

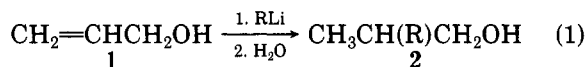
Additions of Organolithium Compounds to Unsaturated Tertiary Amines¹

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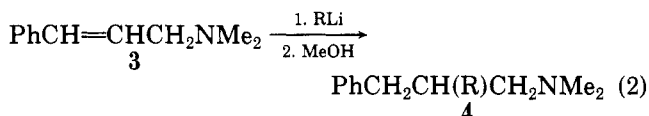
Crandall,² Felkin,³ and their co-workers were the first to note that reactions of allyl alcohol and some other allylic alcohols with an excess of an organolithium compound can lead to formation of addition products (e.g., 1 → 2, eq 1). Since organolithium compounds do not add as readily to



comparable hydrocarbons lacking a hydroxyl group,⁴ an intermediate metalated hydroxyl group must facilitate the additions. Additions to other allylic alcohols⁵ and also to homoallylic⁶ and propargylic alcohols⁷ have since been noted. Furthermore, several observations have indicated that alkoxy groups can assist additions of organolithium compounds to alkenes.⁸⁻¹⁰

We decided to investigate whether additions of organolithium compounds to carbon-carbon multiple bonds could also be assisted by amino groups. Reactions with unsaturated primary amines gave unexpected results, which are described elsewhere.¹¹ Some observations with unsaturated tertiary amines are reported here.

Addition product 4a was isolated in 52% yield from a reaction of 3 (eq 2) with *n*-butyllithium in refluxing hexane

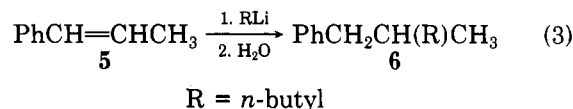


a, R = *n*-butyl; b, R = *tert*-butyl

for 6 h, and 4b was isolated in 56% yield from a similar reaction with *tert*-butyllithium. The ¹H NMR spectra of these products and of the corresponding ammonium ions (generated by dissolving the amines in trifluoroacetic acid)

are considerably more in accord with structure 4 than with PhCHRCH₂CH₂NMe₂, the isomer that would result from the other possible orientation of addition. No addition products were obtained from reactions of 3 with methyl-lithium in refluxing diethyl ether for 11 h or with phenyllithium in refluxing benzene-diethyl ether (70:30 v/v) for 20 h, and substantial amounts of 3 were recovered from both reactions.

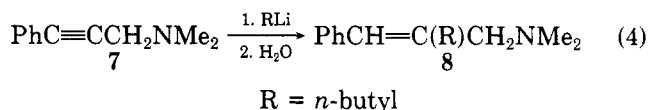
Since organolithium compounds can add to styrene and to other conjugated arylalkenes, the observation of additions to 3 does not necessarily indicate that the tertiary amino function facilitates addition. For that reason, we studied reactions of 5 (eq 3), a related compound lacking



the tertiary amino function. Addition product 6 was isolated in 29% yield from a reaction of 5 and *n*-butyllithium in refluxing hexane for 36 h. A significant amount of higher boiling material also was present, and no significant amount of 5 remained. However, a substantial amount of unreacted 5 and considerably less than 10% of 6 were present after reaction for only 6 h. These results indicate that addition to 5 is slower than to 3. This was confirmed by a reaction of equimolar amounts of 3 and 5 with a deficiency of *n*-butyllithium. Both a ¹H NMR spectrum and GC analysis of the distillate showed that addition product 4a and reactant 5 were the principal components and that addition product 6 was absent. The results of the experiments with 5 alone indicate that 6 would have been detected if a significant amount of addition to 5 had occurred. Therefore, we conclude that addition of *n*-butyllithium to 3 is faster than to 5 and that the tertiary amino function assists addition to 3.

