Ketone Synthesis from Acid Chloride by Means of Organometallic Reagent Derived from R_3Al-$Cu(acac)_2$-PPh_3 System

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Synopsis. Reaction of acid chlorides or thiocarboxylic *S*-esters with the title reagent in tetrahydrofuran provides ketones in good to excellent yields. The coupling reactions with allylic halides to form alkene derivatives are also disclosed.

Synthetic reactions with organoaluminium reagent have received considerable attention recently.[1] The transformation[2] of R′COCl into R′COR fails, however, by means of plain R_3Al, as they react easily with the resultant ketones.[3] Now we wish to report that an organometallic reagent generated from trialkylaluminium, copper(II) bis(acetylacetonate), and triphenylphosphine in 2 : 1 : 2 molar ratio reacts cleanly with carboxylic acid derivatives to give the corresponding ketones, although the identity of the reactive species is not known yet.[4]

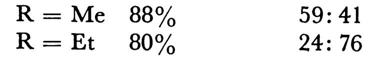
Addition of trialkylaluminium to a mixture of copper(II) bis(acetylacetonate) and triphenylphosphine in tetrahydrofuran produced a homogeneous solution. The absence of triphenylphosphine resulted in a suspension which did not react as expected. Treatment of an acid chloride with the resulting organometallic reagents gave the corresponding ketone in good yield. The results are summarized in Table 1. The reaction proceeded similarly with thiocarboxylic *S*-esters as shown in run 4, 5, 9, and 10. The simplicity and mildness of experimental conditions make the method as useful as other organometallic reagents.[2]

Table 1. Ketone synthesis from carboxylic acid derivatives by means of organometallic reagent derived from R_3Al–$Cu(acac)_2$–PPh_3 system[a]

Run	R′COX		R	Reaction time/h	Yield/%[b] of R′COR
	R′	X			
1	Ph	Cl	Me	0.5	95
2			Et	1	88
3			^{i}Bu	2	55
4	Ph	SPh	Me	1	76
5			Et	1	80
6	$CH_2=CH(CH_2)_8$–	Cl	Me	0.5	90
7			Et	1	91
8			^{i}Bu	1	71
9	$CH_2=CH(CH_2)_8$–	SPh	Me	1	92
10			Et	1	88

a) 2 mol of R_3Al, 1 mol of $Cu(acac)_2$, and 2 mol of PPh_3 were employed per mol of R′COX. b) Isolated yields.

The reagents readily reacted with cinnamyl chloride to provide the cross-coupling products as shown:[5]



R = Me 88% 59:41

R = Et 80% 24:76

Experimental

The IR spectra were determined on a Shimadzu IR-27-G spectrometer; the mass spectra, on a Hitachi RMU-6L machine. The NMR spectra were recorded on a Varian EM-390H spectrometer, using TMS as an internal standard. The analyses were performed at the Elemental Analyses Center of Kyoto University. Tetrahydrofuran (THF) was dried on benzophenone ketyl and distilled. All the experiments were carried out under an argon atmosphere. Purification of the product was performed by preparative thin layer chromatography (TLC) or column chromatography on silica gel (Merck Kiesel gel 60). *S*-Phenyl benzenecarbothioate and *S*-phenyl 10-dodecenethioate were prepared by the reaction of the acid chlorides with an excess of thiophenol in pyridine.

Preparation of Methyl Ketones by Means of Me_3Al–$Cu(acac)_2$–PPh_3 System: A dry flask was charged with copper(II) bis(acetylacetonate) (0.26 g, 1.0 mmol), triphenylphosphine (0.52 g, 2.0 mmol), and THF (10 ml). To the stirred blue suspension at −78 °C was added slowly a hexane solution of trimethylaluminium (1.0 M, 2.0 ml, 2.0 mmol). The mixture was allowed to warm to 0 °C and stirring was continued until the copper(II) salt was completely dissolved and a pale yellow homogeneous solution was obtained (10 min). A solution of acid chloride or thiocarboxylic *S*-ester (1.0 mmol) in THF (2 ml) was added. After stirring at 0 °C for an appropriate time described in Table 1, the resulting mixture was diluted with ether (10 ml) and the ethereal extracts were washed with 1 M hydrochloric acid (20 ml) and brine (2×20 ml), dried over anhydrous sodium sulfate, and concentrated. The crude product was purified by silica gel column chromatography (hexane–ether 20 : 1) and distillation under reduced pressure.

The same procedure was employed for the preparation of organometallic reagents from Et_3Al and $^{i}Bu_3Al$. Dark green and dark brown homogeneous solutions were obtained, respectively.

