Pergamon

Tetrahedron 54 (1998) 8771–8782

TETRAHEDRON

On the Metallation of 2-Isopropylpyridine.

Eric Pasquinet, Patrick Rocca*, Francis Marsais, Alain Godard and Guy Quéguiner.

UPRESA 6014 CNRS - IRCOF/INSA de Rouen BP 08 76131 Mont Saint Aignan cedex - France

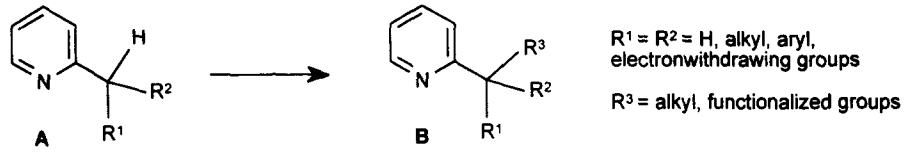
Received 23 February 1998; accepted 28 May 1998

Abstract: 2-Isopropylpyridine has been successfully metallated and functionalized by using potassium diisopropylamide (KDA). Subsequent functionalization has been achieved with a wide range of electrophiles and good to excellent yields have been obtained. The action of other potassium or sodium bases has also been investigated.

Keywords: deprotonation, metallation, potassium compounds, pyridine.

INTRODUCTION

Quaternization of the 2-picolinic carbon of a pyridinic structure, i.e. synthesis of compounds B (R^1, $R^2 \neq$ H) from compounds A (scheme 1), is not a common reaction and has become a challenge since natural or biologically active compounds often bear a quaternary picolinic carbon.[1-5, 13]

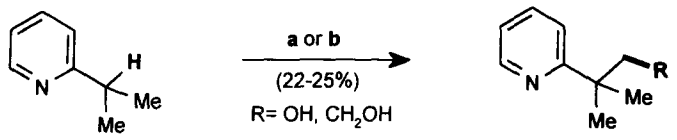


Scheme 1

Obviously, the most straightforward way to make compounds B is hydrogen abstraction on the picolinic carbon of compounds A followed by a functionalization step. Although such a procedure is relatively easy when R^1 (or R^2) is an electron withdrawing group (CN, COOR),[6-10] it is not the case when both R^1 and R^2 are alkyl groups.[11-12, 19] As a matter of fact, there are few reported examples of such direct α-quaternization, the azomethine group (of the pyridine ring) being the only activating group.[13] In a similar way, various pyridylalcohols were synthesized, with poor yields, starting from 2-isopropylpyridine by using alkyl and aryl lithium bases[14-15] (scheme 2).

* Phone : (33) 02 35 52 24 84 E-mail : Patrick.Rocca@insa-rouen.fr

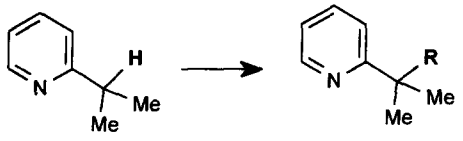
0040-4020/98/$19.00
PII: S0040-4020(98)00507-9



a: PhLi, oxirane (25%, R = CH_2OH) (ref. 14)
b: 1. *n*BuLi/ether/r.t., 2. HCHO gas (22%, R= OH) (ref. 15)

Scheme 2

Other authors have used metallic sodium with anthracene,[16] potassium amide[16] or sodium amide[17-18] as deprotonating agent (scheme 3, a-d). Dialkylamides as base for abstraction of highly hindered picolinic hydrogens have also been reported by Akiba *et al.*[19] who described the preparation of the thio compound (R = CH_2SMe) by using LDA (HMPA was needed as co-solvent and the yield was only moderate: 46%) (scheme 4, e).



R= Et (conditions a-b, ref. 16)
Me (conditions c, ref. 17)
CH_2CH_2OH (conditions d, ref. 18)
CH_2SMe (conditions e, ref. 19)

a: 1. Na/anthracene, 2. ethylene (88%); **b**: 1. KNH_2, 2. EtBr (69%);
c: 1.$NaNH_2$, 2. MeCl (60%); **d**: 1. $NaNH_2$, 2. oxirane (20%);
e: 1.LDA/HMPA, 2. $ClCH_2SMe$ (46%).

Scheme 3

Among the other methods, a mixture of sodium hydride and methyl iodide has also been used on 2,6-dialkyl-*N*-methylpyridinium structures to synthesize highly hindered pyridinium salts but without selectivity.[20]

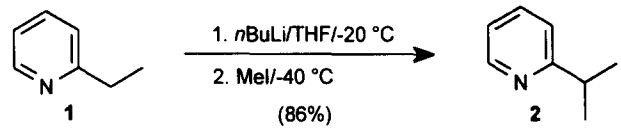
In summary, despite the use of a large number of bases as deprotonating agent of picolin-like compounds, there is no general route to prepare compounds B from compound A and moderate yields have often been observed (scheme 1, $R^1 = R^2$ = alkyls). Consequently, we sought an effective, general synthesis of compounds B with $R^1 = R^2$ = alkyls (scheme 1) with introduction of a wide range of functionalized groups. Although lithiated bases[21] such as alkyllithium or lithium amides are able to achieve the first two hydrogen abstractions[22-25] of the 2-picoline itself, the reported results[26-27] and our own observations in pyridine series suggest that metallation of compounds A (scheme 1, $R^1 = R^2$ = alkyls) by these common bases would be a non effective reaction.

Over the last 15 years, the development of superbases[28-35] as deprotonating agents was quite considerable. So, in this paper, we would like to describe a general route to functionalize 2-isopropylpyridine by using such bases. We essentially used four superbasic mixtures: diisopropylamine(HDA)/*t*BuOK/*n*BuLi; 2,2',6,6'-tetramethylpiperidine(HTMP)/*t*BuOK/*n*BuLi; diisopropylamine/*t*BuONa/*n*BuLi and 2,2',6,6'-tetramethylpiperidine/*t*BuONa/*n*BuLi. Although the actual metallating species is not yet known,[28] and for simplification reasons, these mixtures will be abbreviated as KDA (also called LIDAKOR),[36] KTMP,[35] NDA[37-38] and NaTMP respectively.

RESULTS AND DISCUSSION

Preparation of 2-isopropylpyridine (2)

2-Isopropylpyridine[39-40] **2** was prepared in good yield from commercial 2-ethylpyridine **1** by alkylation with methyl iodide after deprotonation by *n*BuLi (scheme 4).

