, and **5** with CO (40 atm) in the presence of either $Cl_2Ni(PPh_3)_2$ or Li_2CuCl_4 and 2 equiv. of NEt_3 in MeCN at 100 °C yielded widely ranging results summarized in Table 1. For the sake of comparison, the corresponding results with Pd catalysts reported previously[5e] are also presented in the table.

Table 1. Carbonylative Cyclization *via* 5-*C*-*exo* Processes Catalyzed by Ni, Cu, and Pd Complexes [a]

Substrate	Product	Product Yield,[c] %		
		with $Cl_2Ni(PPh_3)_2$	with Li_2CuCl_4	with $Cl_2Pd(PPh_3)_2$
1a	**2**	92	92	85
3	**13**	<10	50	68
4a	**14**	85[d]	60	78
5	**15**	<10	<10	56

[a] The reactions were carried out at 40 atm of CO in the presence of 3-10 mol % of a catalyst and 2 equiv. of NEt_3 in MeCN at 100 °C.

b



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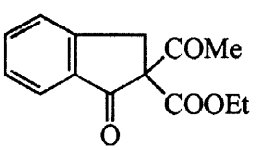

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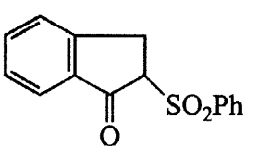

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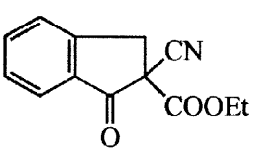

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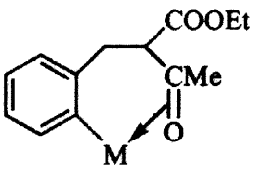
[c] By NMR or GLC. [d] 5 mol% of $Cl_2Ni(PPh)_2$ was reduced with *n*-BuLi (10 mol%).

The results shown in Table 1 indicate the following. While all three transition metals, *i.e.*, Ni, Cu, and Pd, can serve as effective catalysts in the cyclization of **1a** and **4a**, the Ni catalyst was ineffective in the reaction of **3** and **5**, and Li_2CuCl_4 failed to catalyze the cyclization of **5**. Although not yet clear, it is conceivable that the CN and acetyl groups interfere with the desired catalysis by Ni or Cu complexes through chelation as in **16** and **17**. At this point, it has not been established if decarboxylation observed in the conversion of **4a** into **14** is due to the SO_2Ph group or due to the use of the methyl, rather than ethyl, ester. Contrary to our initial expectation, aryl bromides **1b** and **4b** were not reactive enough to give the desired products in >5% yields in the presence of $Cl_2Ni(PPh_3)_2$ under comparable conditions as in the reactions of **1a** and **4a**. Equally disappointing were the reactions of **7-9** using Ni or Cu catalysts. In all cases, the starting iodides remained largely unreacted.



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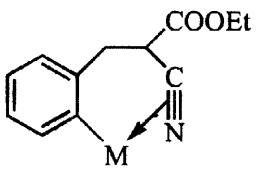

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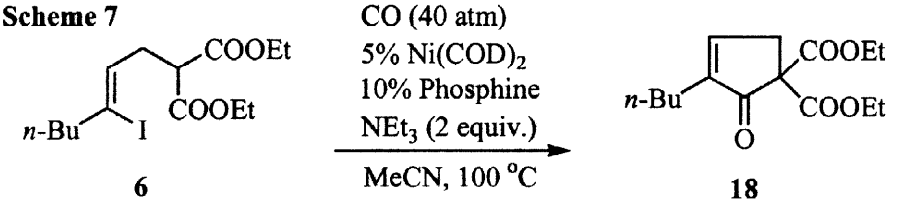
The 5-*C*-*exo* cyclization of alkenyl iodide **6** using Ni catalysts was also initially disappointing in cases where 5% $Cl_2Ni(PPh_3)_2$ and 10% *n*-BuLi, 5% $Ni(PPh_3)_4$, and 5% $Ni(COD)_2$ were used as catalysts. In each case, the desired reaction at 100 °C was very sluggish, and the yields of **18** after 24 h were 5, 20, and 5%, respectively, whereas the corresponding reaction using 10% Li_2CuCl_4 gave **18** in 92% yield. Noting that the balance of the material in the Ni-catalyzed reaction was mostly the unreacted starting compound **6**, we sought a means of accelerating the reaction rate through ligand optimization. To this end, combinations of 5% of $Ni(COD)_2$ and $Ph_2P(CH_2)_nPPh_2$, where n = 2(dppe), n = 3(dppp), and n = 4(dppb), were used as catalysts. Whereas dppe was totally ineffective, dppp and dppb were effective, giving **18** in 85 and 74% yields, respectively (Scheme 7). These results indicate that the catalytic activity of Ni complexes can be significantly modified and improved through optimization of ligands and possibly other parameters as well. When PPh_3 was used, one cyclic byproduct, tentatively identified as the allyl alcohol corresponding to **18** was obtained in about 20% yield, while the reaction involving the use of dppe led to a complex mixture.

