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A Simple Method to Prepare Homoallylic Amines from Secondary Homoallylic Mesylates

Françoise Hénin [a] , Evelyne Mahuet [a] , Caroline Muller [a] & Jacques Muzart [a]
[a] Unité "Réarrangements Thermiques et Photochimiques" Associée au CNRS , Université de Reims Champagne-Ardenne , B.P. 347, 51062, Reims Cedex, France
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A SIMPLE METHOD TO PREPARE HOMOALLYLIC AMINES FROM SECONDARY HOMOALLYLIC MESYLATES

Françoise Hénin*, Evelyne Mahuet, Caroline Muller, Jacques Muzart

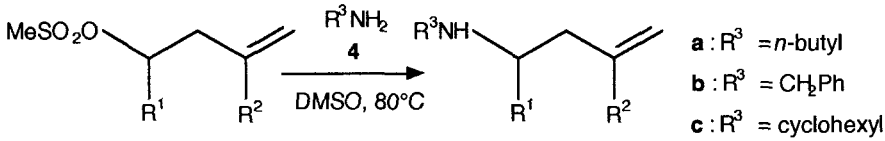
Unité "Réarrangements Thermiques et Photochimiques" Associée au CNRS
Université de Reims Champagne-Ardenne, B.P. 347,
51062 Reims Cedex, France

Abstract: The nucleophilic substitution by primary amines of secondary homoallylic mesylates easily obtained from corresponding alcohols offers a convenient way to prepare homoallylic amines. The relative low yields in pure compounds is counterbalanced by the simplicity of the procedure.

In the course of a research program devoted to the synthesis of methylene lactams by palladium-catalyzed cyclization of unsaturated chloroformamides,[1] it was necessary to synthetize various homoallylic amines where the carbon center of the unsaturated chain connected to the nitrogen atom was tertiary. Such compounds are commonly used as precursors of various functionalized compounds,[2] the most common access to these synthons being the organometallic allylation of imines[3] although other amine derivatives such as chloromethylformamides,[4] *N*-alkyltrimethylsilylalkoxymethylamines[5] and oxazolines[6] also undergo allylation to produce homoallylic amines. Other ways involve cycloadditions as key steps. [7]

The moisture-sensitivity of imines[8] led us to look for a more convenient procedure. Homoallylic amines have been easily obtained by the nucleophilic substitution of the corresponding primary bromides or mesylates by amines.[9] However such a method proved unsuccessful in our hands when applied to a secondary homoallylic mesylate.

In this note, we are pleased to record that such a nucleophilic substitution was nevertheless feasible when carried out under particular conditions (Eq. and Table).



1 : R^1 = *n*-propyl, R^2 = H
2 : R^1 = *n*-hexyl, R^2 = H
3 : R^1 = *n*-propyl, R^2 = Me

5 : R = *n*-propyl, R^2 = H
6 : R = *n*-hexyl, R^2 = H
7 : R^1 = *n*-propyl, R^2 = Me

As we investigated a number of experimental conditions, some of them being compiled in Table, it appeared that i) heating the reaction mixture was required to produce significant amounts of the desired nucleophilic substitution, the optimum temperature being around 80°C; ii) dimethylsulfoxide as solvent led to better results than dimethylformamide, dimethoxyethane and acetonitrile; iii) the nucleophilic amine **4** had to be used not only as a reagent but also as a base, lower yields being reached when using solely one equivalent of this amine in conjunction with either sodium carbonate or triethylamine as trap for the methylsulfonic acid; therefore, two equiv. of **4** were required, a larger amount leading to similar results.

Table: Nucleophilic substitution of secondary homoallylic mesylates by primary amines.[a]

Starting compounds	Reaction temperature (°C)	Reaction time (h)	Homoallylic amine	Yield[b] (%)
1 + 4a	80	2	**5a**	46
"	"	6	"	37
1 + 4b	"	4	**5b**	6
"	"	7	"	33
"	"	13	"	52
" [c]	"	13	"	53
"	"	24	"	40
1 + 4c	"	13	**5c**	52
2 + 4a	20 or 40	24	**6a**	0
"	60	14	"	11
"	80	14	"	34
2 + 4b	"	14	**6b**	50
2 + 4c	"	13	**6c**	50
3 + 4b	"	14	**7b**	34

[a]See experimental part for the procedure. [b]Yield of pure isolated compounds. [c]In using 4 equiv. of benzylamine instead of 2 equiv.

The moderate yields we obtained even under selected conditions were probably due to competitive elimination reactions which were favored from secondary mesylates. However, since the starting material is quickly obtained from the corresponding alcohol without tedious purification, the alcohol being itself easily available,[10] we can think that this method presents some utility in organic synthesis.

EXPERIMENTAL

Amines and DMSO were distilled over calcium hydride. Homoallylic mesylates, prepared from corresponding alcohols[10] using mesyl chloride and pyridine in dichloromathane, were used without purification.

