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Rhodium-catalyzed conjugate addition of arylindium reagents to α,β-unsaturated carbonyl compounds

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Dedicated to the memory of Professor Rafael Suau

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ABSTRACT

A novel rhodium-catalyzed conjugate addition of indium reagents to electron deficient olefins is reported. The reaction takes place in THF/MeOH at 110 °C using arylindium dichlorides, a rhodium(I)-binap complex as catalyst, and α,β-unsaturated ketones and lactones in good yields (45–94%). The addition of MeOH is crucial for an efficient transformation and NMR studies seem to indicate that promotes the catalytic cycle leaving the indium organometallic unaltered. The use of chiral non-racemic ligands allows performing the reaction with moderate enantioselectivities.

1. Introduction

In recent years, indium(III) organometallics have been shown as useful reagents in fundamental organic transformations and provide an alternative to other well-established organometallic reagents.[1] Typically, the use of organoindium compounds is associated with a transition metal complex as catalyst and transmetallation is a key step of the process. Accordingly, in a program devoted to the development of new synthetic applications of indium compounds, we have discovered that triorganoindium reagents (R_3In) participate efficiently in metal-catalyzed reactions, such as conjugate addition (Ni catalyzed),[2] cross-coupling reactions (Pd and Ni catalyzed),[3] and allylic and propargylic substitution reactions (Cu and Pd catalyzed).[4,5] It is remarkable the ability of R_3In to transfer the three organic groups in the palladium-catalyzed cross-coupling reaction.[6]

The 1,4-conjugate addition of organometallic reagents to electron deficient olefins is a fundamental process for carbon–carbon bond formation in organic synthesis.[7] This reaction has been classically associated with organocopper chemistry but nowadays other organometallic species can be used by means of transition metal catalysis. In our group we discovered the nickel-catalyzed conjugate addition of triorganoindium compounds to α,β-unsaturated ketones, esters, and nitriles.[2] This reaction takes place with aryl and alkylindium reagents but only one of the three groups attached to indium is transferred.

Since then, the rhodium-catalyzed conjugate addition reaction of organoboron species to activated olefins has been developed as a modern method for the formation of carbon–carbon bonds under mild conditions in good yields.[8] More recently, other organometallic species have also been applied,[9] including a report showing the utility of diphenylindium hydroxide.[10] In an effort to enlarge the scope of indium reagents in conjugate addition reactions, we decided to study further the rhodium-catalyzed conjugate addition of indium organometallics to α,β-unsaturated carbonyl compounds.

2. Results and discussion

As starting point, we tried to apply the methodology developed for the rhodium-catalyzed conjugate addition of organoboron compounds to electron deficient olefins.[8a] In our first attempt, we found that the reaction of triphenylindium (1.0 equiv) with 2-cyclohexen-1-one (**1**) in THF at 80 °C, using $[Rh(cod)Cl]_2$ (4%) and (±)-binap (8%) as catalytic system, afforded the conjugate addition product **2a** in 41% yield after 6 h (Table 1, entry 1). Alternatively, other rhodium complexes, such as Rh(acac)(cod), or different bidentate phosphine ligands (davephos, dppf) gave similar results (entries 2–4), and the use of substoichiometric quantities of Ph_3In returned lower yields. Although these results probe the utility of

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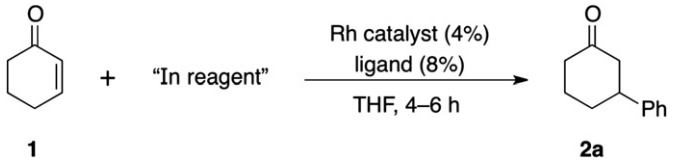
Table 1
Reactions of indium reagents with 2-cyclohexen-1-one (1) under rhodium catalysis



1 2a

Entry	In reagent[a]	Rh catalyst	Ligand	Conditions[a]	Yield[c] (%)
1	Ph_3In (1.0)	$[Rh(cod)Cl]_2$	(±)-binap	80 °C	41
2	Ph_3In (1.0)	Rh(acac)(cod)[b]	(±)-binap	80 °C	35
3	Ph_3In (1.0)	$[Rh(cod)Cl]_2$	davephos	80 °C	40
4	Ph_3In (1.0)	$[Rh(cod)Cl]_2$	dppf	80 °C	39
5	$PhInCl_2$ (1.2)	$[Rh(cod)Cl]_2$	(±)-binap	80 °C	45
6	$PhInCl_2$ (1.2)	$[Rh(cod)Cl]_2$	(±)-binap	110 °C	54
7	$PhInCl_2$ (1.2)	$[Rh(cod)Cl]_2$	(±)-binap	H_2O (1.2), 80 °C	30
8	$PhInCl_2$ (1.2)	$[Rh(cod)Cl]_2$	(±)-binap	MeOH (1.2), 80 °C	48
9	$PhInCl_2$ (1.2)	$[Rh(cod)Cl]_2$	(±)-binap	MeOH (2.4), 80 °C	57
10	$PhInCl_2$ (1.2)	$[Rh(cod)Cl]_2$	(±)-binap	MeOH (2.4), 110 °C	94
11	$PhInCl_2$ (1.2)	$[Rh(cod)Cl]_2$	(±)-binap	MeOH (3.6), 110 °C	83
12	$PhInCl_2$ (1.2)	$[Rh(cod)Cl]_2$	(±)-binap	H_2O (2.4), 110 °C	75
13	$PhInCl_2$ (1.2)	$[Rh(cod)Cl]_2$	(±)-binap	KOH (2.4), 110 °C	34
14	Ph_2InCl (1.2)	$[Rh(cod)Cl]_2$	(±)-binap	MeOH (2.4), 110 °C	93
15	Ph_2InCl (0.6)	$[Rh(cod)Cl]_2$	(±)-binap	MeOH (2.4), 110 °C	58