No addition product was detected and a substantial amount of the substrate was recovered from a reaction of Me₂NCH₂CH=CHCH₂NMe₂ with *n*-butyllithium in refluxing hexane for 24 h. No other allylic amine in which the alkene function is not conjugated with an aromatic ring has been studied. However, since our work was initiated, a brief report appeared of addition of alkylolithium compounds to some tertiary amines with isolated homoallylic alkene functions.⁹

Addition product 8, isolated in 16% yield, and a large amount of undistillable material resulted from a reaction of 7 with *n*-butyllithium (eq 4) in refluxing hexane for 2 h. The configuration of 8 was not established.



Experimental Section

¹H NMR spectra were taken at 60 MHz. Sodium 2,2-dimethyl-2-silapentane-5-sulfonate was used as an internal standard in the trifluoroacetic acid solutions and Me₄Si in all others. Absorptions are reported with the following notations: s, singlet; d, doublet; q, quartet; m, a more complex multiplet or complex overlapping absorptions; br, broad. IR spectra were calibrated with a polystyrene film. High-resolution mass spectra were obtained by using an AEI Model MS-902 spectrometer. Microanalyses were performed by Midwest Microlab. Analytical and preparative GC separations were done with thermal conductivity instruments (helium was the carrier gas) and the following columns: A, 20% SE-30 on Chromosorb W (60-80 mesh), 0.25 in. × 5 ft (copper tubing); B, 15% Carbowax 20M on Gas Chrom P (60-70 mesh), 0.25 in. × 5 ft (aluminum tubing); C, 20% SF-96 on Gas Chrom Z (60-80 mesh), 0.25 in. × 5 ft (aluminum tubing).

(1) Most of this work is taken from: Heyn, A. S. M.S. Dissertation, The Pennsylvania State University, University Park, PA, 1970. Erickson, W. F. Ph.D. Dissertation, The Pennsylvania State University, University Park, PA, 1972.

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Samples were collected by using glass U-shaped tubes inserted into the exit port of the gas chromatograph and cooled in liquid nitrogen.

Materials. Amines 3 and 7 were prepared as described elsewhere.¹² Compound 5, a commercial sample, was distilled before use. Commercial (Alfa Inorganics) solutions of organolithium compounds were used. Hexane was stored over molecular sieves (4A).

Procedure for Reactions with Organolithium Compounds. Except where otherwise noted, the following procedure was used. A solution of the substrate was added slowly (15 min or more) to an ice-cooled, stirred solution of organolithium compound maintained under a positive pressure of nitrogen. The reaction mixture was heated as specified in each experiment and then cooled again before being quenched by slow addition of methanol (5–10 mL). The resulting mixture was filtered (some additional solvent sometimes was added to aid in this). The filtrate was washed with three portions of a saturated sodium bicarbonate solution and then dried (MgSO₄). Solvent was removed by distillation through a small column packed with glass helices (or sometimes by using a rotary evaporator), following which the column was removed and the residue distilled at reduced pressure.