General procedure for the synthesis of ***5*** *to* ***7****:* To a solution of **1** or **3** (1 equiv.) in DMSO (2 ml/g of substrate was added amine **4** (2 equiv.) in one portion. The mixture was stirred and heated to 80°C for the time indicated in Table. After cooling to room temperature, the mixture was basified with 2M NaOH then extracted with methylene chloride. The organic layers were washed with brine and dried over magnesium sulfate. After evaporation of solvents, crude amines were purified by flash-chromatography on silica gel eluting with ethyl acetate/petroleum ether (20/80) or by rapid filtration on a pad of alumina eluting with petroleum ether. Note that the chromatography had to be carried out rapidly because the compounds were rather unstable over these adsorbents. In contrast, they were stored in the fridge for weeks without apparent decomposition.

The spectra properties (NMR in $CDCl_3$, δ in ppm, J in hertz; IR in $CHCl_3$, ν in cm^{-1}) of isolated amines were as followed:

5a. IR: 3500-3250, 2960, 2920, 2860, 1645, 1460, 1110, 920. ^{1}H NMR (250 MHz): 0.91 (t 6H J = 6.9), 1.25-1.51 (9H) 2.05-2.29 (2H), 2.56 (m 3H), 5.04 (br t 1H J = 1.1), 5.09 (br d 1H J = 4.9), 5.70-5.88 (1H). ^{13}C NMR (63 MHz): 13.9, 14.3, 19.1, 20.5, 32.5, 36.4, 38.5, 46.9, 56.8, 116.9, 135.9.

5b. IR (KBr): 3600-3300, 3030, 2958, 2928, 2872, 1640, 1604, 1495, 1200-1000, 914. ^{1}H NMR (250 MHz): O.90 (t 3H J = 7), 1.39 (m 5H), 2.10-2.33 (2H), 2.63 (quint 1H J = 6), 3.77 (s 2H), 5.05 (br t 1H J = 1), 5.10 (br d 1H J = 5.7), 5.70-5.88 (1H), 7.18-7.33 (5H). ^{13}C NMR (63 MHz): 14.2, 18.9, 36.2, 38.4, 51.1, 56.0, 117.0, 126.7, 128.1, 128.3, 135.8, 140.9.

5c. IR: 3400-3100, 3040, 2900, 2820, 1620, 1450, 1435, 1080, 985, 910. ^{1}H NMR (300 MHz): 0.82 (t 3H J = 6.4), 0.90-1.32 (10H), 1.50-1.86 (5H), 2.05 (m 1H), 2.18 (m 1H), 2.46 (tt 1H J = 11, 3.6), 2.64 (m 1H), 5.04 (s 1H), 5.08 (br d 1H J = 4.5), 5.69-5.85 (1H). ^{13}C NMR (675 MHz): 14.2, 19.0, 25.2, 26.1, 34.1, 34.2, 37.1, 39.0, 53.1, 53.6, 116.9, 135.9.

6a. IR: 3400-3100, 3070, 2930, 2860, 1635, 1460, 1110, 1000, 920. ^{1}H NMR (300 MHz): 0.88 (t 3H J = 6.5), 0.91 (t 3H J = 7.2), 1.15-1.60 (15H), 2.13 (m 1H), 2.20 (m 1H), 2.55 (m 3H), 5.04 (br t 1H J = 0.8), 5.09 (br d 1H J = 6.5), 5.76 (m 1H). ^{13}C NMR (75 MHz): 13.8, 13.9, 20.4, 22.5, 25.6, 29.4, 31.7, 32.38, 33.9, 38.3, 46.7, 56.9, 116.8, 135.7.

6b. IR: 3400-3100, 3060, 2920, 2860, 1640, 1600, 1490, 1450, 1100, 1000, 920. ^{1}H NMR (300 MHz): 0.89 (t 3H J = 6.8), 1.27 (m 9H), 1.40 (m 2H), 2.16 (m 1H), 2.27 (m 1H), 2.61 (quint 1H J = 6.2), 3.77 (s 2H), 5.05 (s 1H), 5.09 (br d 1H J = 6.8), 5.70-5.85 (1H), 7.30 (m 5H). ^{13}C NMR (75 MHz): 14.0, 22.6, 25.6, 29.5, 31.8, 33.9, 33.3, 51.1, 56.2, 117.0, 126.7, 128.1, 128.3, 135.8, 140.8.

6c. IR: 3470-3100, 3070, 2920, 2850, 1635, 1450, 1100, 1000, 920. ^{1}H NMR (300 MHz): 0.88 (t 3H J = 6.9), 0.96-1.40 (14H), 1.55-1.89 (5H), 2.10 (m 1H), 2.21 (m 1H), 2.45 (m 1H), 2.67 (quint 1H J = 5.7), 5.03 (s 1H), 5.08 (br d 1H J = 5.0), 5.70-5.83 (1H). ^{13}C NMR (75 MHz): 13.9, 22.5, 25.1, 25.1, 25.7, 26.0, 29.4, 31.7, 34.0, 34.1, 38.9, 53.3, 53.5, 116.8, 135.8.