[a] In parentheses, number of equivalents with respect to **1**.
[b] Catalyst (8%) was used.
[c] Isolated yield.

organoindium reagents in rhodium-catalyzed conjugation addition reactions, the low yield led us to look for a more efficient procedure.

In an effort to improve the efficiency of the reaction, we studied the reactivity of monoorganoindium dihalides ($RInX_2$). Although indium organometallic chemistry is generally associated with triorganoindium compounds, $RInCl_2$ can be prepared from equimolecular amounts of organometallic reagent and $InCl_3$[11] or from aryl iodides using In(0).[12] Under the previous conditions, we found that the reaction of $PhInCl_2$ (1.2 equiv) with **1** gave the conjugate addition product in 45% yield as a single reaction product, after 6 h at 80 °C (entry 5) and 54% yield when the reaction is carried out at 110 °C (entry 6). It is worth noting that although the same chemical yield when using Ph_3In was obtained, the atom economy is higher.[13]

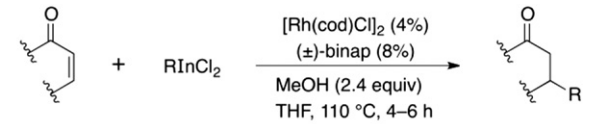
In the rhodium-catalyzed reaction of arylboronic acids to α,β-unsaturated ketones the addition of water increases the efficiency of the process, presumably because the hydrolysis of an (oxa-π-allyl)rhodium intermediate favors the regeneration of the rhodium active catalyst.[14] Taking into account that the hydrolysis of alkyl and arylindium reagents is relatively slow,[6a,11b] and the presence of stoichiometric amounts of water are tolerated,[6a,10,15] we studied the effect of a protic cosolvent in the conjugate addition reactions using monoorganoindium dihalides.

Under the previous conditions (1.2 equiv of $PhInCl_2$, 80 °C), we observed that the addition of 1.2 equiv of H_2O to the reaction mixture led to a lower yield (30%, entry 7). However, the addition of 1.2 equiv of methanol retained the yield (48%, entry 8) and 2.4 equiv slightly increased the yield up to 57% (entry 9).[16,17] Additionally, when the reaction temperature was increased to 110 °C, the conjugate addition product was obtained in a high 94% yield (entry 10). On the other hand, the use of larger amounts of MeOH or water as proton source gave lower yields (entries 11 and 12).[18]

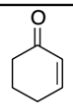
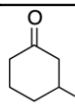
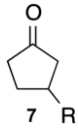
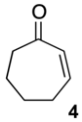
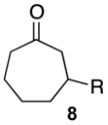
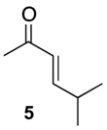
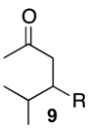
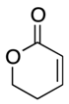
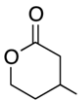
As in the rhodium-catalyzed conjugate addition of boronic acids we also explored the reaction under basic conditions.[9] In this case we found that the use of KOH (2.4 equiv) as additive gave the conjugate addition product in lower yields (34%, entry 13). Finally, we also found that other organoindium species, such as Ph_2InCl (1.2 equiv) reacted with **1** under the optimized conditions to afford **2a** in a good 93% yield (entry 14), although it should be noted that the atom efficiency of this reaction is lower than using $PhInCl_2$. Unfortunately, using 0.6 equiv of Ph_2InCl the yield decreased to 58% (entry 15), a result that can be explained by to the lower reactivity of the Ph_2InCl reagent.

Once the experimental conditions for the rhodium-catalyzed conjugate addition of dichlorophenylindium to 2-cyclohexen-1-one were optimized (2.4 equiv of MeOH, 110 °C, Table 2, entry 1), we explored the versatility of the methodology by using other unsaturated carbonyl compounds and different monoarylindium reagents. Following this approach, we found that dichlorophenylindium reacted efficiently with enones, such as 2-cyclopenten-1-one (**3**), 2-cyclohepten-1-one (**4**), and the acyclic enone **5**, to afford the corresponding conjugate addition products (**7a**, **8a**, and **9a**, respectively) in good yields (63–80%, entries 5, 8, and 10). Additionally, the rhodium-catalyzed reaction of $PhInCl_2$ with the α,β-unsaturated lactone **6** also occurs in a good 76% yield, giving the lactone **10a**.