Reactions of *N,N*-Dimethyl-3-phenyl-2-propen-1-amine (3). (a) **With *n*-Butyllithium; Isolation of 2-Benzyl-*N,N*-dimethyl-1-hexanamine (4a).** A solution of 3 (4.00 g, 24.8 mmol) in hexane (50 mL) was added to a hexane solution of *n*-butyllithium (27 mL, 2.35 M, 63 mmol). The resulting solution was heated at reflux temperature for 6 h, during which a suspension developed. Distillation gave 4a: 2.85 g (13.0 mmol, 52%); bp 90–95 °C (0.7 torr); ¹H NMR (CCl₄) δ 0.90 (m, 3, CH₂CH₃), 1.28 (m, 6, (CH₂)₃), 1.78 (m, 1, CH), ~2.0 (partially obscured m, 2, CH₂Ph or CH₂N), 2.15 (s, 6, N(CH₃)₂), 2.49 (d of d, *J* = 13, 7 Hz, 1, CHHPh or CHHN), 2.70 (d of d, *J* = 13, 5 Hz, 1, CHHPh or CHHN), 7.15 (m, 5, Ph); ¹H NMR (CF₃CO₂H) δ 0.92 (m, 3, CH₂CH₃), 1.40 (m, 6, (CH₂)₃), 2.16 (m, 1, CH), 2.74 (d, *J* = 5 Hz, 3, CH₃NCH₃), 2.84 (d, *J* = 5 Hz, 3, CH₃NCH₃), ~2.9 (partially obscured m, 2, CH₂Ph or CH₂N), 3.05 (m, 2, CH₂Ph or CH₂N), 7.28 (m, 5, Ph); mass spectrum, *m/z* 219.1992 (M⁺, calcd for C₁₅H₂₅N 219.1987). Anal. Calcd for C₁₅H₂₅N: C, 82.13; H, 11.49; N, 6.38. Found: C, 81.86; H, 11.34; N, 6.62. GC analysis (column A) showed only one significant peak.

(b) **With *tert*-Butyllithium; Isolation of 2-Benzyl-3,3-dimethyl-*N,N*-dimethyl-1-butanamine (4b).** A solution of 3 (3.00 g, 18.6 mmol) in pentane (40 mL) was added to a solution of *tert*-butyllithium (26 mL, 1.82 M, 47 mmol). The resulting suspension was heated at reflux temperature for 6 h. Distillation gave 4b: 2.30 g (10.5 mmol, 56%); bp 67–70 °C (0.4 torr); ¹H NMR (CCl₄) δ 0.92 (s, 9, C(CH₃)₃), 1.56 (m, at 100 MHz this absorption roughly resembled a quintet with *J* = 6 Hz, 1, CH), 1.98 (s, 6, N(CH₃)₂), 2.00 (partially obscured, probably d of d, *J* = 12.5, 7 Hz, 1, CHHPh or CHHN), 2.24 (d of d, *J* = 12.5, 5 Hz, 1, CHHPh or CHHN), 2.45 (d of d, *J* = 14, 7 Hz, 1, CHHPh or CHHN), 2.68 (d of d, *J* = 14, 5 Hz, 1, CHHPh or CHHN), 7.14 (m, 5, Ph); ¹H NMR (CF₃CO₂H) 1.06 (s, 9, C(CH₃)₃), 1.85 (m, 1, CH), 2.35 (d, *J* = 5 Hz, 3, CH₃NCH₃), 2.69 (d, *J* = 5 Hz, 3, CH₃NCH₃), 3.16 (m, 4, CH₂Ph and CH₂N), 7.38 (br s, 5, Ph); mass spectrum, *m/z* 219.1971 (M⁺, calcd for C₁₅H₂₅N 219.1987). Anal. Calcd for C₁₅H₂₅N: C, 82.13; H, 11.49; N, 6.38. Found: C, 82.31; H, 11.42; N, 6.49. GC analysis (column A) showed only one significant peak.

Reaction of 1-Phenyl-1-propene (5) with *n*-Butyllithium. Isolation of 2-Benzylhexane (6). A solution of 5 (4.0 g, 33.8 mmol) in hexane (40 mL) was added to a hexane solution of *n*-butyllithium (36.6 mL, 2.35 M, 86 mmol), and the resulting solution was heated at reflux temperature for 36 h. Distillation gave 6: 1.7 g (9.6 mmol, 29%); bp 44–47 °C (0.25 torr); ¹H NMR (CCl₄) δ 0.80 (d, *J* = 6 Hz, 3, CHCH₃), 0.88 (m, 3, CH₂CH₃), 1.24 (m, 6, (CH₂)₃), ~1.70 (m, 1, CH), 2.33 (d of d, *J* = 13, 6 Hz, 1, CHHPh), 2.59 (d of d, *J* = 13, 6 Hz, 1, CHHPh), 7.14 (m, 5, Ph). A second fraction (1.0 g) was obtained [bp 122–130 °C (0.15 torr)], but the material responsible for it was not identified.

