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Palladium-catalyzed Ketone Synthesis from Acyl Chloride and Organoaluminum Reagents

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Synopsis. The reaction of organoaluminum reagents with acyl chloride catalyzed by $Pd(PPh_3)_4$ in tetrahydrofuran provides ketones in fair yields.

During the past decade, a wide variety of organometallics are examined to react with acyl halides to give ketones. Among them, those containing Mg,[1] Mn,[2] Zn,[3] and Cu[4] have been widely used. The transformation of R^1COCl into R^1COR fails, however, by means of plain R_3Al, because they react easily with the resulting ketones. Several attempts have been made to overcome this difficulty. A ketone synthesis reported previously[5] is based on the organometallic reagent generated from trialkylaluminum, bis(acetylacetonato)copper(II), and triphenylphosphine in 2:1:2 molar ratio. Here we wish to report another effective method for the preparation of ketones from acyl chlorides with organoaluminum reagents in the presence of Pd(0) catalyst.[6]

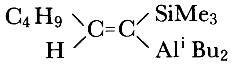
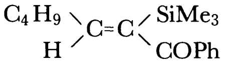
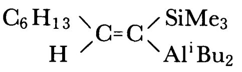
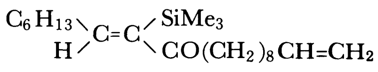
$$R^1COCl + R_3Al \xrightarrow[THF]{Pd(PPh_3)_4} R^1COR$$

Treatment of benzoyl chloride with triethylaluminum in tetrahydrofuran in the presence of a catalytic amount of $Pd(PPh_3)_4$ gave propiophenone in 70% yield. The uncatalyzed reaction gave <5% yield of propiophenone under the same reaction conditions. Palladium catalyst generated *in situ* from $Pd(OAc)_2$ and triphenylphosphine (1:2) was also efficient for the transformation.[7] Other catalysts such as $RuCl_2(PPh_3)_3$, $NiCl_2(PPh_3)_2$, and $RhCl(PPh_3)_3$ were not effective for this ketone synthesis. The use of tetrahydrofuran as a solvent is critical. In benzen or dichloromethane, the complex mixture was obtained since the resulting ketones were attacked by organoaluminum reagents. The results are summarized in Table 1. Alkynyl and alkenyl groups were introduced selectively in preference to the ubiquitous alkyl substituents on aluminum to give ynones and enones, respectively.

Experimental

The IR spectra were determined on a Shimadzu IR-27-G spectrometer; the mass spectra, on a Hitachi X-80 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 was dried in 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

TABLE 1. PALLADIUM-CATALYZED ACYLATION OF ORGANOALUMINUM REAGENTS[a]

Entry	RCOCl	Reagent	Product	Yield[b] %
1	PhCOCl	Et_3Al	PhCOEt	70
2	PhCOCl	Me_3Al	PhCOMe	(74)[c]
3	PhCH=CHCOCl	Et_3Al	PhCH=CHCOEt	68
4	$CH_2=CH(CH_2)_8COCl$	Et_3Al	$CH_2=CH(CH_2)_8COEt$	71
5	$CH_2=CH(CH_2)_8COCl$	Me_3Al	$CH_2=CH(CH_2)_8COMe$	59
6	PhCOCl	$C_4H_9C\equiv CAlEt_2$	$C_4H_9C\equiv CCOPh$	67
7	$C_7H_{15}COCl$	$C_4H_9C\equiv CAlEt_2$	$C_4H_9C\equiv CCOC_7H_{15}$	65
8	PhCH=CHCOCl	$C_4H_9C\equiv CAlEt_2$	$C_4H_9C\equiv CCOCH=CHPh$	74
9	$C_7H_{15}COCl$	$PhC\equiv CAlEt_2$	$PhC\equiv CCOC_7H_{15}$	61
10	$CH_2=CH(CH_2)_8COCl$	$C_6H_{13}C\equiv CAlEt_2$	$C_6H_{13}C\equiv CCO(CH_2)_8CH=CH_2$	55
11	$CH_2=CH(CH_2)_8COCl$	$Me_3SiC\equiv CAlEt_2$	$Me_3SiC\equiv CCO(CH_2)_8CH=CH_2$	51
12	PhCOCl	 $(C_4H_9)(H)C=C(SiMe_3)(Al^iBu_2)$	 $(C_4H_9)(H)C=C(SiMe_3)(COPh)$	51
13	$CH_2=CH(CH_2)_8COCl$	 $(C_6H_{13})(H)C=C(SiMe_3)(Al^iBu_2)$	 $(C_6H_{13})(H)C=C(SiMe_3)(CO(CH_2)_8CH=CH_2)$	53

a) The reactions were performed in THF at 0—25 °C. Organoaluminum reagent (1.0—2.0 mmol), acid chloride (1.0 mmol), and $Pd(PPh_3)_4$ (0.05 mmol) were employed. b) Isolated yields unless otherwise stated. c) GLPC yield.

(Merck Kiesel gel 60).

General Procedure for the Preparation of Ketones with Trialkylaluminum: The reaction of benzoyl chloride with triethylaluminum is representative. Triethylaluminum (1.0 M[†] hexane solution, 2.0 ml, 2.0 mmol) was added to a tetrahydrofuran solution of benzoyl chloride (0.14 g, 1.0 mmol) and $Pd(PPh_3)_4$ (58 mg, 0.05 mmol) at 0 °C under an argon atomosphere. The whole was stirred at 25 °C for 4 h. The resulting mixture was poured into 1 M HCl and extracted with ethyl acetate. The combined organic layer was dried (Na_2SO_4) and concentrated *in vacuo*. Purification by preparative TLC on silica gel (hexane:ethyl acetate=10:1) gave propiophenone (90 mg, 70% yield) as an oil which was identical with the authentic sample.