Table 2
Reaction of arylindium dichlorides with α,β-unsaturated carbonyl compounds



(1.0 equiv) (1.2 equiv)

Entry	α,β-Unsaturated compounds	R	Product		Yield[a] (%)
1	 1	Ph	 2	**2a**	94
2		4-CF_3–C_6H_4		**2b**	69
3		4-F–C_6H_4		**2c**	46
4		3-F–C_6H_4		**2d**	66
5	 3	Ph	 7	**7a**	80
6		4-CF_3–C_6H_4		**7b**	57
7		4-F–C_6H_4		**7c**	56
8	 4	Ph	 8	**8a**	70
9		4-CF_3–C_6H_4		**8b**	62
10	 5	Ph	 9	**9a**	63
11		4-CF_3–C_6H_4		**9b**	45
12	 6	Ph	 10	**10a**	76
13		4-CF_3–C_6H_4		**10b**	58
14		4-F–C_6H_4		**10c**	47
15		3-F–C_6H_4		**10d**	56

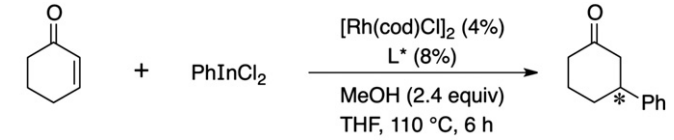
[a] Isolated yield.

The scope of the conjugate addition reaction was extended to functionalized arylindium dichlorides, such as 4-trifluoromethylphenylindium dichloride, 4-fluorophenylindium dichloride, and 3-fluorophenylindium dichloride. The reaction of 4-trifluoromethylphenylindium dichloride with the enones **1**, **3**, **4**, and **5** and with the lactone **6**, provided the conjugate addition products **2b**, **7b**, **8b**, **9b**, and **10b**, in good yields (45–69%, entries 2,

6, 9, 11, and 13). Analogously, the reaction of 4- and 3-fluorophenylindium dichloride with the previous enones and lactone also afforded the addition products in moderate to good yields (46–66%, entries 3, 4, 7, 14, and 15).

After studying the rhodium-catalyzed conjugate addition of monoarylindium reagents with various α,β-unsaturated carbonyl compounds, we turned our interest into the development of enantioselective reactions by using chiral non-racemic catalyst. Under the optimized reaction conditions, the reaction of $PhInCl_2$ with **1** using (*S*)-binap (8%) as catalyst afforded, after 6 h at 110 °C, the conjugate addition product **2a** in 96% yield and 40% ee (Table 3, entry 1). Other chiral ligands afforded moderate enantioselectivities, with the best results obtained using (*S*)-segphos (85% yield, 52% ee, entry 2). Non-biaryl ligands, such as (*R*)-MeO-biphep, (*R*,*R*)-dipamp, (*R*)-(*S*)-josiphos, (*S*,*S*)-diop, and (1*R*,4*R*)-2,5-diphenylbicyclo[2.2.2]octa-2,5-diene gave lower enantioselectivities (33–94% yield, 8–18% ee).

Table 3
Reaction of $PhInCl_2$ with 2-cyclohexen-1-one under asymmetric catalysis

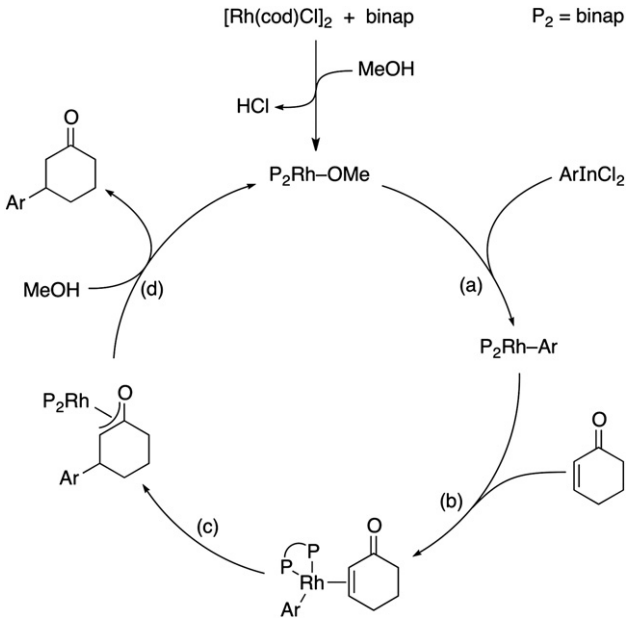


Entry	Ligand	Yield[a] (%)	ee[b] (%)
1	(*S*)-binap	96	40 (*S*)
2	(*S*)-segphos	85	52 (*S*)
3	(*R*,*R*)-quinoxP*	65	35 (*R*)

[a] Isolated yield.
[b] Determined by HPLC using a Chiralcel OD-H column.