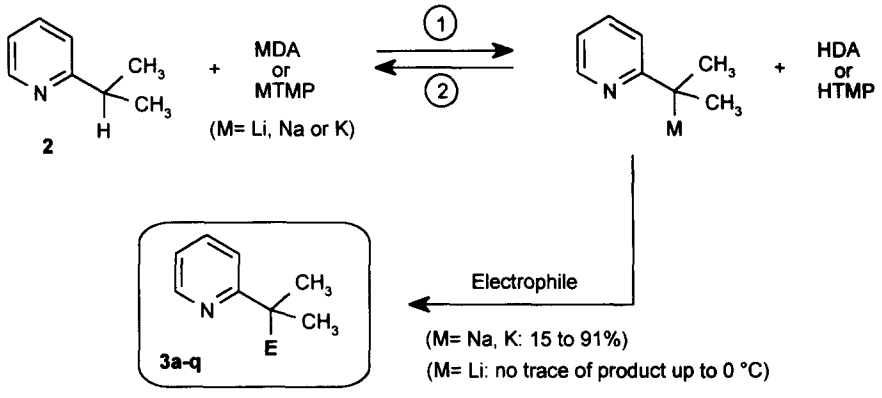


Scheme 4

Metallation of 2-isopropylpyridine (2)

Optimization of metallation conditions. When *n*butyllithium (*n*BuLi) or lithium diisopropylamide (LDA) was used, no metallated 2-isopropylpyridine **2** had been observed even at 0 °C (no deuterium incorporation and the typical picolinic red colored anion did not appear). This lack of reactivity may largely be ascribed to an unfavorable deprotonation equilibrium (scheme 5). Similarly, with LiTMP,[41] no hydrogen abstraction had been observed though LiTMP is a stronger base than LDA.[41-44, 49]

At this stage, we decided to carry out our experiments with potassium amides[45-46] which have higher reactivity and basicity than the corresponding lithium amides.[28, 42-44, 47-48] Thus, by carrying out the metallation of **2** with a 10% excess of KDA (prepared *in situ* by adding *n*BuLi to a diisopropylamine (HDA)-*t*BuOK mixture in THF) during 30 minutes at –75°C followed by action of benzaldehyde, benzylic alcohol **3f** was obtained in a 63% isolated yield. Significantly better results were obtained by increasing the amount of base and temperature (Scheme 5, Table 1).



Scheme 5

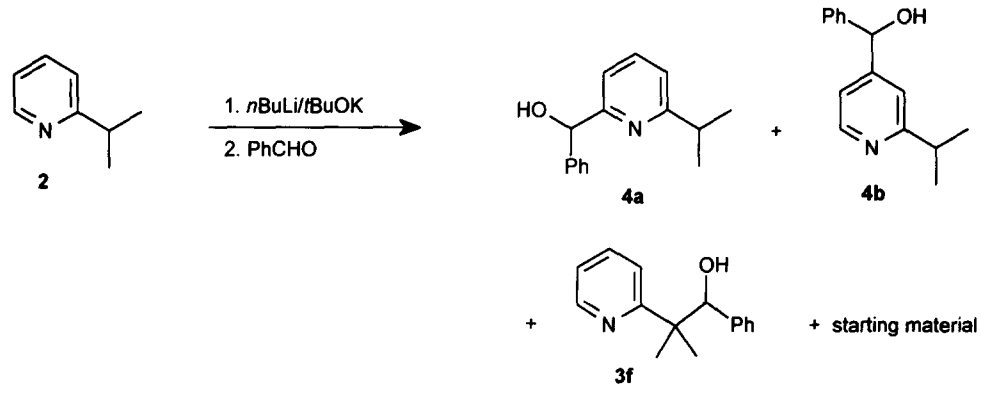
Table 1. Metallation of 2-Isopropylpyridine with KDA and Subsequent Functionalization with Benzaldehyde. Optimization of the Reaction Conditions.

Entry	Solvent	HDA-*t*BuOK : *n*BuLi (KDA)	Temperature (T °C)	Time (t min)	% Yield[a] (isolated)
1	THF	1.1 : 1.1	−75	30	75 (63)
2	"	"	−50	"	82 (71)
3	"	"	"	60	90
4	"	"	−30	"	84
5	Diethylether	"	"	"	80
6	THF	1.5 : 1.2	−50	30	83
7	**THF**	**1.5 : 1.5**	**−50**	**30**	**100 (90)**
8	"	"	−30	60	100

[a] ^{1}H NMR integration.

Variation of the base. Other strong bases such as NDA, NaTMP and KTMP were also used in various conditions (Table 2). Although KTMP is a stronger base than KDA in a thermodynamic sense,[49] no difference could be made between these two deprotonating agents (steric hindrance seems to lower the kinetic basicity of KTMP). When comparing sodium and potassium dialkylamides, we found a similar reactivity between NaTMP and KTMP towards **2** (Table 2, entry 2 *versus* entry 7). However, NDA required slightly longer reaction times for complete deprotonation than its potassium analogue (Table 2, entries 1, 4 and 5) but remained much more reactive than the corresponding lithium analogue (no deprotonation for the latter).

Interestingly, the superbasic mixture *n*BuLi/*t*BuOK[28-32] proved to be less effective and selective than the previous bases in the metallation of **2**. Indeed, in that case (scheme 6), the crude product was a mixture of four compounds : **2/3f/4a/4b** in the following ratio: 1/1.4/0.5/0.4 (**4a** and **4b** were identified by their ^{1}H and ^{13}C NMR spectra: see experimental). It should be noted that neither **4a** nor **4b** have been observed after metallation with MDA or MTMP (M= Na and K).



Scheme 6

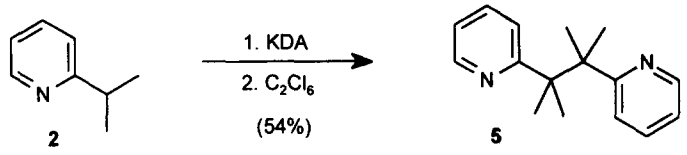
Table 2. Metallation of 2-Isopropylpyridine and Subsequent Functionalization with Benzaldehyde. Variation of the Base.

Entry	Base[a] (1.5 eq in THF)	Temperature (°C)	Time (min)	Yield (%)[b]
1[c]	HDA/*n*BuLi/*t*BuOK	-50	30	100
2	HTMP/*n*BuLi/*t*BuOK	-50	30	100
3	"	-30	60	69[d]
4	HDA/*n*BuLi/*t*BuONa	-50	30	83
5	"	"	60	100
6	"	-30	30	100
7	HTMP/*n*BuLi/*t*BuONa	-50	"	100

[a] amine/*n*BuLi/*t*BuOM: 1.5/1.5/1.5 for 1 equivalent of **2**
[b] ^{1}H NMR integration
[c] optimum conditions (identical to entry 7 of Table 1)
[d] presumed instability of KTMP at this temperature[49]

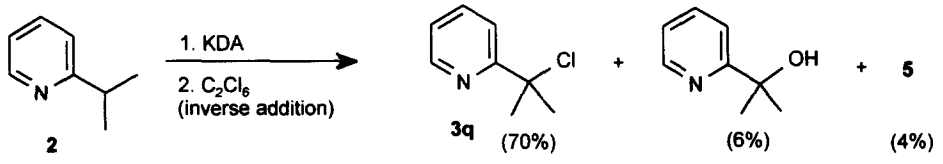
Functionalization of metallated picoline. Functionalization experiments with 2-isopropylpyridine **2** (metallated under optimized conditions with KDA (Table 2, entry 1)) were carried out with various electrophiles (Table 3). Good to excellent results were obtained with alkyl halides, non-enolisable carbonyl compounds and thio electrophiles. Low yields (21 to 34%) were obtained with other electrophiles mainly due to elimination processes (Table 3, entries 14 and 15) or formation of enolates of the carbonyl compounds (Table 3, entries 8 and 9). Generally, lower yields have been observed when NDA was used with subsequent reaction with non-enolisable electrophiles (except for diethylcarbonate). In contrast, the use of NDA instead of KDA, proved to be fruitful with enolisable electrophiles such as acetaldehyde or cyclopentanone (Table 3, entries 7 and 9).