1-Trimethylsilyl-12-tridecen-1-yn-3-one: Butyllithium (1.6 M hexane solution, 1.3 ml, 2.0 mmol) was added to a solution of trimethylsilylacetylene (0.25 g, 2.5 mmol) in hexane (2.0 ml) at 0 °C. After stirring for 15 min at 0 °C, diethylaluminum chloride (1.0 M hexane solution, 2.0 ml, 2.0 mmol) was added and the resulting mixture was stirred for 15 min at 0 °C. Tetrahydrofuran (3.0 ml), $Pd(PPh_3)_4$ (46 mg, 0.04 mmol), and 10-undecenoyl chloride (0.14 g, 0.7 mmol) were added successively and the whole was stirred for additional 60 min at 25 °C. Workup and purification by silica gel column chromatography gave the desired ketone in 51% yield: Bp 100 °C (bath temp, 2 Torr[††]); IR (neat) 3080, 2930, 2860, 2150, 2100, 1680, 1640, 1460, 1250, 850, 760 cm^{-1}; NMR (CCl_4) δ=0.25 (s, 9H), 1.08—1.77 (m, 12H), 1.77—2.13 (m, 2H), 2.27—2.57 (m, 2H), 4.83 (d, J=11 Hz, 1H), 4.87 (d, J=18 Hz, 1H), 5.67 (ddt, J=18, 11, 7.5 Hz, 1H). Found: m/z 249.1699. Calcd for $C_{15}H_{25}OSi$: M−CH_3, 249.1678.

18-Nonadecen-7-yn-9-one: Bp 115—120 °C (bath temp, 2 Torr); IR (neat) 3080, 2930, 2850, 2210, 1740, 1680, 1640, 1460, 1160, 1000, 910 cm^{-1}; NMR (CCl_4) δ=0.88 (m, 3H), 1.17—1.80 (m, 23H), 1.80—2.17 (m, 2H), 2.17—2.53 (m, 4H), 4.88 (d, J=12 Hz, 1H), 4.93 (d, J=18 Hz, 1H), 5.73 (ddt, J=18, 12, 7 Hz, 1H). Found: m/z 276.2444. Calcd for $C_{19}H_{32}O$: M, 276.2451.

(Z)-12-Trimethylsilyl-1,12-nonadecadien-11-one: Diisobutylaluminum hydride (1.5 M hexane solution, 1.3 ml, 2.0 mmol) was added to a solution of 1-trimethylsilyl-1-octyne (0.37 g, 2.0 mmol) in hexane (3.0 ml) and ether (1.5 ml) at 25 °C under an argon atmosphere.[8] After stirring for 40 min, tetrahydrofuran (4.0 ml) was added, then $Pd(PPh_3)_4$ (0.04 g, 0.05 mmol) and a solution of 10-undecenoyl chloride (0.14 g, 0.7 mmol) in tetrahydrofuran (3.0 ml) was added. The resulting mixture was stirred for 1.5 h. Workup (1 M HCl, ethyl acetate) and purification by preparative TLC on silica gel (hexane:ethyl acetate=10:1) provided the title compound (0.13 g, 53% yield) as an oil: Bp 115—120 °C (bath temp, 2 Torr); IR (neat) 3080, 2940, 2860, 1675, 1600, 1465, 1250, 850, 760 cm^{-1}; NMR (CCl_4) δ=0.01 (s, 9H), 0.68—0.93 (m, 3H), 0.97—1.67 (m, 20H), 1.70—2.43 (m, 6H), 4.70 (d, J=11 Hz, 1H), 4.75 (d, J=18 Hz, 1H), 5.55 (ddt, J=18, 11, 7 Hz, 1H), 6.5 (t, J=7.5 Hz, 1H). Found: C,75.28; H, 12.09%. Calcd for $C_{22}H_{42}OSi$: C, 75.36; H, 12.07%.

(Z)-1-Trimethylsilyl-1-hexenyl Phenyl Ketone: Bp 110 °C (bath temp, 2 Torr); IR (neat) 2960, 2860, 1655, 1600, 1450, 1250, 840, 710 cm^{-1}; NMR (CCl_4) δ=0.20 (s, 9H), 0.83—1.05 (m, 3H), 1.17—1.55 (m, 4H), 2.17—2.45 (m, 2H), 6.28 (t, J=7.5 Hz, 1H), 7.30—7.93 (m, 5H). Found: m/z 260.1602. Calcd for $C_{16}H_{24}OSi$: M, 260.1595.

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6) Negishi has reported about palladium-catalyzed acylation of organoaluminum reagents briefly in the literature 3a. We wish to report here our independent work.

7) Palladium(II) acetate (23 mg, 0.1 mmol) and triphenylphosphine (50 mg, 0.2 mmol) were added to a solution of $^{n}C_4H_9C{\equiv}CAlEt_2$ (2.0 mmol) in tetrahydrofuran (5.0 ml). Then a solution of benzoyl chloride (0.14 g, 1.0 mmol) in tetrahydrofuran (2.0 ml) was added and the whole was stirred at 25 °C for 3 h. Purification of the product gave the corresponding ketone (0.1 g) in 52% yield. $PdCl_2(PPh_3)_2$ was catalytically as effective as $Pd(PPh_3)_4$.

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[†] 1 M=1 mol dm^{-3}.

[††] 1 Torr=133.322 Pa.