Scheme 7

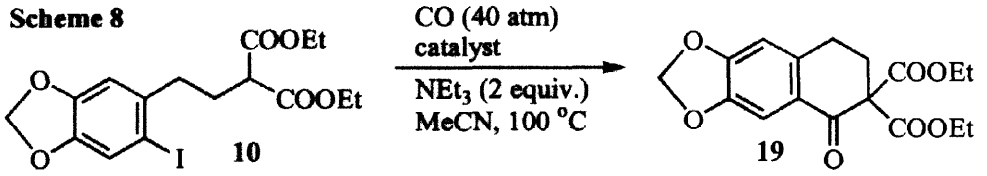


6 18

Phosphine	Time (h)	Yield of **18** (%)	**6** (%)
none	24	5	95
PPh_3	24	20	40
dppe	40	<5	<5
dppp	40	85	<2
dppb	40	74	10

The feasibility of achieving the 6-*C*-*exo* carbonylative cyclization has been demonstrated only with one substrate **10** by its conversion to **19** with either 3 mol % of $Cl_2Ni(PPh_3)_2$ or 10 mol % of Li_2CuCl_4 as a catalyst in 92 or 98% yield, respectively (Scheme 8). Although no other substrates for the 6-*C*-*exo* process have so far been tested, the results shown in Scheme 8 suggest that it may well be a very favorable process of reasonable scope.

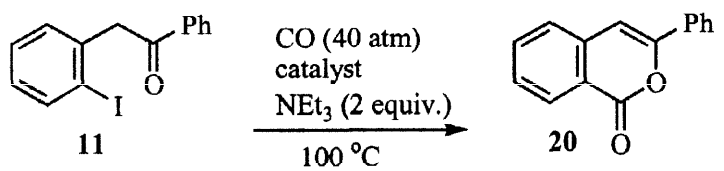
Scheme 8



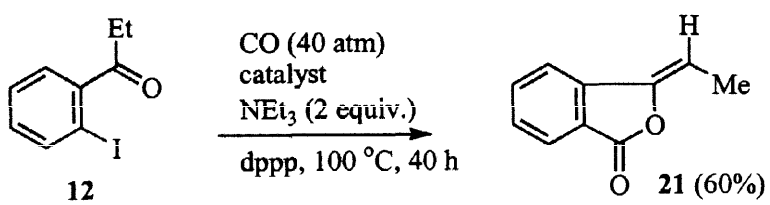
Catalyst	19 (%)
3 mol% $Cl_2Ni(PPh_3)_2$	92
10 mol% Li_2CuCl_4	98

6-*O*-*endo* and 5-*O*-*endo* Processes. The reaction of **11** and **12** with CO (40 atm), 2 equiv. of NEt_3 in MeCN at 100 °C in the presence of a Ni or Cu catalysts was briefly investigated. Under these conditions, neither 5 mol % of $Ni(PPh_3)_4$ nor 10 mol % of Li_2CuCl_4 was an effective catalyst. In either case, the desired product **20** was produced only in 20% yield even after 1 day, with 70-75% of the starting compound remaining unreacted. On the other hand, a combination of 5 mol% of $Ni(COD)_2$ and 10 mol % of dppb in conjunction with the use of DMF as a solvent led to a 95% yield of **20** (Scheme 9). The Cu-catalyzed reaction has not been improved. Under these improved conditions, **12** also underwent the expected 5-*O*-*endo* cyclization catalyzed by Ni(dppp) generated *in situ* by mixing $Ni(COD)_2$ with dppp to produce **21** in 60% yield.[14]

Scheme 9



Catalyst	Solvent	Time (h)	20 (%)	11 (%)
5 mol% $Ni(PPh_3)_4$	DMF	24	20	75
10 mol% Li_2CuCl_4	MeCN	40	20	70
5 mol% $Ni(COD)_2$ 10 mol% dppb	DMF	40	95	<2



In a recent study of the corresponding Pd-catalyzed carbonylative cyclization,[5e] the following two generalizations regarding the preferred cyclization mode have been made: (1) Formation of five- and six-membered rings is favored over potentially competitive three-, four-, seven-, or eight-membered rings. (2) In cases where trapping with *C*- and *O*-enolates can, in principle, produce ketones and lactones, respectively, of the same

ring size, trapping with *O*-enolates is favored (Table 2). All of the results of the carbonylative cyclization observed in this study are in full agreement with these generalizations.

