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14. Since β_{lg} for the MNPA system is not reported, we choose the known value for *p*-cyanophenyl acetate (PCPA) system ($\beta_{lg} = -0.51$). It is because *p*-cyanophenol and *m*-nitrophenol have similar p*Ka* values and therefore β_{lg} of MNPA would be close to that of PCPA.
15. A similar argument could be obtained from an analysis of the effective charges on the oxygen atoms of the attacking and leaving aryloxides at the TS. The effective charges on the oxygen atoms of both attacking and leaving aryloxides are suggested to be −0.25 for PNPA system by Williams *et al.*[3c] However our present data give the effective charges of −0.1 and +0.2 for the oxygens of attacking and leaving aryloxides, respectively, indicating a stepwise mechanism. We are grateful to one of the referees for the kind suggestion concerning the effective charge.

One-Pot Synthesis of Ketones Using *N*-Methyl-*N*-(2-Pyridinyl)-*N'*-Propylene Urea

Jae In Lee

Department of Chemistry, College of Natural Science, Duksung Women's University, Seoul 132-714

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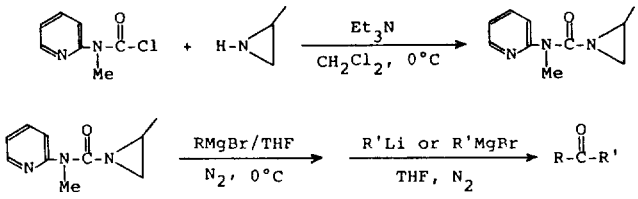
Reaction of carboxylic acid derivatives with organometallics is well-known and widely used for the synthesis of ketones. However, its synthetic application is limited due to the formation of undesired tertiary alcohols, produced by the further addition of the organometallics to the product.[1] Several types of active esters[2] having pyridinyl ligand have been developed to circumvent this limitation. For instance, the reaction of *S*-(2-pyridinyl) thioates,[2c] 2-pyridinyl esters,[2d] and *N*-methyl-*N*-(2-pyridinyl) carboxamides[2f] with Grignard reagents is especially useful for the successful synthesis of ketones. Active amides[3] have also been proposed as acylating reagents to prevent such a side reaction by generating tetrahedral intermediates with Grignard or organolithium reagents. However, there are few reports on the ketone synthesis by sequential additions of two organometallic reagents to the substrate such as *S*-phenyl carbonochloridothioate.[4]

We now wish to report a one-pot synthesis of ketones from Grignard and organolithium reagents using *N*-methyl-*N*-(2-pyridinyl)-*N'*-propylene urea.[5] The reagent was conveniently prepared by the reaction of *N*-methyl-2-pyridinecarbamoyl chloride,[6] generated from 2-(methylamino)pyridine and phosgene, with 2-methylaziridine in the presence of triethylamine in methylene chloride at 0 °C. The reagent was



easily separated by aqueous work-up and obtained in 92% yield after a short pathway silica gel column chromatography.

The success of ketone synthesis using *N*-methyl-*N*-(2-pyridinyl)-*N'*-propylene urea depends largely on, in the first step, selective substitution of 2-(methylamino)pyridinyl group without concomitant displacement of the 2-methylaziridyl group. We have achieved this goal by dropwise addition of Grignard reagents to *N*-methyl-*N*-(2-pyridinyl)-*N'*-propylene urea at 0 °C. Thus, when *N*-methyl-*N*-(2-pyridinyl)-*N'*-propylene urea was treated with 1 equiv of phenylmagnesium bromide at 0 °C over a period of 15-20 min, 1-benzoyl-2-methylaziridine was obtained in 93% yield and there were no observable side products such as benzophenone. However, the reaction was carried out in a one-pot way; After completion of the first step, the second organolithium or Grignard reagent was added to the mixture without the isolation of *N*-acylaziridine intermediates.

The result of the synthesis of various ketones was summarized in the Table 1 and the present method appeared especially effective for the synthesis of aromatic ketones. The reaction of the first step works well for aliphatic and aromatic magnesium bromide and was not influenced by the kind of electron withdrawing or donating group in 4-substituted phenylmagnesium bromide under the present reaction conditions. In the second step, reaction of Grignard reagents with the *N*-acylaziridine intermediates required a little longer time than organolithium reagents in most cases. Sig-

Table 1. Preparation of Ketones from *N*-Methyl-*N*-(2-Pyridinyl)-*N'*-Propylene Urea and Grignard/Organolithium Reagents