It should also be noted the impossibility to obtain the chloroderivative **3q** [50] in the same conditions (by using hexachloroethane (C_2Cl_6) as electrophile). In that case, the dimer **5** [18, 51-52] had been obtained (Scheme 7).



Scheme 7

However, chloroderivative **3q** has been prepared, in good yield, by pouring the potassium derivative of **2** onto an excess of hexachloroethane (Table 3, entry 18). In that case, small amounts of the dimer **5** and of an alcohol have been observed (scheme 8).



Scheme 8

By carrying out an experiment with **3q** as electrophile in regular conditions, dimer **5** was obtained in 51% isolated yield, thus suggesting that **3q** was an intermediate in the formation of **5**.

Table 3. Functionalization of Metallated 2-Isopropylpyridine.

Entry	Electrophile	E	Product	% Yield[a] (KDA)	% Yield[a] (NDA)
1	MeI	Me	**3a**	86	-
2	EtI	Et	**3b**	85	-
3	*n*BuI	*n*Bu	**3c**	88	-
4	allyl bromide	allyl	**3d**	91	83
5	$ClCH_2SMe$	CH_2SMe	**3e**	72[b]	54
6	PhCHO	PhCH(OH)	**3f**	90	-
7	MeCHO	MeCH(OH)	**3g**	58	73
8	Butanone (MEK)	EtC(Me)(OH)	**3h**	34	-
9	cyclopentanone	Cyclopentyl(OH)	**3i**[e]	29	53
10	Ph_2CO	$Ph_2C(OH)$	**3j**[f]	62	-
11	HCO_2Et	CHO	**3k**	63	-
12	N-formylpiperidine	"	"	63	-
13	diethylcarbonate	CO_2Et	**3l**	78	86
14	$Cl(CH_2)_2CN$	$(CH_2)_2CN$	**3m**	31	15
15	$Br(CH_2)_2CO_2Me$	$(CH_2)_2CO_2Me$	**3n**	21	17
16	Me_2S_2	SMe	**3o**	86	77
17	oxirane	$(CH_2)_2OH$	**3p**	78[c]	77
18	C_2Cl_6[d]	Cl	**3q**	70	-

[a] All yields are for isolated products by column chromatography on silica gel otherwise stated. For low yields, starting material is recovered but not completely because of strong volatility. With NDA as base, a "-" symbol means that the experiment has not been carried out.

[b] Reported yield for this product: 46%[19]

[c] Reported yields for this product: 20%[18] and 25%[14]

[d] 10 equivalents and inverse addition. Reported yield for this product: 59%[50]

[e] purified by Kugelrohr distillation.

[f] purified by recristallization in ethanol.

CONCLUSION

2-Isopropylpyridine **2** has been successfully metallated and functionalized by using potassium diisopropylamide (KDA) followed by action of various electrophiles. The method is quite general and good yields have been obtained. This study is currently being extended to the total synthesis of pyridinic analogues of natural products bearing a highly hindered picolinic carbon.

ACKNOWLEDGEMENTS

We thank the *Centre National de la Recherche Scientifique* and the *Ministère de l'Education Nationale, de la Recherche et de la Technologie* (Aide MRT n° 9625) for financial support.

EXPERIMENTAL

General

IR: Perkin-Elmer FTIR 1600. NMR: Bruker AM 200 (for ^1H and ^{13}C). For ^1H NMR, $CDCl_3$ as solvent δ_H = 7.27, TMS as internal standard, [d_6]DMSO as solvent δ_H = 2.50, HMDS as internal standard; for ^{13}C NMR $CDCl_3$ δ_H = 77.0, [d_6]DMSO δ_C = 39.7. ^1H-^1H coupling constants are in good agreement with the common values for 2-alkyl substituted pyridines and are not given ($J_{3-4} = J_{4-5} \sim 8$ Hz, $J_{5-6} \sim 5$ Hz, $J_{4-6} \sim 2$ Hz). MS: JEOL AX500 (CI positive, 200eV). Melting points were measured on a Kofler apparatus. Elemental analyses were performed on a Carlo Erba 1160 CHN apparatus. Refractive index were recorded on an Abbe Refractometer at 20 °C. Diethyl ether (Et_2O) and tetrahydrofuran (THF) were distilled from benzophenone / sodium and their water content was estimated by the modified Karl-Fischer method[53]: Et_2O < 10 ppm, THF < 45 ppm. Sodium and potassium tertbutoxide were commercial and used as received. Diisopropylamine (HDA) was distilled over CaH_2. 2,2',6,6'-Tetramethylpiperidine (HTMP) was stored over molecular sieves. Commercial 2.5 M solutions of *n*butyllithium in hexanes were stored and transfered under a deoxygenated and dehydrated argon atmosphere. Liquid electrophiles were distilled and stored under an argon atmosphere before use.

Preparation of 2-isopropylpyridine (**2**)*:*

Commercial 2-ethylpyridine **1** (22.9 ml, 200 mmol) in anhydrous THF (120 ml) was placed in a dried, argon-flushed 500 ml 3-necked flask equipped with mechanical stirring, and cooled to −30°C. *n*BuLi (84 ml, 210 mmol) was added over 30 min, temperature being kept between −30°C and −20°C. After an additional hour of stirring at −20°C, the deep red solution was cooled to −50°C. Methyl iodide (13.7 ml, 220 mmol) in anhydrous THF (50 ml) was then carefully, slowly added between −50°C and −40°C (orange). After 30 min stirring at −40°C and subsequent hydrolysis (100 ml of water), the reaction mixture was made acidic with 25 ml concentrated HCl and extracted with ether (200 ml). The aqueous layer was treated with solid K_2CO_3 and extracted with CH_2Cl_2 (3 × 150 ml). After drying ($MgSO_4$) and filtration, the solvent was removed *in vacuo* at room temperature. Further distillation under atmospheric pressure gave pure 2-isopropylpyridine **2** as a colorless liquid in a 86% yield, b.p. 155-157°C (lit. b.p. 162°C[39], 155-157°C[40]), n^{20}_D = 1.4883 (lit.[40] n^{20}_D = 1.4910). IR (film): ν = 2963, 1591, 1570, 1476, 1433. ^1H NMR ($CDCl_3$): δ = 1.22 (d, J = 6.9 Hz, 6 H, $2CH_3$), 2.98 (sept, J = 6.9 Hz, 1 H, CH), 6.98 (dd, 1 H, H-5), 7.07 (d, 1 H, H-3), 7.49 (td, 1 H, H-4), 8.45 (dd, 1 H, H-6). $C_8H_{11}N$ (121.18): calcd. C 79.29, H 9.15, N 11.56; found C 79.12, H 9.00, N 11.32.