Table 2. Possible and Competing Cyclization Processes and Predicted Preferences

Competition and Favored Process[a]		
3-*C*-*exo*	vs.	**5-*O*-endo**
4-*C*-*exo*	vs.	**6-*O*-endo**
5-*C*-*exo*	vs.	7-*O*-endo
6-*C*-*exo*	vs.	8-*O*-endo

[a] The favored process in each case is highlighted.

CONCLUSIONS

1. Carbonylative cyclization of iodoarenes containing a proximal enolate precursor in the *ortho* position and related iodoalkenes can be selectively converted to either cyclic ketones or lactones in the presence of Ni or Cu catalysts *via* trapping of putative acylmetal intermediates with *C*- or *O*-enolates, respectively. Together with Pd, the synthetic chemists now have three transition metals, *i.e.*, Ni, Cu, and Pd, to choose from as catalysts.

2. The results obtained in this study are in full agreement with the two predictive generalizations derived from a related earlier study of the Pd-catalyzed reaction: (1) Formation of five- and six-membered rings is favored over potentially competitive three, four, seven, or eight-membered rings. (2) In cases where trapping with *C*- and *O*-enolates can, in principle, produce ketones and lactones, respectively, of the same ring size, trapping with *O*-enolates is favored. Specifically, β- and γ-iodo carbonyl compounds may undergo selective 5-*O*-endo and 6-*O*-endo processes, respectively, while δ- and ϵ-iodo carbonyl derivatives favor 5-*C*-*exo* and 6-*C*-*exo* processes, respectively.

3. The current scopes of the Ni- or Cu-catalyzed reactions are still somewhat narrower than that of the Pd-catalyzed reaction, and the Ni- or Cu-catalyzed versions appear to be more strongly substrate dependent. This study has, however, clearly demonstrated that, through optimization of ligands, solvents, and other changeable parameters, substantial improvements leading to highly satisfactory results can be made in various cases. Further investigation is clearly needed to delineate the relative merits and demerits of Ni, Cu, and Pd.

EXPERIMENTAL SECTION

General Procedures. All reactions were conducted under a dry Ar atmosphere. Gas chromatographic measurements were performed on SE-30 (Chromosorb W) columns with appropriate saturated hydrocarbon internal standards. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on Varian Gemini-200 and GE QE-300 NMR spectrometers using Me_4Si as an internal standard unless otherwise noted. NMR yields were determined by using dibromomethane as internal reference. All commercially available reagents were used without further purification unless otherwise noted. THF was distilled from sodium benzophenone ketyl. CH_3CN, DMF, CH_2Cl_2, and NEt_3 were dried over molecular sieves 4A. Ni- or Cu-catalyzed high-pressure carbonylation reaction were carried out in a 22-mL autoclave (Parr Instrument Co.) using a cylinder of 99.99% pure CO (Matheson).

Preparation of Carbonylative Cyclization Precursors. Iodoarenes **1**, **3-5**, **8**, and **12** as well as iodoalkene **6** were prepared as described below. The preparation of **7** and **9-11** were previously reported in detail.[5e]

Preparation of Doubly Stabilized Enolates. (i) Diethyl 2-(*o*-Iodobenzyl)malonate (1a).[5b] **Representative Procedure.** To a supension of NaH (0.29 g, 12 mmol) in THF (20 mL) and HMPA (4.2 mL, 24 mmol) were sequentially added diethyl malonate (1.92g, 12 mmol) in THF (20 mL, 23 °C, 30 min) and 2-iodobenzyl bromide (3.56 g, 12 mmol, 23 °C, 2 h). After the standard workup, column chromatography (ethyl acetate/hexane = 1/4) provided **1a** (91%): IR (neat) 1734 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 1.21 (t, J = 7.1 Hz, 6 H), 3.34 (d, J = 7.8 Hz, 2 H), 3.83 (t, J = 7.8 Hz, 1 H), 4.15 (q, J = 7.1 Hz, 2 H), 4.16 (q, J = 7.1 Hz, 2 H), 6.8-7.9 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 13.92, 39.18, 51.60, 61.40, 100.33, 128.17, 128.57, 130.49, 139.55, 140.16, 168.41.