In order to gain insight about the reaction mechanism, the structure of the organoindium reagents prepared was studied by ^{13}C NMR.[19] Initially, we found that the mixture of equimolar amounts of PhLi and $InCl_3$ in THF provides, after stirring at room temperature overnight, a 21:79 ratio of Ph_2InCl and $PhInCl_2$.[20] This Schlenk-type equilibrium show correspondence with the observation by Clark in methylindium halides,[11a] and more recently by Baba in allyl,[21] homoallyl,[22] and alkenylindium species.[23] When the reaction mixture is heated 1 h at 80 °C, the equilibrium is displaced to the 3:97 ratio, and to 0:100 after 1 h at 110 °C, a result reproduced during the preparation of dimethylindium chloride.[11a] Although the presence of Ph_3In could be envisaged as kinetic initial product,[11a] this compound is not detected, probably due to an equilibration process during the preparation and acquisition of NMR data.

The influence of the methanol in the reaction mixture was also studied by NMR. When MeOH (2 equiv) was added to the $PhInCl_2$ reagent prepared as before, the ^{13}C NMR spectra showed the reagents $Ph_2InCl/PhInCl_2$ in the same 7:93 ratio, and when the reaction mixture was heated at 110 °C for 1 h, $PhInCl_2$ was the only product detected. These results seem to indicate that the nucleophilic displacement of the chlorine atoms in $PhInCl_2$ is not produced.[20] This behavior is coincident with previously results about the stability of organoindium halides in aqueous media.[21c,24] Therefore it seems that the role of MeOH in the rhodium-catalyzed conjugate addition reactions is associated with the generation of the catalytic specie and/or the methanolysis of the oxoallyl rhodium enolate intermediate (Scheme 1).



Scheme 1. Proposed catalytic cycle for the rhodium-catalyzed conjugate addition of arylindium dichlorides to enones. Key: (a) Transmetallation. (b) Coordination to the electron-deficient olefin. (c) Alkene insertion into the Rh–Ar bond. (d) Methanolysis of the (oxa-π-allyl)rhodium intermediate.

3. Conclusions

In summary, arylindium dihalides react with α,β-unsaturated carbonyl ketones and lactones under rhodium(I) catalysis in THF at 110 °C. The reaction proceeds efficiently when methanol (2.4 equiv) is added to the reaction mixture. NMR studies seem to indicate that the organoindium reagents remain unaltered and MeOH promotes the catalytic cycle. Additionally, when chiral ligands are used the conjugate addition reaction proceeds with moderate enantioselectivity. Further studies about the reactivity of organoindium reagents with other unsaturated carbonyl systems, as well as the development of a highly enantioselective version are under investigation and will be reported in due course.

4. Experimental section

4.1. General methods

All reactions were carried out in flame dried glassware, under argon atmosphere, using standard gastight syringes, cannulae, and septa. Reaction temperatures refer to external bath temperatures. Anhydrous THF was obtained by distillation from the sodium ketyl of benzophenone. α,β-Unsaturated carbonyl compounds were purified, immediately before use, by distillation in a high-vacuum line and were trapped at −78 °C in a dry ice-acetone bath. Dry MeOH and all other commercially available reagents were used as received. Organolithium reagents were titrated prior to use. Organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated by using a rotary evaporator at aspirator pressure. TLC was carried out on precoated silica gel 60 F_{254} plates (layer thickness 0.2 mm) and components were located by observation under UV light and by treating the plates with a phosphomolybdic acid or *p*-anisaldehyde solutions. Flash column chromatography was performed on silica gel (230–400 mesh). ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ at 300 MHz and 75 MHz, respectively, at ambient temperature, and calibrated to the solvent peak. ^{13}C NMR spectra of organoindium species were recorded in THF-d_8 at 125 MHz, at room temperature, in an NMR spectrometer equipped with a cryoprobe, and calibrated to the solvent peak.[20] DEPT spectroscopy was used to assign carbon

types. Mass spectra were obtained with EI ionization at 70 eV. IR spectra were recorded on an FT-IR spectrometer with an ATR (Attenuated Total Reflectance) accessory. The enantioselectivity of chiral products was determined by comparison of the chiral stationary phase HPLC traces with those of the corresponding racemic products. The absolute configurations of the products were assigned by comparison with published data.