General procedure A: metallation of 2-isopropylpyridine (**2**) *with KDA (optimization and subsequent reaction with benzaldehyde, see Table 1):*

In a dried, argon-flushed 50 ml flask was placed potassium tertbutoxide (1.1 or 1.5 eq.), anhydrous THF (10 ml) and diisopropylamine (1.1 or 1.5 eq.). The mixture was cooled to (T − 20)°C and *n*BuLi (1.1, 1.2 or 1.5 eq.) was slowly added. The reaction mixture was then warmed up to T°C over 15 min before adding 2-isopropylpyridine (5 mmol). After t min of metallation, the mixture was cooled to −75°C, benzaldehyde (15 mmol) was slowly added and reacted for 2 h at −75°C. After hydrolysis (10 ml water), dichloromethane extraction (3 × 15 ml) and drying ($MgSO_4$), the solvent was removed *in vacuo* at room temperature. Conversion was determined by comparing the ^1H-NMR integration of the starting material C-H signal (septuplet at 2.98 ppm) to that of the product C-H signal (singlet at 4.83 ppm).

Metallation of 2-isopropylpyridine (**2**) *with nBuLi / tBuOK:*

In a dried, argon-flushed flask was placed potassium tertbutoxide (505 mg, 4.5 mmol) in anhydrous THF (9 ml). After cooling to −75°C, *n*BuLi (1.8 ml, 4.5 mmol) was slowly added and the reaction mixture stirred for 10 min. 2-isopropylpyridine **2** (4.1 mmol) was added and the reaction stirred at −75°C for 1 h. Benzaldehyde (12 mmol) was then slowly added and allowed to react for 2 h at −75°C. Standard work-up was then carried out and the products separated by column chromatography on silica gel (eluant: cyclohexane/ethyl acetate 9/1 to 5/5).

1-Phenyl-1-(6-isopropyl-(2-pyridyl))methanol (**4a**):

^{1}H NMR ($CDCl_3$): δ = 1.37 (d, *J* = 6.9 Hz, 6 H, $2CH_3$), 3.13 (sept, *J* = 6.9 Hz, 1 H, CH), 5.72 (s, 1 H, C*H*OH), 6.03 (s, 1 H, OH), 6.90 (d, 1 H, H-3_{pyr} or H-5_{pyr}), 7.07 (d, 1 H, H-3_{pyr} or H-5_{pyr}), 7.25-7.42 (m, 5 H, phenyl H), 7.52 (t, 1 H, H-4_{pyr}). ^{13}C NMR ($CDCl_3$) δ = 22.32 ($2CH_3$), 35.80 (CH), 74.35 (C-OH), 118.50 (C-3_{pyr} or C-5_{pyr}), 119.20 (C-3_{pyr} or C-5_{pyr}), 127.02 (C-2_{phen} + C-6_{phen} or C-3_{phen} + C-5_{phen}), 128.36 (C-2_{phen} + C-6_{phen} or C-3_{phen} + C-5_{phen}), 127.56 (C-4_{phen}), 137.16 (C-4_{pyr}), 143.45 (C-1_{phen}), 159.29 (C-6_{pyr}), 165.11 (C-2_{pyr}).

1-Phenyl-1-(2-isopropyl-4-pyridyl)methanol (**4b**):

m.p. 111 °C; ^{1}H NMR ([D_6]DMSO) δ = 1.19 (d, *J* = 6.9 Hz, 6 H, $2CH_3$), 2.96 (sept, *J* = 6.9 Hz, 1 H, CH), 5.67 (s, 1 H, C*H*OH), 6.07 (s, 1 H, OH), 7.15-7.36 (m, 7 H, H-3_{pyr} + H-5_{pyr} + phenyl H), 8.36 (d, 1 H, H-6_{pyr}). ^{13}C NMR ([D_6]DMSO) δ = 22.84 ($2CH_3$), 35.89 (CH), 73.63 (C-OH), 118.26 (C-3_{pyr} or C-5_{pyr}), 119.14 (C-3_{pyr} or C-5_{pyr}), 126.67 (C-2_{phen} + C-6_{phen} or C-3_{phen} + C-5_{phen}), 128.59 (C-2_{phen} + C-6_{phen} or C-3_{phen} + C-5_{phen}), 127.47 (C-4_{phen}), 144.84 (C-1_{phen}), 148.91 (C-6_{pyr}), 154.80 (C-4_{pyr}), 166.65 (C-2_{pyr}).

General procedure B: metallation of 2-isopropylpyridine with other sodium or potassium amides:

The procedure was identical to procedure A. For sodium amides, *t*BuOK was replaced by *t*BuONa. For metallation with NaTMP or KTMP, HDA was replaced by HTMP.

General procedure C: reactivity of MDA-metallated 2-isopropylpyridine towards various electrophiles:

Experiments were carried out on 3 mmol of 2-isopropylpyridine **2**, according to the optimized procedure, i.e.: metallation at −50°C (30 min with KDA, 60 min with NDA) and reaction with electrophiles at −75°C for 0.5 to 2 h. Electrophiles (3-fold excess) were added pure if liquid (except alkyl iodides) or in solution in anhydrous THF (2 to 5 ml) if solid.

2-Tertiobutylpyridine[54] (**3a**):

The foregoing procedure, with methyl iodide as electrophile, gave 86% (KDA) of **3a**, $n^{20}D$ = 1.4938 (lit.[17-18] $n^{20}D$ = 1.4891). IR (film): ν = 2959, 1588, 1569, 1480, 1430. ^{1}H NMR ($CDCl_3$) δ = 1.35 (s, 9 H, $3CH_3$), 7.03 (dd, 1 H, H-5), 7.30 (d, 1 H, H-3), 7.56 (td, 1 H, H-4), 8.54 (dd, 1 H, H-6). ^{13}C NMR ($CDCl_3$) δ = 29.81 ($3CH_3$), 37.07 (C-α), 118.68 (C-3 or C-5), 120.28 (C-3 or C-5), 135.77 (C-4), 148.27 (C-6), 168.91 (C-2). $C_9H_{13}N$ (135.21): calcd. C 79.95, H 9.69, N 10.36; found: C 79.62, H 9.40, N 10.65.

2-Methyl-2-(2-pyridyl)butane (**3b**):

The foregoing procedure, with ethyl iodide as electrophile, gave 85% (KDA) of **3b**, $n^{20}D$ = 1.4902 (lit.[16] $n^{20}D$ = 1.4924). IR (film): ν = 2964, 1587, 1569, 1475, 1430. ^{1}H NMR ($CDCl_3$) δ = 0.67 (t, *J* = 7.4 Hz, 3 H, CH_2CH_3), 1.32 (s, 6 H, $2CH_3$), 1.74 (q, *J* = 7.4 Hz, 2 H, CH_2), 7.04 (dd, 1 H, H-5), 7.26 (d, 1 H, H-3), 7.57 (td, 1 H, H-4), 8.56 (dd, 1 H, H-6); ^{13}C NMR ($CDCl_3$) δ = 8.87 (CH_2CH_3), 27.17 ($2CH_3$), 35.63 (CH_2), 40.39 (C-α), 119.79 (C-3 or C-5), 120.23 (C-3 or C-5), 135.64 (C-4), 148.41 (C-6), 167.99 (C-2). $C_{10}H_{15}N$ (149.24): calcd. C 80.48, H 10.13, N 9.39; found C 80.55, H 10.42, N 9.05.