(ii) Diethyl 2-(*o*-Bromobenzyl)malonate (1b).[5b] Using 2-bromobenzyl bromide (3.00 g, 12 mmol), **1b** was prepared in 83% yield: IR (neat) 1734 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 1.21 (t, J = 7.1 Hz, 3 H), 3.33 (d, J = 7.8 Hz, 2 H), 3.85 (t, J = 7.8 Hz,1 H), 4.14 (q, J = 7.1 Hz, 2 H), 4.15 (q, J = 7.1 Hz, 2 H), 7.05-7.6 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 13.94, 34.98, 51.42, 61.42, 124.50, 127.34, 128.52, 131.40, 132.85, 137.01, 168.59.

(iii) Ethyl 2-(*o*-Iodobenzyl)acetoacetate (3).[5b] This compound was prepared from 2-iodobenzyl bromide (3.56 g, 12 mmol) and ethyl acetoacetate (1.56 g, 12 mmol) in 91% yield: IR (neat) 1745 (s) , 1720 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.20 (t, J = 7.4 Hz, 1 H), 2.25 (s, 3 H), 3.25 (d, J = 7.4 Hz, 2 H), 3.95 (t, J = 7.4 Hz, 1 H), 4.16 (q, J = 7.1 Hz, 2 H), 6.85-7.85 (m, 4 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 13.93, 29.70, 38.34, 58.92, 61.41, 100.29, 128.28, 128.53, 130.76, 139.53, 140.47, 168.55, 201.96.

(iv) Methyl 2-(*o*-Iodobenzyl)phenylsulphonylacetate (4a).[5b] This compound was prepared from 2-iodobenzyl bromide (3.56 g, 12 mmol) and methyl phenylsulphonyl acetate (2.56 g, 12 mmol) in 88% yield: IR (Nujol) 1750 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 3.37 (d, J = 9 Hz, 1 H), 3.40 (d, J = 6.2 Hz, 1 H), 3.59 (s, 3 H), 4.41 (dd, J = 9, 6.2 Hz, 1 H), 6.8-8.1 (m, 9 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 37.54, 52.95, 69.54, 99.92, 128.56, 129.23, 129.32, 130.78, 134.44, 137.13, 137.76, 139.83, 165.16.

(v) Methyl 2-(*o*-Bromobenzyl)pehenylsulfonylacetate (4b).[5b] Using 2-bromobenzyl bromide (3.00 g,

12 mmol) **4b was prepared in 83% yield: IR (Nujol) 1750 (s) cm^{-1}**; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 3.30 (dd, J = 13.6, 11.6 Hz, 1 H), 3.50 (dd, J = 13.6, 3.5 Hz, 1 H), 3.58 (s, 3 H), 4.41 (dd, J = 11.6, 3.5 Hz, 1 H), 7.05-8.05 (m, 9 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 33.31, 52.91, 69.33, 124.24, 127.68, 129.16 (2 C), 131.50, 133.03, 134.40, 134.60, 137.09, 165.28.

(vi) Ethyl 2-(*o*-Iodobenzyl)cyanoacetate (5).[5b] This compound was prepared from 2-iodobenzyl bromide (1.78 g, 6 mol) and ethyl cyanoacetate (0.68 g, 6 mmol) in 44% yield: IR (Nujol) 1738 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 1.31 (t, J = 7.1 Hz, 3 H), 3.22 (dd, J = 13.9, 9.6 Hz, 1 H), 3.47 (dd, J = 13.9, 6.2 Hz, 1 H), 3.92 (dd, J = 9.6, 6.2 Hz, 1 H), 4.28 (q, J = 7.1 Hz, 2 H), 6.95-8.0 (m, 4 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 13.93, 37.65, 40.43, 63.05, 99.97, 115.71, 128.79, 129.64, 130.98, 137.88, 139.85, 165.14.