4.2. Dichloroorganoindium reagents

Dichloroarylindium reagents were prepared by the dropwise addition of the corresponding aryllithium reagent (1 equiv, ~1.5 M in dry THF) to a solution of $InCl_3$ (1.1 equiv, ~0.5 M in dry THF) at −78 °C and warming to room temperature during 4 h. Phenyllithium was commercially available and was used as received. Other aryllithium reagents were prepared by the dropwise addition of *n*-BuLi (1.0 equiv, 2.0 M in hexanes) to a solution of the corresponding bromoaryl compound (1.0 equiv, ~0.5 M in dry THF) at −78 °C and stirring for 30 min.

4.3. General procedure for the rhodium-catalyzed 1,4-addition

To a solution of $[Rh(cod)Cl]_2$ (0.04 mmol) and (±)-binap (0.08 mmol) in dry THF (2 mL) placed in an argon filled Schlenk tube, a solution of $ArInCl_2$ (1.2 mmol, ~0.3 M in dry THF), the α,β-unsaturated carbonyl compound (1 mmol) and dry MeOH (2.4 mmol) were successively added. The resulting mixture was heated at 110 °C for 4–6 h and then the reaction was quenched by the addition of a few drops of MeOH. The mixture was concentrated and EtOAc (25 mL) was added. The organic phase was successively washed with aqueous HCl (5%, 15 mL), saturated aqueous $NaHCO_3$ (15 mL) and brine (15 mL), then dried, filtered, and concentrated. The residue was purified by flash chromatography (EtOAc/hexanes) to afford the 1,4-addition products.

*4.3.1. 3-Phenylcyclohexanone (**2a**)*[25]. Pale yellow oil (168 mg, 94%); ν_{max} 3027, 2934, 2865, 1707 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.75–1.95 (m, 2H), 2.07–2.20 (m, 2H), 2.35–2.65 (m, 4H), 2.97–3.08 (m, 1H), 7.22–7.27 (m, 3H), 7.32–7.38 (m, 2H); δ_C (75 MHz, $CDCl_3$) 25.5 (CH_2), 32.7 (CH_2), 41.1 (CH_2), 44.7 (CH), 48.9 (CH_2), 126.5 (2× CH), 126.7 (CH), 128.7 (2× CH), 144.3 (C), 210.9 (C); *m*/*z* (EI) 174 (100, M^+); HRMS (EI): M^+, found 174.1037. $C_{12}H_{14}O$ requires 174.1039. In the reactions using chiral ligands, the enantiomeric excess was determined by HPLC (Chiralcel OD-H, hexane/*i*-PrOH=98:2, 1.0 mL/min, 254 nm) t_R (*S*)=12.5 min, t_R (*R*)=13.8 min.

*4.3.2. 3-[4-(Trifluoromethyl)phenyl]cyclohexanone (**2b**)*[26]. Light brown oil (118 mg, 69%); ν_{max} 2938, 1708 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.69–1.94 (m, 2H), 2.08–2.22 (m, 2H), 2.35–2.65 (m, 4H), 3.04–3.14 (m, 1H), 7.34 (d, *J* 8.1 Hz, 2H), 7.59 (d, *J* 8.1 Hz, 2H); δ_C (75 MHz, $CDCl_3$) 25.3 (CH_2), 32.4 (CH_2), 41.0 (CH_2), 44.4 (CH), 48.4 (CH_2), 124.1 (q, $^1J_{CF}$ 271.9 Hz, CF_3), 125.6 (q, $^3J_{CF}$ 3.8 Hz, 2× CH), 126.9 (2× CH), 129.0 (q, $^2J_{CF}$ 32.4 Hz, C), 148.1 (C), 210.2 (C); *m*/*z* (EI) 242 (81, M^+), 199 (100); HRMS (EI): M^+, found 242.0907. $C_{13}H_{13}OF_3$ requires 242.0913.

*4.3.3. 3-(4-Fluorophenyl)cyclohexanone (**2c**)*[27]. Light brown oil (50 mg, 46%); ν_{max} 3344, 2916, 2848, 1707 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.74–1.90 (m, 2H), 2.01–2.20 (m, 2H), 2.32–2.63 (m, 4H), 2.96–3.06 (m, 1H), 6.98–7.06 (m, 2H), 7.15–7.22 (m, 2H); δ_C (75 MHz, $CDCl_3$) 25.3 (CH_2), 32.8 (CH_2), 41.1 (CH_2), 43.9 (CH), 49.0 (CH_2), 115.4 (d, $^2J_{CF}$ 21.2 Hz, 2× CH), 127.9 (d, $^3J_{CF}$ 7.9 Hz, 2× CH), 140.0 (d, $^4J_{CF}$ 3.2 Hz, C), 161.5 (d, $^1J_{CF}$ 244.7 Hz, CF), 210.7 (C); *m*/*z* (EI) 192 (84, M^+), 135 (100); HRMS (EI): M^+, found 192.0943. $C_{12}H_{13}OF$ requires 192.0945.