2-Methyl-2-(2-pyridyl)hexane (**3c**):

The foregoing procedure, with butyl iodide as electrophile, gave 88% (KDA) of **3c**, $n^{20}D$ = 1.4850. IR (film): ν = 2957, 2931, 2859, 1588, 1570, 1475, 1430. ^{1}H NMR ($CDCl_3$) δ = 0.75 (t, *J* = 7.1 Hz, 3 H, CH_2CH_3), 0.89-1.22 (m, 4 H, CH_2CH_3 + $CH_2CH_2CH_3$), 1.28 (s, 6 H, $2CH_3$), 1.65 [m, 2 H, $CH_2C(CH_3)_2$], 6.97 (dd, 1 H, H-5), 7.21 (d, 1 H, H-3), 7.50 (td, 1 H, H-4), 8.51 (dd, 1 H, H-6). ^{13}C NMR ($CDCl_3$) δ 13.68 (CH_3), 22.99 (CH_2CH_3), 26.60 ($CH_2CH_2CH_3$), 27.49 ($2CH_3$), 39.94 (C-α), 42.91 [$CH_2C(CH_3)_2$], 119.33 (C-3 or C-5), 119.98 (C-3 or C-5), 135.38 (C-4), 148.21 (C-6), 167.96 (C-2). $C_{12}H_{19}N$ (177.29): calcd C 81.30, H 10.80, N 7.90; found: C 81.07, H 10.97, N 7.99.

4-Methyl-4-(2-pyridyl)pentene (**3d**):

The foregoing procedure, with allyl bromide as the electrophile, gave 91% (KDA) and 83% (NDA) of **3d**, $n^{20}D$ = 1.4998. IR (film): ν = 2963, 1588, 1474, 1430. ^{1}H NMR ($CDCl_3$) δ = 1.35 (s, 6 H, $2CH_3$), 2.48 (d, J = 7.2 Hz, 2 H, CH_2), 4.93 (d, J = 9.9 Hz, 1 H, H_{cis}), 4.95 (d, J = 17.2 Hz, 1 H, H_{trans}), 5.57 (ddt, J = 17.2, 9.9 & 7.2 Hz, 1 H, H_{vinyl}), 7.08 (dd, 1 H, H-5), 7.28 (d, 1 H, H-3), 7.60 (td, 1 H, H-4), 8.58 (dd, 1 H, H-6). ^{13}C NMR ($CDCl_3$) δ = 27.29 ($2CH_3$), 40.22 (C-α), 47.38 (CH_2), 116.80 (C=CH_2), 119.69 (C-3 or C-5), 120.49 (C-3 or C-5), 135.26 (*C*=CH_2), 135.81 (C-4), 148.50 (C-6), 167.64 (C-2). $C_{11}H_{15}N$ (161.25): calcd. C 81.94, H 9.38, N 8.69; found: C 82.08, H 9.45, N 8.53.

Methyl 2-methyl-2-(2-pyridyl)propyl sulfide (**3e**):

The foregoing procedure, with chloromethyl methyl sulfide as electrophile, gave 72% (KDA) and 54% (NDA) of **3e**, $n^{20}D$ = 1.5325. IR (film): ν = 2963, 1588, 1569, 1473, 1431. ^{1}H NMR ($CDCl_3$) δ = 1.40 (s, 6 H, $2CH_3$), 1.82 (s, 3 H, SCH_3), 2.90 (s, 2 H, CH_2S), 7.05 (dd, 1 H, H-5), 7.28 (d, 1 H, H-3), 7.56 (td, 1 H, H-4), 8.51 (dd, 1 H, H-6). ^{13}C NMR ($CDCl_3$) δ = 17.41 (SCH_3), 27.10 ($2CH_3$), 41.89 (C-α), 48.31 (CH_2), 120.72 (C-3 or C-5), 121.08 (C-3 or C-5), 136.14 (C-4), 148.00 (C-6), 164.72 (C-2). $C_{10}H_{15}NS$ (181.30): calcd C 66.25, H 8.34, N 7.73; found: C 66.42, H 8.18, N 7.85.

2-Methyl-1-phenyl-2-(2-pyridyl)propanol (**3f**):

The foregoing procedure, with benzaldehyde as electrophile, gave 90% (KDA) of **3f**, m.p. 64°C. IR (KBr): ν = 3354, 2974, 1594, 1566, 1470, 1467. ^{1}H NMR ($CDCl_3$) δ = 1.27 (s, 3 H, CH_3), 1.39 (s, 3 H, CH'_3), 4.83 (s, 1 H, CH), 6.62 (s, 1 H, OH), 7.02-7.19 (m, 7 H, H-3_{pyr} + H-5_{pyr} + phenyl H), 7.55 (td, 1 H, H-4_{pyr}), 8.51 (dd, 1 H, H-6_{pyr}). ^{13}C NMR ($CDCl_3$) δ = 23.06 (CH_3), 27.04 (CH'_3), 43.92 (C-α), 61.86 (C-OH), 120.72 (C-3 or C-5), 121.41 (C-3 or C-5), 126.90 ($C4_{phen}$), 127.23 (C-4_{phen} + C-6_{phen} or C-3_{phen} + C-5_{phen}), 127.28 (C-4_{phen} + C-6_{phen} or C-3_{phen} + C-5_{phen}), 136.92 (C-4), 141.90 (C-1_{phen}), 147.45 (C-6), 166.62 (C-2). $C_{15}H_{17}NO$ (227.31): calcd. C 79.26, H 7.54, N 6.16; found: C 79.53, H 7.75, N 6.14.

3-Methyl-3-(2-pyridyl)butan-2-ol (**3g**):

The foregoing procedure, with acetaldehyde as electrophile, gave 58% (KDA) and 73% (NDA) of **3g**, $n^{20}D$ = 1.5110. IR (film) ν = 3384, 2971, 1591, 1570, 1470, 1431. ^{1}H NMR ($CDCl_3$) δ = 1.05 (d, , J = 6.4 Hz, 3 H, CHCH_3), 1.31 (s, 3 H, CH_3), 1.36 (s, 3 H, CH'_3), 3.87 (q, J = 6.4 Hz, 1 H, CH), 5.75 (s, 1 H, OH), 7.13 (dd, 1 H, H-5), 7.30 (d, 1 H, H-3), 7.66 (td, 1 H, H-4), 8.47 (dd, 1 H, H-6). ^{13}C NMR ($CDCl_3$) δ = 18.32 (CHCH_3), 23.02 (CH_3), 26.48 (CH'_3), 43.47 (C-α), 74.86 (C-OH), 120.37 (C-3 or C-5), 120.97 (C-3 or C-5), 136.71 (C-4), 147.42 (C-6), 167.55 (C-2). $C_{10}H_{15}NO$ (165.24): calcd. C 72.69, H 9.15, N 8.48; found: C 72.81, H 9.36, N 8.60.