A distillate of 2.2 g was obtained from a similar reaction that was heated at reflux for only 6 h. The distillate was mainly 5, containing less than 10% of 6.

Competition of 3 and 5 for a Limited Amount of *n*-Butyllithium. A solution of 3 (2.20 g, 13.6 mmol), 5 (1.61 g, 13.6 mmol), and decane (1.94 g, 13.6 mmol) in hexane (30 mL) was added to a hexane solution of *n*-butyllithium (5.0 mL, 2.35 M, 11.8 mmol) which had been diluted with additional hexane (10 mL). The resulting solution was heated at reflux temperature for 24 h. Distillation gave a liquid: 4.4 g; bp 25–150 °C (0.5 torr). The ¹H NMR spectrum showed principally absorptions due to 4, 5, and decane. GLC analysis (column B, the decane served as an internal standard) showed substantial peaks due to 4 and 5 and a small peak due to 3. No other significant peaks were observed.

Reaction of *N,N*-Dimethyl-3-phenyl-2-propyn-1-amine (7) with *n*-Butyllithium. Isolation of 2-Butyl-*N,N*-dimethyl-3-phenyl-2-propen-1-amine (8). A solution of 7 (2.00 g, 12.6 mmol) in hexane (25 mL) was added to a hexane solution of *n*-butyllithium (16 mL, 2.37 M, 38 mmol). The resulting solution was heated at reflux for 2 h. A precipitate appeared soon after refluxing began. Methanol (5 mL) and water (5 mL) were added carefully followed by diethyl ether and more water. The layers were separated, and the aqueous layer was extracted with two additional portions of diethyl ether. The combined organic layers were dried (MgSO₄), and most of the solvent was removed at reduced pressure. Distillation gave 8: 0.43 g (2.0 mmol, 16%); bp 84–95 °C (1.0 torr); ¹H NMR (CDCl₃) δ 0.93 (m, 3, CH₂CH₃), 1.35 (m, 4, (CH₂)₂CH₃), 2.24 (m, 8, N(CH₃)₂ and =CCH₂CH₂), 2.93 (br s, 2, CH₂N), 6.57 (br s, 1, =CH), 7.28 (m, 5, Ph); IR (CCl₄) 1650 cm⁻¹ (C=C). A sample of the distillate was purified by GC (column C, 175 °C) to free it from a trace of 7. Anal. Calcd for C₁₅H₂₃N: C, 82.89; H, 10.67; N, 6.44. Found: C, 82.82; H, 10.52; N, 6.74. A considerable amount of tar remained in the distillation flask.

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Registry No. 3, 33962-90-2; 4a, 33083-85-1; 4b, 33083-84-0; 5, 637-50-3; 6, 3200-11-1; 7, 2568-65-2; 8, 86969-86-0.

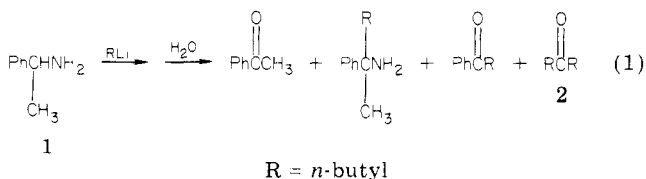
Fragmentation of Metalated Primary Amines Having Tertiary Organic Groups¹

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We have previously reported^{2,3} reactions, such as the example in eq 1, of primary amines and organolithium



compounds that lead to formation of (1) primary amines in which the organic group of the organolithium compound is incorporated at the α-carbon and (2) imines or compounds such as ketones that result from transformations of the imines following quenching of the reactions. The

(1) Most of this work is taken from: Cabré, S. M.S. Dissertation, The Pennsylvania State University, University Park, PA, 1975.

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