*4.3.4. 3-(3-Fluorophenyl)cyclohexanone (**2d**)*[27]. Yellow oil (89 mg, 66%); ν_{max} 1709, 2866, 2935 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.74–1.90 (m, 2H), 2.06–2.20 (m, 2H), 2.32–2.63 (m, 4H), 2.96–3.07 (m, 1H), 6.89–7.01 (m, 3H), 7.25–7.32 (m, 1H); δ_C (75 MHz, $CDCl_3$) 25.3 (CH_2), 32.5 (CH_2), 41.0 (CH_2), 44.3 (d, $^4J_{CF}$ 1.7 Hz, CH), 48.6 (CH_2), 113.4 (d, $^2J_{CF}$ 21.4 Hz, CH), 113.5 (d, $^2J_{CF}$ 21.0 Hz, CH), 122.2 (d, $^4J_{CF}$ 2.8 Hz, CH), 130.1 (d, $^3J_{CF}$ 8.3 Hz, CH), 146.9 (d, $^3J_{CF}$ 6.8 Hz, C), 163.0 (d, $^1J_{CF}$ 245.9 Hz, CF), 210.3 (C); *m*/*z* (EI) 192 (93, M^+), 149 (100); HRMS (EI): M^+, found 192.0941. $C_{12}H_{13}OF$ requires 192.0945.

*4.3.5. 3-Phenylcyclopentanone (**7a**)*[28]. Yellow oil (115 mg, 80%); ν_{max} 3028, 2961, 1737 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.93–2.08 (m, 1H), 2.25–2.53 (m, 4H), 2.64–2.73 (m, 1H), 3.38–3.50 (m, 1H), 7.24–7.29 (m, 3H), 7.34–7.39 (m, 2H); δ_C (75 MHz, $CDCl_3$) 31.1 (CH_2), 38.8 (CH_2), 42.2 (CH), 45.7 (CH_2), 126.7 (3× CH), 128.6 (2× CH), 143.0 (C), 218.3 (C); *m*/*z* (EI) 160 (100, M^+); HRMS (EI): M^+, found 160.0881. $C_{11}H_{12}O$ requires 160.0883.

*4.3.6. 3-[4-(Trifluoromethyl)phenyl]cyclopentanone (**7b**)*[29]. Pale yellow oil (85 mg, 57%); ν_{max} 2916, 2848, 1741 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.94–2.09 (m, 1H), 2.27–2.55 (m, 4H), 2.66–2.75 (m, 1H), 3.43–3.55 (m, 1H), 7.38 (d, *J* 8.1 Hz, 2H), 7.61 (d, *J* 8.1 Hz, 2H); δ_C (75 MHz, $CDCl_3$) 30.9 (CH_2), 38.6 (CH_2), 42.0 (CH), 45.4 (CH_2), 124.1 (q, $^1J_{CF}$ 271.9 Hz, CF_3), 125.6 (q, $^3J_{CF}$ 3.8 Hz, 2× CH), 127.1 (2× CH), 129.0 (q, $^2J_{CF}$ 32.5 Hz, C), 147.1 (C), 217.3 (C); *m*/*z* (EI) 228 (87, M^+), 172 (100); HRMS (EI): M^+, found 228.0752. $C_{12}H_{11}OF_3$ requires 228.0757.

*4.3.7. 3-(4-Fluorophenyl)cyclopentanone (**7c**)*[30]. Yellow oil (64 mg, 56%); ν_{max} 2960, 1739 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.89–2.03 (m, 1H), 2.24–2.52 (m, 4H), 2.63–2.71 (m, 1H), 3.35–3.47 (m, 1H), 6.99–7.07 (m, 2H), 7.19–7.25 (m, 2H); δ_C (75 MHz, $CDCl_3$) 31.3 (CH_2), 38.8 (CH_2), 41.5 (CH), 45.8 (CH_2), 115.4 (d, $^2J_{CF}$ 21.2 Hz, 2× CH), 128.1 (d, $^3J_{CF}$ 7.8 Hz, 2× CH), 138.7 (d, $^4J_{CF}$ 3.2 Hz, C), 161.6 (d, $^1J_{CF}$ 244.9 Hz, CF), 217.9 (C); *m*/*z* (EI) 178 (100, M^+); HRMS (EI): M^+, found 178.0782. $C_{11}H_{11}OF$ requires 178.0788.

*4.3.8. 3-Phenylcycloheptanone (**8a**)*[28]. Yellow oil (92 mg, 70%); ν_{max} 3027, 2925, 2854, 1696 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.45–1.58 (m, 1H), 1.66–1.82 (m, 2H), 1.95–2.13 (m, 3H), 2.58–2.73 (m, 3H), 2.87–3.00 (m, 2H), 7.17–7.24 (m, 3H), 7.27–7.34 (m, 2H); δ_C (75 MHz, $CDCl_3$) 24.1 (CH_2), 29.2 (CH_2), 39.2 (CH_2), 42.7 (CH), 43.9 (CH_2), 51.2 (CH_2), 126.3 (CH), 126.4 (2× CH), 128.6 (2× CH), 146.9 (C), 213.4 (C); *m*/*z* (EI) 188 (97, M^+), 104 (100); HRMS (EI): M^+, found 188.1190. $C_{13}H_{16}O$ requires 188.1196.