2,3-Dimethyl-2-(2-pyridyl)pentan-3-ol (**3h**):

The foregoing procedure, with butanone as electrophile, gave 34% (KDA) of **3h**, $n^{20}D$ = 1.5071. IR (film) ν = 3328, 2972, 1590, 1570, 1469, 1436. ^{1}H NMR ($CDCl_3$) δ = 0.87 (t, 3 H, CH_2CH_3), 1.03 (s, 3 H, CH_3C-OH), 0.9-1.2 (comp, 2 H, CH_2), 1.38 (s, 3 H, CH_3), 1.41 (s, 3 H, CH'_3), 6.47 (s, 1 H, OH), 7.12 (dd, 1 H, H-5), 7.33 (d, 1 H, H-3), 7.65 (td, 1 H, H-4), 8.47 (dd, 1 H, H-6). ^{13}C NMR ($CDCl_3$) δ = 7.79 (CH_2CH_3), 20.72 (aliph. C), 23.21 (aliph. C), 24.15 (aliph. C), 29.54 (aliph. C), 46.41 (C-α), 76.33 (C-OH), 120.09 (C-3 or C-5), 120.77 (C-3 or C-5), 136.76 (C-4), 147.25 (C-6), 168.44 (C-2). $C_{12}H_{19}NO$ (193.29): C 74.57, H 9.91, N 7.25; found: C 74.25, H 9.87, N 7.53.

1-(1,1-dimethyl-1-(2-pyridyl)methyl)cyclopentanol (**3i**):

The foregoing procedure, with cyclopentanone as electrophile, gave 29% (KDA) and 53% (NDA) of **3i**, b.p. 120°C/2 mmHg, $n^{20}D$ = 1.5207. IR (film): ν = 3330, 2964, 2867, 1591, 1570, 1470, 1434. ^{1}H NMR ($CDCl_3$) δ = 1.40 (s, 6 H, $2CH_3$), 1.40-1.90 (m, 8 H, cyclopentyl H), 6.51 (s, 1 H, OH), 7.13 (dd, 1 H, H-5), 7.34 (d, 1 H, H-3), 7.65 (td, 1 H, H-4), 8.46 (dd, 1 H, H-6). ^{13}C NMR ($CDCl_3$) δ = 24.41 ($2CH_3$), 24.66 (*C*-C-C-OH), 36.00 (*C*-C-OH), 44.96 (C-α), 86.69 (C-OH), 119.91 (C-3 or C-5), 120.93 (C-3 or C-5), 136.72 (C-4), 147.15 (C-6), 168.23 (C-2). $C_{13}H_{19}NO$ (205.30): calcd C 76.06, H 9.33, N 6.82; found: C 76.28, H 9.38, N 6.97.

1,1-Diphenyl-2-methyl-2-(2-pyridyl)propanol (**3j**):

The foregoing procedure, with benzophenone as electrophile, gave 62% (KDA) of **3j**, m.p. 171-173°C. IR (KBr): ν = 3190, 2992, 1590, 1568, 1469. ^{1}H NMR ($CDCl_3$) δ = 1.51 (s, 6 H, $2CH_3$), 7.04-7.34 (m, 11 H, phenyl H + H-5), 7.62 (d, 1 H, H-3), 7.72 (td, 1 H, H-4), 8.32 (dd, 1 H, H-6), 8.60 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$) δ = 27.05 (broad, $2CH_3$), 46.48 (C-α), 83.92 (C-OH), 120.13 (C-3_{pyr} or C-5_{pyr}), 120.76 (C-3_{pyr} or C-5_{pyr}), 125.90 (2C-4_{phen}), 126.62 (2C-4_{phen} + 2C-6_{phen} or 2C-3_{phen} + 2C-5_{phen}), 129.35 (2C-4_{phen} + 2C-6_{phen} or 2C-3_{phen} + 2C-5_{phen}), 137.19 (C-4_{pyr}), 147.18 (broad, 2C-1_{phen}), 147.22 (C-6_{pyr}), 169.16 (C-2_{pyr}). $C_{21}H_{21}NO$ (303.41): calcd. C 83.13, H 6.98, N 4.62; found: C 83.47, H 7.23, N 4.41.

2-Methyl-2-(2-pyridyl)propionaldehyde (**3k**):

The foregoing procedure, with ethyl formate or *N*-formyl piperidine as electrophile, gave 63% (KDA) of **3k** (unstable product). ^{1}H NMR ($CDCl_3$) δ = 1.46 (s, 6 H, $2CH_3$), 7.15 (dd, 1 H, H-5), 7.26 (d, 1 H, H-3), 7.66 (td, 1 H, H-4), 8.55 (dd, 1 H, H-6), 9.74 (s, 1 H, CHO).

Ethyl 2-methyl-2-(2-pyridyl)propionate (**3l**):

The foregoing procedure, with diethyl carbonate as electrophile, gave 78% (KDA) and 86% (NDA) of **3l**, $n^{20}D$ = 1.4868. IR (film): ν = 2979, 1730, 1588, 1571, 1474, 1431. – ^{1}H NMR ($CDCl_3$) δ = 1.13 (t, *J* = 7.1 Hz, 3 H, CH_2CH_3), 1.58 (s, 6 H, $2CH_3$), 4.10 (q, *J* = 7.1 Hz, 2 H, CH_2), 7.09 (dd, 1 H, H-5), 7.25 (d, 1 H, H-3), 7.60 (td, 1 H, H-4), 8.50 (dd, 1 H, H-6). ^{13}C NMR ($CDCl_3$) δ = 13.84 (CH_2CH_3), 25.42 ($2CH_3$), 49.33 (C-α), 60.56 (CH_2), 119.62 (C-3 or C-5), 121.37 (C-3 or C-5), 136.26 (C-4), 148.67 (C-6), 163.63 (C-2), 176.00 (C=O). $C_{11}H_{15}NO_2$ (193.25): calcd C 68.37, H 7.82, N 7.25; found: C 68.42, H 7.68, N 7.38.

4-Methyl-2-(2-pyridyl)pentanenitrile (**3m**):

The foregoing procedure, with 3-chloropropionitrile as electrophile, gave 31% (KDA) and 15% (NDA) of **3m**, $n^{20}D$ = 1.5010. IR (film): ν = 2986, 2245, 1588, 1570, 1477, 1431. ^{1}H NMR ($CDCl_3$) δ = 1.35 (s, 6 H, $2CH_3$), 2.11 (m, 4 H, CH_2 + CH_2CN), 7.10 (dd, 1 H, H-5), 7.26 (d, 1 H, H-3), 7.62 (td, 1 H, H-4), 8.53 (dd, 1 H, H-6). ^{13}C NMR ($CDCl_3$) δ = 12.82 (*C*-CN), 27.46 ($2CH_3$), 38.06 (*C*-C-CN), 39.89 (C-α), 119.72 (C-3 or C-5), 121.11 (C-3 or C-5), 120.09 (CN), 136.36 (C-4), 148.77 (C-6), 165.44 (C-2). $C_{11}H_{14}N_2$ (174.25): calcd C 75.82, H 8.10, N 16.08; found: C 76.02, H 8.14, N 15.93.