7b. IR (KBr): 3600-3300, 2957, 2930, 2872, 1645, 1603, 1495, 1454, 1095-1028, 889. ^{1}H NMR (250 MHz): 0.93 (t 3H J = 7.1), 1.24-1.60 (5H), 1.66 (t 3H J = 1.15), 2.16 (dd 2H J = 6.9, 0.8), 2.70 (quint 1H J = 6.9), 3.73 (d 1H J = 6.5), 3.84 (d 1H J = 6.5), 4.76 (sext 1H J = 0.8), 4.82 (sext 1H J = 0.8), 7.20-7.38 (5H). ^{13}C NMR (63 MHz): 14.3, 18.8, 22.2, 36.4, 43.3, 51.3, 54.0, 112.7, 126.8, 128.1, 128.3, 143.6.

REFERENCES AND NOTES

1. Hénin F., Muzart J. and Pète J.P. *Tetrahedron Lett.* **1986**, *27*, 6339.

2. See for examples, a) Keck G. E. and Enholm E. J. *J. Org. Chem.* 1985, *50*, 146; b) Laschat S. and Kunz H. *Synlett* **1990**, 51; c) ref. cited in these two papers.

3. Various allylic organometallics have been used in addition to imines:

- allyl boranes and boronates, a) Yamamoto Y., Komatsu T. and Maruyama K. *J. Org. Chem.* 1985, *50*, 3115; b) Yamamoto Y., Nishii S., Maruyama K., Komatsu T. and Ito W. *J. Amer. Chem. Soc.* **1986**, *108*, 7778; c) Wuts P.G.M. and Jung Y.W. *J. Org. Chem.* **1991**, *56*, 365;

- allyl-Mg, -Cu and -Li, d) Bocoum A., Boga C., Savoia D. and Umani-Ronchi A. *Tetrahedron Lett.* **1991**, *32*, 1367; e) Huet J. *Bull. Soc. Chim. Fr.* **1964**, 952;

- allyl silanes and stannanes in the presence of a Lewis acid, f) ref. 2a; g) Ciufolini M. A. and Spencer G. O. *J. Org. Chem.* **1989**, *54*, 4739; h) Laschat S. and Kunz H. *Synlett* **1990**, 629; i) Laschat S. and Kunz H. *J. Org. Chem.* **1991**, *56*, 5883; j) Kira M., Hino T. and Sakurai H. *Chem. Lett.* **1991**, 277;

- "Barbier type reactions", k) Blomberg C. *The Barbier Reaction and Related One-Step Processes* Springer-Verlag: Berlin, **1993**; the organometallic species being generated in situ in presence of:

. Zn, l) Dembélé Y.A., Belaud C. and Villiéras J. *Tetrahedron: Asymmetry* **1992**, *3*, 511; m) Bocoum A., Savoia D. and Umani-Ronchi A. *J. Chem. Soc., Chem. Commun.* **1993**, 1542;

. Ta or Bi, n) Bhuyan P. J., Prajapati D. and Sandhu J. S. *Tetrahedron Lett.* **1993**, *34*, 7975;

. In, o) Beuchet P., Le Marrec N. and Mosset P. *Tetrahedron Lett.* **1992**, *33*, 5959; p) Jin S. J., Araki S. and Butsugan Y. *Bull. Chem. Soc. Jpn* **1993**, *66*, 1528;

. Cd, q) Sain B., Prajapati D. and Sandhu J. S. *Tetrahedron Lett.* **1992**, *33*, 4795;

. Cr^{2+}, r) Giammaruco M., Taddei M. and Ulivi P. *Tetrahedron Lett.* **1993**, *34*, 3635;

. metal redox couples - Pb^{II} and Ti^{IV} - reduced by metallic aluminium, s) Tanaka H., Yamashita S., Ikemoto Y. and Torii S. *Chemistry Lett.* **1987**, 673; t) Tanaka H., Inoue K., Pokorski U., Taniguchi M. and Torii S. *Tetrahedron Lett.* **1990**, *31*, 3023; or Pb^{II} electroreduced, u) Tanaka H., Nakahara T., Dhimane H. and Torii S. Tetrahedron Lett. **1989**, *30*, 4161.

4. Courtois G., Mesnard D., Mahoungou J. R. and Miginiac L. Bull. Soc. Chim. Fr. **1986**, 449.

5. Courtois G. and Miginiac L. Tetrahedron Lett. **1987**, *28*, 1659.

6. Wu M. J. and Pridgen L. N. Synlett **1990**, 636.

7. a) De Shong P. , Leginus J.M. and Landler S.W. J. Org. Chem. **1986**, *51*, 574; b) Garigipati R. S., Cordova R., Parvez M. and Weinreb S. M. Tetrahedron **1986**, *42*, 2979.

8. a) Sandler S. R. and Karo W. *Organic Functional Group Preparation* Academic Press: New York, **1986**, Vol. II, p. 291; b) ref. 3g.

9. See for example: Sisko J., Henry J.R. and Weinreb S.M. *J. Org. Chem.* **1993**, *58*, 4945.

10. a) Katzenellenbogen J.A. and Lenox R.S. *J. Org. Chem.* **1973**, *38*, 326; b) Wilson W.R. and Guazzaroni M.E. *J. Org. Chem.* **1989**, *54*, 3087; c) ref. 3k.

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