(vii) (*Z*)-Diethyl 4-Iodo-oct-3-ene-1,1-dicarboxylate (6).[5b] This compound was prepared from (*Z*)-1-bromo-3-iodo-2-heptene (2.29 g, 6 mmol) and diethyl malonate (0.96 g, 6 mmol) in 84% yield: IR (neat) 1739 (s), 960 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.90 (t, J = 7.1 Hz, 3 H), 1.2-1.6 (m, 10 H), 2.46 (t, J = 7 Hz, 2 H), 2.71 (dd, J = 7.6, 6.7 Hz, 2 H), 3.46 (t, J = 7.5 Hz, 1 H), 4.21 (q, J = 7.1 Hz, 4 H), 5.54 (t, J = 6.8 Hz, 1 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ13.71, 13.98, 21.08, 31.21, 35.35, 44.82, 50.72, 61.37, 112.58, 129.96, 168.53.

Ethyl 3-*o*-Iodophenylpropionate (8).[5b] To a solution of 2 *M* solution of lithium isopropylamide (2.5 mL, 5 mmol) in THF were added ethyl acetate (0.49 mL, 5 mmol) in THF (15 mL, -78 °C, 30 min), HMPA (1.4 mL, 8 mmol), and 2-iodobenzyl bromide (1.2 g, 4.1 mmol) in THF (10 mL, -78 °C, 2 h). Column chromatography (ethyl acetate/ hexane = 20:1) provided **8** (0.39 g, 44%): IR (neat) 1736 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 1.25 (t, J = 7.1 Hz, 3 H), 2.62 (t, J = 7.8 Hz, 2 H), 3.06 (t, J = 7.8 Hz, 2 H), 4.15 (q, J = 7.1 Hz, 2 H), 6.8-7.9 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 14.24, 34.47, 35.98, 60.62, 128.50, 128.78, 129.86, 139.92, 143.41, 172.88.

2,2-Bis(ethoxycarbonyl)-1-indanone (2). (a) Representative Procedure of Carbonylative Cyclization Using Ni Catalysts. (Procedure I).[5b] To a solution of **1a** (0.38 g, 1 mmol) in 2 mL of MeCN were added sequentially NEt_3(0.28 mL, 2 mmol) and $Cl_2Ni(PPh_3)_2$ (21 mg, 0.03 mmol). The mixture was placed in an autoclave, which was charged with CO (40 atm), heated to 100 °C, and stirred for 30 h. After cooling, the mixture was worked up with ether and brine, washed with aqueous $NaHCO_3$, and dried over $MgSO_4$. Evaporation of volatiles (50 °C, 0.1 mmHg) followed by a short-path chromatography (silica gel) provided 253 mg (92%) of the titled compound:[5b] IR (neat) 1728 (s), 1590 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 1.28 (t, J = 7.1 Hz, 6 H), 3.82 (s, 2 H), 4.26 (q, J = 7.1 Hz, 4 H), 7.40 (t, J = 7.3 Hz, 1 H), 7.49 (d, J = 7.5 Hz, 1 H), 7.63 (t, J = 7.5 Hz, 1 H), 7.79 (d, J = 7.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 13.77, 36.01, 62.36, 67.08, 125.05, 126.12, 127.94, 134.14, 135.58, 151.72, 166.72, 194.35; HRMS calcd for $C_{15}H_{16}O_5$ 276.0997, found 276.0997.

(b) Representative Procedure of Carbonylative Cyclization Using Copper Catalysts. (Procedure II).[5b] To a solution of **1a** (0.38 g, 1 mmol) in 3 mL of THF-MeCN (1:1) were added sequentially NEt_3 (0.28 mL, 2 mmol) and Li_2CuCl_4 (0.1 *M* in THF, 1 mL, 0.1 mmol). The mixture was placed in an autoclave, and CO (40 atm) was introduced. The mixture was heated to 100 °C and stirred for 40 h. After the standard workup, column

chromatography (hexane/ethyl acetate = 3/1) provided 251 mg (91%) of the titled compound.

2-Acetyl-2-ethoxycarbonyl-1-indanone (13).[5b] This compound was prepared following Procedure II except that **3** (0.69 g, 2 mmol) was used in place of **1a** (reaction time, 40 h). Column chromatography (hexane/ethyl acetate = 10/1) provided **13** (202 mg, 41%, 50% by GLC): IR (neat) 1740 (s), 1718 (s) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 1.27 (t, J = 7.1 Hz, 3 H), 2.49 (s, 3 H), 3.43 (d, J = 18 Hz, 1 H), 4.07 (d, J = 18 Hz, 1 H), 4.26 (q, J = 7.1 Hz, 2 H), 7.1-7.9 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 13.98, 27.64, 34.12, 62.61, 74.69, 125.50, 126.76, 128.42, 134.60, 136.25, 153.22, 168.71, 196.45, 198.45; HRMS calcd for $C_{14}H_{14}O_4$ 246.0892, found 246.0897.