Methyl 4-methyl-4-(2-pyridyl)pentanoate (**3n**):

The foregoing procedure, with methyl 3-bromopropionate as electrophile, gave 21% (KDA) and 17% (NDA) of **3n**, $n^{20}D$ = 1.5095. IR (film): ν = 2955, 1738, 1588, 1570, 1477, 1432. ^{1}H NMR ($CDCl_3$) δ = 1.35 (s, 6 H, $2CH_3$), 2.09 (m, 4 H, CH_2 + CH_2COO), 3.59 (s, 3 H, $COOCH_3$), 7.08 (dd, 1 H, H-5), 7.28 (d, 1 H, H-3), 7.60 (td, 1 H, H-4), 8.56 (dd, 1 H, H-6). ^{13}C NMR ($CDCl_3$) δ = 27.44 ($2CH_3$), 29.75 (CH_2COO), 37.63 (CH_2), 39.70 (C-α), 51.16 (OCH_3), 119.60 (C-3 or C-5), 120.58 (C-3 or C-5), 135.92 (C-4), 148.53 (C-6), 166.69 (C-2) 174.02 (C=O). $C_{12}H_{17}NO_2$ (207.27): C 69.54, H 8.27, N 6.76; found: C 69.69, H 8.38, N 6.93.

Methyl 1-methyl-1-(2-pyridyl)ethyl sulfide (**3o**):

The foregoing procedure, with dimethyl disulfide as electrophile, gave 86% (KDA) and 77% (NDA) of **3o**, $n^{20}D$ = 1.5383. IR (film): ν = 2970, 1587, 1567, 1470, 1427. ^{1}H NMR ($CDCl_3$) δ =1.73 (s, 6 H, $2CH_3$), 1.82 (s, 3 H, SCH_3), 7.10 (dd, 1 H, H-5), 7.61 (m, 2 H, H-3 + H-4), 8.53 (dd, 1 H, H-6). ^{13}C NMR ($CDCl_3$) δ = 12.03 (SCH_3), 28.03 ($2CH_3$), 48.17 (C-α), 120.72 (C-3 or C-5), 121.08 (C-3 or C-5), 136.14 (C-4), 148.00 (C-6), 164.72 (C-2). $C_9H_{13}NS$ (167.28): C 64.62, H 7.83, N 8.37; found: C 64.85, H 7.99, N 8.55.

2-Methyl-2-(2-pyridyl)butanol (**3p**):

The foregoing procedure, with oxirane as electrophile, gave 78% (KDA) and 77% (NDA) of **3p**, $n^{20}D$ = 1.5192. IR (film): ν = 3371, 2962, 1591, 1570, 1477, 1431. ^{1}H NMR ($CDCl_3$) δ = 1.39 (s, 6 H, $2CH_3$), 2.01 (t, 2 H, CH_2CH_2OH), 3.68 (t, 2 H, CH_2OH), 4.66 (s, 1 H, OH), 7.13 (dd, 1 H, H-5), 7.36 (d, 1 H, H-3), 7.66 (td, 1 H, H-4), 8.50 (dd, 1 H, H-6). ^{13}C NMR ($CDCl_3$) δ = 28.85 ($2CH_3$), 40.25 (C-α), 44.35 (CH_2CH_2OH), 59.14

(CH_2OH), 120.00 (C-3 or C-5), 120.84 (C-3 or C-5), 136.64 (C-4), 147.72 (C-6), 167.64 (C-2). $C_{10}H_{15}N0$ (165.24): C 72.69, H 9.15, N 8.48; found: C 72.78, H 8.98, N 8.66.

2-Chloro-2-(2-pyridyl)propane[50] (**3q**):

The modified foregoing procedure (the potassio intermediate was poured on an excess of electrophile), with hexachloroethane as electrophile, gave 70% (KDA) of **3q**, $n^{20}D$ = 1.5112 (lit.[50] $n^{20}D$ = 1.5153). IR (film): ν = 2984, 1588, 1571, 1471, 1431. ^{1}H NMR ($CDCl_3$) δ = 2.01 (s, 6 H, $2CH_3$), 7.18 (dd, 1 H, H-5), 7.70 (m, 2 H, H-3 + H-4), 8.56 (dd, 1 H, H-6). ^{13}C NMR ($CDCl_3$) δ = 32.82 ($2CH_3$), 70.09 (C-α), 120.19 (C-3 or C-5), 122.16 (C-3 or C-5), 136.56 (C-4), 148.16 (C-6), 163.48 (C-2). MS (CI, 200eV, *t*BuH); *m/z* (%): 156/158 (100) [M+1], 120 (65) [M+1 – HCl] . $C_8H_{10}ClN$ (155.63): C 61.74, H 6.48, N 9.00; found: C 61.98, H 6.35, N 9.32.

2,3-dimethyl-2,3-bis(2-pyridyl)butane[51] (**5**):

The foregoing procedure, with hexachloroethane as electrophile, gave 54% of **5**, m.p. 123°C (lit.[51] m.p. 121°C, lit.[52] m.p. 116-117°C). IR (film): ν = 2968, 1582, 1564, 1466, 1426. ^{1}H NMR ($CDCl_3$) δ = 1.41 (s, 6 H, $2CH_3$), 6.82 (d, 1 H, H-3), 7.01 (dd, 1 H, H-5), 7.37 (td, 1 H, H-4), 8.51 (dd, 1 H, H-6). ^{13}C NMR ($CDCl_3$) δ = 24.15 ($2CH_3$), 46.14 (C-α), 120.38 (C-3 or C-5), 122.20 (C-3 or C-5), 134.40 (C-4), 147.11 (C-6), 166.12 (C-2). $C_{16}H_{20}N_2$ (240.35): C 79.96, H 8.39, N 11.66; found: C 79.65, H 8.68, N 11.53.