*4.3.9. 3-[4-(Trifluoromethyl)phenyl]cycloheptanone (**8b**)*[31]. Colorless oil (107 mg, 62%); ν_{max} 2929, 1698 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.44–1.58 (m, 1H), 1.66–1.80 (m, 2H), 1.98–2.11 (m, 3H), 2.52–2.68 (m, 3H), 2.89–3.01 (m, 2H), 7.30 (d, *J* 8.1 Hz, 2H), 7.56 (d, *J* 8.1 Hz, 2H); δ_C (75 MHz, $CDCl_3$) 24.0 (CH_2), 29.1 (CH_2), 38.9 (CH_2), 42.5 (CH), 43.8 (CH_2), 50.7 (CH_2), 124.1 (q, $^1J_{CF}$ 271.9 Hz, CF_3), 125.6 (q, $^3J_{CF}$ 3.8 Hz, 2× CH), 126.8 (2× CH), 128.7 (q, $^2J_{CF}$ 32.5 Hz, C), 150.7 (C), 212.6 (C); *m*/*z* (EI) 256 (71, M^+), 199 (100); HRMS (EI): M^+, found 256.1068. $C_{14}H_{15}OF_3$ requires 256.1070.

*4.3.10. 5-Methyl-4-phenyl-2-hexanone (**9a**)*[28]. Pale yellow oil (82 mg, 63%); ν_{max} 3028, 2958, 2928, 2872, 1711 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 0.75 (d, *J* 6.7 Hz, 3H), 0.94 (d, *J* 6.7 Hz, 3H), 1.78–1.90 (m, 1H), 1.99 (s, 3H), 2.79–2.82 (m, 2H), 2.89–2.96 (m, 1H), 7.14–7.22 (m, 3H), 7.25–7.31 (m, 2H); δ_C (75 MHz, $CDCl_3$) 20.3 (CH_3), 20.7 (CH_3), 30.5 (CH_3), 33.3 (CH), 47.6 (CH_2), 48.0 (CH), 126.2 (CH), 128.1 (2× CH), 128.2 (2× CH), 143.2 (C), 208.3 (C); *m*/*z* (EI) 190

(12, M^+), 132 (100); HRMS (EI): M^+, found 190.1349. $C_{13}H_{18}O$ requires 190.1352.

*4.3.11. 5-Methyl-4-[4-(trifluoromethyl)phenyl]-2-hexanone (**9b**)*[32]. Colorless oil (61 mg, 45%); ν_{max} 2962, 1716 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 0.74 (d, *J* 6.7 Hz, 3H), 0.94 (d, *J* 6.7 Hz, 3H), 1.79–1.91 (m, 1H), 2.02 (s, 3H), 2.75–2.91 (m, 2H), 2.98–3.06 (m, 1H), 7.27 (d, *J* 8.1 Hz, 2H), 7.53 (d, *J* 8.1 Hz, 2H); δ_C (75 MHz, $CDCl_3$) 20.2 (CH_3), 20.5 (CH_3), 30.5 (CH_3), 33.0 (CH), 47.2 (CH_2), 47.5 (CH), 124.2 (q, $^1J_{CF}$ 271.8 Hz, CF_3), 125.0 (q, $^3J_{CF}$ 3.8 Hz, 2× CH), 128.5 (q, $^2J_{CF}$ 32.3 Hz, C) 128.5 (2× CH), 147.7 (C), 207.3 (C); *m*/*z* (EI) 258 (2, M^+), 200 (100); HRMS (EI): M^+, found 258.1219. $C_{14}H_{17}OF_3$ requires 258.1226.

*4.3.12. Tetrahydro-4-phenyl-2H-pyran-2-one (**10a**)*[33]. Colorless oil (116 mg, 76%); ν_{max} 3028, 2956, 1727 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.97–2.10 (m, 1H), 2.14–2.23 (m, 1H), 2.64 (dd, *J* 17.6, 10.6 Hz, 1H), 2.92 (ddd, *J* 17.6, 6.0, 1.6 Hz, 1H), 3.19–3.30 (m, 1H), 4.39 (ddd, *J* 11.4, 10.3, 3.9 Hz, 1H), 4.51 (ddd, *J* 11.4, 4.9, 3.9 Hz, 1H), 7.21–7.31 (m, 3H), 7.34–7.40 (m, 2H); δ_C (75 MHz, $CDCl_3$) 30.2 (CH_2), 37.4 (CH), 37.4 (CH_2), 68.6 (CH_2), 126.4 (2× CH), 127.2 (CH), 128.9 (2× CH), 142.8 (C), 170.6 (C); *m*/*z* (EI) 176 (100, M^+); HRMS (EI): M^+, found 176.0829. $C_{11}H_{12}O_2$ requires 176.0832.