2-Phenylsulfonyl-1-indanone (14).[5b] **(a) Using a Nickel Catalyst.** This compound was prepared following Procedure I except that *n*-BuLi in hexanes was used to generate an active Ni catalyst (-78 °C to 25 °C, 2 equiv. relative to Ni) and that **4a** (0.43g, 1 mmol) was used as the substrate (reaction time, 24 h). Column chromatography (hexane/ethyl acetate = 3/1) provided **14** (198 mg, 73%, 85% by NMR): IR (neat) 1732 (s), 1609 (s), 1449 (s) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 3.53 (dd, J = 18, 8.3 Hz, 1 H), 3.81 (dd, J = 18, 3.3 Hz, 1 H), 4.30 (dd, J = 8.3, 3.3 Hz, 1 H), 7.3-8.0 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 28.04, 68.59, 124.79, 126.36, 128.17, 129.03, 129.21, 134.19, 135.69, 135.90, 137.45, 151.77, 194.41; HRMS (M+1) calcd for $C_{15}H_{13}O_3S$ 273.0585, found 273.0588.

(b) Using a Copper Catalyst. This compound was prepared following Procedure II except that **4a** (0.43g, 1 mmol) was used in place of **1a** (reaction time, 19 h). Column chromatography (hexane/ethyl acetate = 3/1) provided **14** (0.09 g, 30%) along with 0.11 g (30%) of 2-methoxycarbonyl-2-phenylsulfonyl-1-indanone and 0.13 g (30%) of the starting material.

2-(*n*-Butyl)-5,5-bis(ethoxycarbonyl)-2-cyclopenten-1-one (18).[5b] **(a) Using $Ni(COD)_2$-dppp.** This compound was prepared following Procedure I, except that **6** (191 mg, 0.5 mmol), and a combination of $Ni(COD)_2$ (5.4 mg, 0.025 mmol) and 1,4-bis(diphenylphosphino)propane (20 mg, 0.05 mmol) were used as the starting compounds and catalyst, respectively (reaction time, 24 h). Column chromatography (hexane/ethyl acetate = 4/1) provided **18** (111 mg, 79%, 85% by NMR): IR (neat) 1745 (s), 1715 (s) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 0.90 (t, J = 7.1 Hz, 3 H), 1.28 (t, J = 7.1 Hz, 6 H), 1.25-1.55 (m, 4 H), 2.20 (t, J = 7.1 Hz, 2 H), 3.21 (dd, J = 4.7, 2.1 Hz, 2 H), 4.23 (q, J = 7.1 Hz, 4 H), 7.3-7.35 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 13.67, 13.84 (2 C), 22.17, 24.63, 29.44, 36.45, 62.25 (2 C), 64.99, 144.02, 155.23, 166.74, 197.25 (2 C); HRMS cald for $C_{15}H_{22}O_5$ 282.1467, found 282.1462.

(b) Using $Ni(COD)_2$ and dppb. Using **6** (191 mg, 0.5 mmol), MeCN (2 mL), NEt_3 (0.14 mL, 1 mmol),$Ni(COD)_2$ (5.4 mg, 0.025 mmol), and dppb (21 mg, 0.05 mmol), (reaction time, 24 h), **18** was obtained in 69% yield (97 mg, 74% by NMR) along with 8 mg (6%, 10% by NMR) of **6**.

(c) Using $Ni(PPh_3)_4$. Using **6** (382 mg, 1 mmol), MeCN (3 mL), NEt_3 (0.28 mL, 2 mmol), $Ni(PPh_3)_4$ (55 mg, 0.05 mmol) (reaction time, 24 h), **18** was obtained in 14 % yield (40 mg, 20% by NMR) along with 2-(*n*-butyl)-5,5-bis(ethoxycarbonyl)-2-cyclopenten-1-ol (34 mg, 12%, 20% by NMR) and 103 mg (27%, 40% by NMR)