REFERENCES

1. Ishikaw, K.; Fukami, T.; Niiyama, K.; Nagase, T.; Hioki, Y.; Takeshita, H. *JP Patent* **1991**, 03 72,458 [91 72,458] (*Chem. Abstr.* **1991**, *115*, 114362t).
2. Saito, K.; Goto, T.; Kobayashi, A.; Kojo, K.; Oguchi, S.; Narita, S. *JP Patent* **1987**, 62,289,560 [87,289,560] (*Chem. Abstr.* **1988**, *109*, 110408r).
3. Bernhart, C.; Cautreels, W.; Gautier, P. *FR Patent* **1984**, 2,535,722 (*Chem. Abstr.* **1984**, *101*, 171070f).
4. Esanu, A. *DE Patent* **1986**, 3,538,063 (*Chem. Abstr.* **1986**, *105*, 191053p).
5. Desmaële, D.; Mekouar, K.; d'Angelo, J. *J. Org. Chem.* **1997**, *62*, 3890-3901.
6. Czuba, W.; Kowalski, P.; Rutkowski, K. Pol. J. Chem. **1979**, *53(7-8)*, 1477-1487.
7. Hurst, D. T.; Viney, M. *Tetrahedron Lett.* **1968**, 3895-3896.
8. Bohlmann, F.; Winterfeldt, E.; Studt, P.; Laurent, H.; Boroschewski, G.; Kleine, K. M. *Chem. Ber.* **1961**, *94*, 3151-3174.
9. Kato, T.; Atsumi, T.; Sasaki, H. *Yakugaku Zasshi* **1965**, *85(9)*, 812-816 (*Chem. Abstr.* **1965**, *63*, 18018g).
10. Kubo, K.; Ukawa, K.; Kuzuna, S.; Nohara, A. *Chem. Pharm. Bull.* **1986**, *34(3)*, 1108-1117.
11. Siemeling, U.; Neumann, B.; Stammler, H. G. *Z. Naturforsch.* **1994**, *49b*, 683-686.
12. Hogen-Esch, T. E.; Smith, R. A.; Ades, D.; Fontanille, M. *J. Polym. Sci., Polym. Lett. Ed.* **1981**, *19*, 309-314.
13. Ward, T. J.; Warrellow, G. J. *UK Patent* **1991**, 2,248,449 A.
14. Reinecke, M. G.; Kray, L. R. *J. Org. Chem.* **1964**, *29*, 1736-1739.
15. Eisch, J. J.; Kovacs, C. A.; Chobe, P.; Boleslawski, M. P. *J. Org. Chem.* **1987**, *52*, 4427-4437.
16. Pines, H.; Notari, B. *J. Am. Chem. Soc.* **1960**, *82*, 2209-2213.
17. Brown, H. C.; Murphey, W. A. *J. Am. Chem. Soc.* **1951**, *73*, 3308-3312.
18. Fraenkel, G.; Cooper, J. W. *J. Am. Chem. Soc.* **1971**, *93*, 7228-7238.
19. Akiba, K.-Y.; Takee, K.; Shimizu, Y.; Ohkata, K. *J. Am. Chem. Soc.* **1986**, *108*, 6320-6327.
20. Weber, H.; Pant, J. *Arch. Pharm.* **1980**, *313*, 307-310.
21. Wakefield, B. J. *Best Synthetic Methods: Organolithium Methods*; Academic Press: San Diego, 1988.
22. Katritzky, A. R.; Rees, C. W. *Comprehensive Heterocyclic Chemistry*; Pergamon Press: Oxford, 1984 ; *2*, p. 333.
23. Mathis, C.; Hogen-Esch, T. E. *J. Am. Chem. Soc.* **1982**, *104*, 634-635.

24. Crabb, T. A.; Fallah, A. *J. Chem. Soc. Perkin Trans. 2* **1992**, 1335-1342.
25. Beumel, O. F. Jr; Smith, W. N.; Rybalka, B. *Synthesis* **1974**, 43-45.
26. Osuch, C.; Levine, R. *J. Org. Chem.* **1956**, *21*, 1099-1101.
27. Doering, W. E.; Pasternak, V. Z. *J. Am. Chem. Soc.* **1950**, *72*, 143-147.
28. Mordini, A. *Adv. Carbanion Chem.* **1992**, *1*, 1-44.
29. Schlosser, M. *J. Organomet. Chem.* **1967**, *8*, 9-16.
30. Hartmann, J.; Schlosser, M. *Helv. Chim. Acta* **1976**, *59*, 453-466.
31. Mordini, A.; Ben Rayana, E.; Margot, C.; Schlosser, M. *Tetrahedron* **1990**, *46*, 2401-2410.
32. Margot, C.; Matsuda, H.; Schlosser, M. *Tetrahedron* **1990**, *46*, 2425-2430.
33. Gualtieri, F.; Mordini, A.; Pecchi, S.; Scapecchi, S. *Synlett* **1996**, 447-448.
34. Ricci, A.; Guerrini, A.; Seconi, G.; Mordini, A.; Constantieux, T.; Picard, J.-P.; Aizpurua, J.-M.; Palomo, C. *Synlett* **1994**, 955-957.
35. Klusener, P. A. A.; Tip, L.; Brandsma, L. *Tetrahedron* **1991**, *47*, 2041-2064 and references cited therein.
36. Margot, C.; Schlosser, M. *Tetrahedron Lett.* **1985**, *26*, 1035-1038.
37. Barr, D.; Dawson, A. J.; Wakefield, B. J. *J. Chem. Soc. Chem. Comm.* **1992**, *2*, 204.
38. Andrews, P. C.; Barnett, N. D. R.; Mulvey, R. E.; Clegg, W.; O'Neil, P. A.; Barr, D.; Cowton, L.; Dawson, A. J.; Wakefield, B. J. *J. Organomet. Chem.* **1996**, *518*, 85-95 and references cited therein.
39. Chelucci, G.; Gladiali, S. *J. Heterocyclic Chem.* **1988**, *25*, 1761-1765.
40. Wakatsuki, Y.; Yamazaki, H. *Synthesis* **1976**, 26-28.
41. Olofson, R. A.; Dougherty, C. M. *J. Am. Chem. Soc.* **1973**, *95*, 582-584.
42. Herrmann, J. L.; Kieczykowski, G. R.; Schlessinger, R. H. *Tetrahedron Lett.* **1973**, 2433-2436.
43. Fraser, R. R.; Mansour, T. S.; Savard, S. *J. Org. Chem.* **1985**, *50*, 3232-3234.
44. Fraser, R. R.; Mansour, T. S. *Tetrahedron Lett.* **1986**, *27*, 331-334.
45. Renger, B.; Hügel, H.; Wykypiel, W.; Seebach, D. *Chem. Ber.* **1978**, *111*, 2630-2645.
46. Raucher, S.; Koolpe, G. A. *J. Org. Chem.* **1978**, *43*, 3794-3796.
47. Lochmann, L.; Trekoval, J. *J. Organomet. Chem.* **1979**, *179*, 123-132.
48. Symons, E. A.; Powell, M. F.; Schnittker, J. B.; Clermont, M. J. *J. Am. Chem. Soc.* **1979**, *101*, 6704-6709.
49. Ahlbrecht, H.; Schneider, G. *Tetrahedron* **1986**, *42*, 4729-4741.
50. Feuer, H.; Doty, J. K. *J. Heterocyclic Chem.* **1978**, *15*, 1517.
51. Feuer, H.; Doty, J.; Lawrence, J. P. *J. Org. Chem.* **1973**, *38*, 417-422.
52. Canty, A. J.; Mirchin, N. J. *Aust. J. Chem.* **1986**, *39*, 1063-1069.
53. Bizot, J. *Bull. Soc. Chim. Fr.* **1967**, *1*, 151.
54. Among other methods to prepare 2-tertiobutylpyridine **3a**, see reference 17 and the procedure described by Russell, G. A.; Rajaratnam, R.; Wang, L.; Zhi Shi, B.; Hyu Kim, B.; Fa Yao, C. *J. Am. Chem. Soc.* **1993**, *115*, 10596-10604.