Isobutyl Phenyl Ketone: Bp 85 °C (bath temp, 2 Torr, 1 Torr =133.322 Pa); IR (neat) 2955, 1690, 1600, 1584, 1450, 1365, 1210, 1005, 750, 688 cm^{-1}; NMR (CCl_4) δ 1.02 (d, 6H, J=7 Hz), 2.29 (qt, 1H, J=7 Hz), 2.76 (d, 2H, J=7 Hz), 7.30—8.05 (m, 5H); MS *m/e* (%) 162 (M^+, 13), 147 (6), 120 (28), 105 (100), 77 (54), 51 (24). The compound was identical with the authentic sample.[6]

11-Dodecen-2-one: Bp 85 °C (bath temp, 2 Torr), IR (neat) 2940, 2860, 1724, 1644, 1358, 1160, 990, 908 cm^{-1}; NMR (CCl_4) δ 1.15—1.70 (m, 12H), 1.85—2.20 (m, 2H), 2.04 (s, 3H), 2.32 (t, 2H, J=6 Hz), 4.88 (d, 1H, J=9 Hz), 4.94 (d, 1H, J=18 Hz), 5.50—6.00 (m, 1H); MS *m/e* (%) 182 (M^+, 1), 124 (6), 82 (13), 71 (27), 58 (63), 55 (35), 43 (100), 41 (44).

Found: C, 79.07; H, 12.29%. Calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.16%.

12-Tridecen-3-one: Bp 87 °C (bath temp. 2 Torr); IR (neat) 2925, 2850, 1715, 1642, 1460, 1108, 990, 904 cm^{-1}; NMR (CCl_4) δ 1.00 (t, 3H, J=7 Hz), 1.15—1.75 (m, 12H), 1.85—2.15 (m, 2H), 2.15—2.50 (m, 4H), 4.90 (d, 1H, J=10 Hz), 4.94 (d, 1H, J=18 Hz), 5.50—6.00 (m, 1H); MS *m/e* (%) 196 (M^+, 1), 167 (6), 149 (11), 139 (8), 85 (26), 83 (26), 72 (76), 57 (100), 55 (73).

Found: C, 79.29; H, 12.58%. Calcd for $C_{13}H_{24}O$: C, 79.53; H, 12.32%.

2-Methyl-13-tetradecen-4-one: Bp 108 °C (bath temp, 2 Torr); IR (neat) 2940, 2860, 1712, 1642, 1468, 1365, 988, 905 cm^{-1}; NMR (CCl_4) δ 0.89 (d, 6H, $J=7$ Hz), 1.10—1.80 (m, 12H), 1.80—2.36 (m, 7H), 5.88 (d, 1H, $J=10$ Hz), 5.94 (d, 1H, $J=18$ Hz), 5.50—6.00 (m, 1H); MS *m/e* (%) 224 (M^+, 2), 209 (3), 167 (10), 149 (11), 113 (13), 100 (19), 85 (86), 69 (25), 67 (22), 58 (80), 57 (100).

Found: C, 80.11; H, 12.72%. Calcd for $C_{15}H_{28}O$: C, 80.29; H, 12.58%.

Methylation of Cinnamyl Chloride by Means of Me_3Al–Cu(acac)$_2$–PPh_3 System: A pale yellow organometallic reagent derived from trimethylaluminium (2.0 mmol), copper(II) bis(acetylacetonate) (0.26 g, 1.0 mmol), and triphenylphosphine (0.52 g, 2.0 mmol) in THF (10 ml) was prepared as described above. A solution of cinnamyl chloride (0.15 g, 1.0 mmol) in THF (2 ml) was added slowly to the solution at 0 °C, and the resulting mixture was stirred at the same temperature for an additional 15 min. The mixture was diluted with ether (10 ml) and the ethereal extracts were washed with 1 M hydrochloric acid (20 ml) and brine (2×20 ml), dried over anhydrous sodium sulfate, and concentrated. The crude product was purified by preparative TLC with hexane as an eluent to give two isomeric methylated products (0.12 g, 88%) whose ratio was determined by GLPC (20% PEG 6000, 2 m, 100 °C). 1-Phenyl-1-butene ($T_r=16.1$ min, 59%) and 3-phenyl-1-butene ($T_r=6.3$ min, 41%) were identical with the authentic samples.(7)

The same procedure was employed for the coupling reaction of cinnamyl chloride and the organometallic reagent derived from triethylaluminium. GLPC (20% PEG 6000, 2 m, 100 °C) indicated two peaks, $T_r=9.3$ min (3-phenyl-1-pentene, 76%) and $T_r=25.7$ min (1-phenyl-1-pentene, 24%).

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