of **6**. The 2-cyclopentenol derivative displayed the following spectral data: IR(neat) 3502 (s), 1730 (s) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 0.90 (t, J = 7.2 Hz, 3 H), 1.26 (t, J = 7.2 Hz, 3 H), 1.27 (t, J = 7.2 Hz, 3 H), 1.25-1.65 (m, 4 H), 2.14 (t, J = 7.5 Hz, 2 H), 2.50 (br, 1 H), 2.65-2.8 (m, 1 H), 3.1-3.25 (m, 1 H), 4.19 (q, J = 7.2 Hz, 2 H), 4.20 (q, J = 7.2 Hz, 2 H), 5.10 (br, 1 H), 5.45 (d, J = 2.2 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 13.89, 13.97, 14.03, 22.46, 27.71, 29.49, 37.81, 61.52, 61.59, 64.24, 81.39, 124.13, 144.57, 169.92, 171.06; MS(EI) M^+ 284.

(d) Using Li_2CuCl_4. Following Procedure II except that **6** (382 mg, 1 mmol) was used in place of **1a** (reaction time, 40 h). **18** was obtained in 92% yield (259 mg).

2,2-Bis(ethoxycarbonyl)-6,7-methylenedixoy-1-tetralone (19).[5b] **(a) Using a Nickel Catalyst.** This compound was prepared following Procedure I, except that **10** (432 mg, 1 mmol) and $Cl_2Ni(PPh_3)_2$ (33 mg, 0.05 mmol) were used (reaction time, 24 h). Short column chromatography provided **19** (307 mg, 92%): IR (neat) 1852 (s), 1728 (s), 1618 cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 0.90 (t, J = 7.1 Hz, 3 H), 1.28 (t, J = 7.1 Hz, 6 H), 1.25-1.55 (m, 4 H), 2.20 (t, J = 7.1 Hz, 2 H), 3.21 (dd, J = 4.7, 2.1 Hz, 2 H), 4.23 (q, J = 7.1 Hz, 4 H), 7.3-7.35 (m, 1 H); ^{13}C NMR ($CDCl_3$,) δ 13.67, 13.84 (2 C), 22.17, 2463, 29.44, 36.45, 62.25 (2 C), 64.99, 144.02, 155.23, 166.74, 197.25 (2C); HRMS calcd for $C_{15}H_{22}O_5$ 282.1467, found 282.1462.

(b) Using a Cu Catalyst. Following Procedure II except that **10** (432 mg, 1 mmol) was used in place of **1a** (reaction time, 40 h), **19** was obtained in 98% yield.

3-Phenyl-2-benzopyran-1(1*H*)-one (20).[5e] This compound was prepared following Procedure I except that **11** (161 mg, 0.5 mmol) in DMF (2 mL) and a combination of $Ni(COD)_2$ (5.5 mg, 0.025 mmol) and dppb (21 mg, 0.05 mmol) were used as the starting compounds and catalyst, respectively (reaction time, 40 h). Column chromatography (hexane/ether = 10/1) provided **20** (93 mg, 84%, 95% by NMR): IR (Nujol) 1724 (s), 1639 (s), 1069 (s) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 6.93 (s, 1 H), 7.4-7.9 (m, 8 H), 8.25-8.35 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 101.75, 120.49, 125.19, 125.93, 128.09, 128.77, 129.59, 129.91, 131.91, 134.81, 137.46, 153.57, 162.24.

(*Z*)-3-Ethylidene-4-benzofuran-1(3*H*)-one (21). This compound was prepared following Procedure I, except that **12** (130 mg, 0.5 mmol), and a combination of $Ni(COD)_2$ (5.4 mg, 0.025 mmol) and dppp (20 mg, 0.05 mmol) were used as the starting compounds and catalyst, respectively (reaction time, 40 h). Column chromatography (hexane/ether = 10/1) provided **21** (46 mg, 57%, 60% by NMR):[5h] ^1H NMR ($CDCl_3$, Me_4Si) δ 2.01 (d, J = 7.2 Hz, 3 H), 5.67 (q, J = 7.2 Hz, 1 H), 7.4-7.55 (m, 1 H), 7.55-7.75 (m, 2 H), 7.86 (d, J = 7.7 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 11.29, 104.23, 119.58, 124.33, 125.14, 129.32, 134.29, 139.48, 146.36, 167.13.

Acknowledgements. We thank the National Institutes of Health (GM 36792) for support of this research and Johnson-Matthey for Pd compounds. We also thank Japan Society for Promotion of Science for a postdoctoral fellowship (HM).

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