Step 1[a] RMgBr, R	Step 2 R'Li or R'MgBr	Reaction conditions[b] temp. °C	time, h	Isolated yield, %[c]
CH_3	$CH_3(CH_2)_4C{=}CLi$	0→r.t.	1	50
$C_6H_5(CH_2)_3$	EtMgBr	r.t.	1	63
	n-BuLi	0	0.3	86
$CH_3(CH_2)_4C{=}C$	*t*-BuLi	0	1	48
c-C_6H_{11}	*n*-BuLi	0	0.3	77
	sec-BuLi	r.t.	0.5	43
C_6H_5	$CH_2{=}CHCH_2MgBr$	r.t.	0.5	71
	C_6H_5MgBr	0→r.t.	2	93
	n-BuLi	0	0.2	93
	n-BuLi (2 eq)	0	0.2	78
4-Cl-C_6H_4	CH_3Li	0→r.t.	0.5	76
	C_6H_5MgBr	0→r.t.	2	80
	C_6H_5Li	0→r.t.	0.5	74
4-Me-C_6H_4	CH_3Li	0→r.t.	0.5	78
	sec-BuLi	0	0.5	79
	t-BuLi	0	1	71
4-MeO-C_6H_4	$CH_3(CH_2)_4MgBr$	r.t	2	77
	n-BuLi	0	0.2	90
	t-BuLi	0	1	74

[a]The Grignard reagent was added over a period of 15–20 min at 0 °C. [b]Reaction conditions indicate step 2. [c]The numbers indicate overall yield of two steps and all the products, purified by Kugelrohr distillation, were identified by comparison of their physical and spectral properties with reported data.

nificantly, the reaction was not limited to primary organolithium reagents and the *N*-acylaziridine intermediates react effectively with secondary and tertiary organolithiums. However, the steric hindrance of aliphatic Grignard reagents in the first step has fairly influenced the yield, and thus sequential reaction of cyclohexyl-magnesium bromide and *sec*-butyl lithium gave the corresponding ketone in 43% yield.

A representative experimental procedure is as follows. To the solution of *N*-methyl-*N*-(2-pyridinyl)-*N'*-propylene urea (306 mg, 1.6 mmol) in dry THF (3 m*l*) was added 6.4 m*l* of phenylmagnesium bromide (0.25 *M* in THF, 1.6 mmol) dropwise over a period of 15–20 min at 0 °C. After completion of the addition, stirring was continued for an additional 5–10 min at the same temperature, and then 1 m*l* of *n*-butyl lithium (1.6 *M* in hexane, 1.6 mmol) was added to the reaction mixture at 0 °C. After being stirred for 0.3 h, reaction mixture was quenched with 3% aqueous HCl and extracted with methylene chloride (30 m*l*) three times. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and concentrated under vacuum. The crude product was purified by Kugelrohr distillation (95–100 °C/5 mm, lit.[3c] 90–91 °C/2.8 mm) to give 259.3 mg (93%) of valerophenone: ^{1}H NMR ($CDCl_3$) 1.01 (t, 3H, J = 7 Hz), 1.15–2.08 (m, 4H), 2.98 (t, 2H, J = 7 Hz), 7.35–7.67 (m, 3H), 7.85–8.15 (m, 2H); IR (neat) 1680 cm^{-1} (C = O).

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5. ^{1}H NMR ($CDCl_3$) 1.12 (d, J = 6 Hz, 3H), 1.86–2.00 (m, 1H), 2.35–2.55 (m, 2H), 3.54 (s, 3H), 6.94–7.20 (m, 1H), 7.54–7.83 (m, 2H), 8.35–8.55 (m, 1H); IR (neat) 1665 (C = O), 3060 cm^{-1} (aromatic CH); MS (70 eV), *m/z* 191 (M^+, 15.0), 135 ($CO{-}N(CH_3){-}2{-}Py^+$, 76.3), 107 ($N(CH_3){-}2{-}Py^+$, 65.0), 78 ($2{-}Py^+$, 100). Anal. Calcd. for $C_{10}H_{13}N_3O$: C, 62.81; H, 6.85; N, 21.97. Found: C, 61.45; H, 6.75; N, 21.79.
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Convenient Synthesis of Carboxylic Anhydrides Using *N*-Methyl-2-Pyridinecarbamoyl Chloride

Jin Hee Kim and Jae In Lee*

Department of Chemistry, Duksung Women's University, Seoul 132-714

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One-step synthesis of carboxylic anhydrides from the corresponding acids is usually accomplished by dehydration. This can be generally carried out with various dehydrating agents. They include *N,N'*-carbonyldiimidazole,[1] *N,N'*-dicyclohexylcarbodiimide,[2] tetracyanoethylene,[3] or thionyl chloride.[4] It has also been reported that triethylamine salts of carboxylic acids can be converted to anhydrides by reaction with phosgene,[5] *N,N*-diphenylcarbamoyl chloride,[6] organophosphorus reagents,[7] chlorosulfonyl isocyanate,[8] *N,N,N',N'*-tetramethylchloroformamidinium chloride,[9] mesyl chloride,[10] or phosphonium anhydride.[11] The advantage of these