*4.3.13. Tetrahydro-4-[4-(trifluoromethyl)phenyl]-2H-pyran-2-one (**10b**)*[33]. Yellow oil (92 mg, 58%); ν_{max} 2925, 1730 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 2.00–2.13 (m, 1H), 2.17–2.27 (m, 1H), 2.64 (dd, *J* 17.6, 10.6 Hz, 1H), 2.95 (ddd, *J* 17.6, 6.0, 1.6 Hz, 1H), 3.28–3.39 (m, 1H), 4.42 (ddd, *J* 11.5, 10.4, 3.8 Hz, 1H), 4.54 (ddd, *J* 11.5, 5.0, 3.8 Hz, 1H), 7.35 (d, *J* 8.1 Hz, 2H), 7.64 (d, *J* 8.1 Hz, 2H); δ_C (75 MHz, $CDCl_3$) 30.0 (CH_2), 37.1 (CH_2), 37.3 (CH), 68.3 (CH_2), 126.0 (q, $^3J_{CF}$ 3.8 Hz, 2× CH), 126.9 (2× CH), 127.5 (q, $^1J_{CF}$ 271.6 Hz, CF_3), 129.6 (q, $^2J_{CF}$ 32.6 Hz, C), 146.6 (C), 169.9 (C); *m*/*z* (EI) 244 (90, M^+), 172 (100); HRMS (EI): M^+, found 244.0703. $C_{12}H_{11}O_2F_3$ requires 244.0706.

*4.3.14. 4-(4-Fluorophenyl)tetrahydro-2H-pyran-2-one (**10c**)*[34]. Pale yellow oil (48 mg, 47%); ν_{max} 2955, 2919, 1727 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.95–2.08 (m, 1H), 2.13–2.22 (m, 1H), 2.60 (dd, *J* 17.6, 10.6 Hz, 1H), 2.92 (ddd, *J* 17.6, 5.9, 1.7 Hz, 1H), 3.19–3.29 (m, 1H), 4.39 (ddd, *J* 11.5, 10.4, 3.8 Hz, 1H), 4.51 (ddd, *J* 11.5, 5.0, 3.8 Hz, 1H), 7.01–7.09 (m, 2H), 7.15–7.22 (m, 2H); δ_C (75 MHz, $CDCl_3$) 30.4 (CH_2), 36.8 (CH), 37.6 (CH_2), 68.5 (CH_2), 115.8 (d, $^2J_{CF}$ 21.4 Hz, 2× CH), 127.9 (d, $^3J_{CF}$ 8.0 Hz, 2× CH), 138.5 (d, $^4J_{CF}$ 3.3 Hz, C), 161.8 (d, $^1J_{CF}$ 245.8 Hz, CF), 170.3 (C); *m*/*z* (EI) 194 (53, M^+), 135 (100); HRMS (EI): M^+, found 194.0735. $C_{11}H_{11}O_2F$ requires 194.0738.

*4.3.15. 4-(3-Fluorophenyl)tetrahydro-2H-pyran-2-one (**10d**).* Light brown oil (71 mg, 56%); ν_{max} 2923, 2853, 1727 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.97–2.10 (m, 1H), 2.16–2.25 (m, 1H), 2.62 (dd, *J* 17.6, 10.7 Hz, 1H), 2.94 (ddd, *J* 17.6, 5.9, 1.6 Hz, 1H), 3.21–3.31 (m, 1H), 4.40 (ddd, *J* 11.5, 10.4, 3.8 Hz, 1H), 4.52 (ddd, *J* 11.5, 4.9, 3.8 Hz, 1H), 6.90–7.02 (m, 3H), 7.30–7.38 (m, 1H); δ_C (75 MHz, $CDCl_3$) 30.1 (CH_2), 37.2 (d, $^4J_{CF}$ 1.8 Hz, CH), 37.3 (CH_2), 68.4 (CH_2), 113.5 (d, $^2J_{CF}$ 21.7 Hz, CH), 114.2 (d, $^2J_{CF}$ 21.0 Hz, CH), 122.0 (d, $^4J_{CF}$ 2.9 Hz, CH), 130.5 (d, $^3J_{CF}$ 8.4 Hz, CH), 145.2 (d, $^3J_{CF}$ 6.8 Hz, C), 163.1 (d, $^1J_{CF}$ 246.9 Hz, CF), 170.1 (C); *m*/*z* (EI) 194 (100, M^+); HRMS (EI): M^+, found 194.0734. $C_{11}H_{11}O_2F$ requires 194.0738.

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Supplementary data

Experimental procedures for the characterization of organoindium compounds by ^{13}C NMR experiments and copies of NMR spectra for compounds prepared. Supplementary data related to this article can be found online at doi:10.1016/j.tet.2011.11.075.

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