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Reaction of 1-*t*-Butyl-2-cyanoazetidine with Silver Nitrate or Silver Perchlorate

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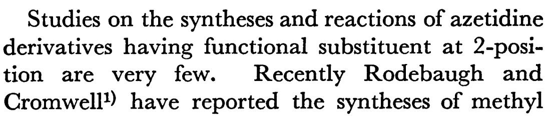
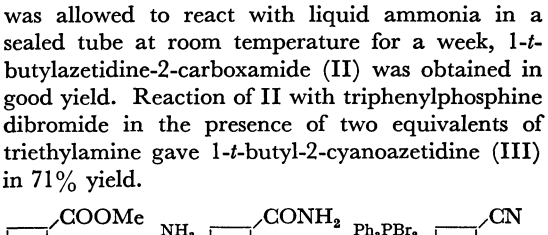
Studies on the syntheses and reactions of azetidine derivatives having functional substituent at 2-position are very few. Recently Rodebaugh and Cromwell[1] have reported the syntheses of methyl 1-alkylazetidine-2-carboxylates by the reaction of primary amines with methyl α,γ-dibromobutyrate, and these azetidine-2-carboxylates are suitable for our studies on the preparation and reactions of various azetidine derivatives.

We wish to report on the synthesis of 1-*t*-butyl-2-cyanoazetidine and its reactions with silver nitrate or silver perchlorate in ethanol anticipating the intermediacy of 1-*t*-butyl-1-azetinium salt.

When methyl 1-*t*-butylazetidine-2-carboxylate (I) was allowed to react with liquid ammonia in a sealed tube at room temperature for a week, 1-*t*-butylazetidine-2-carboxamide (II) was obtained in good yield. Reaction of II with triphenylphosphine dibromide in the presence of two equivalents of triethylamine gave 1-*t*-butyl-2-cyanoazetidine (III) in 71% yield.



It is known that α-aminonitriles afford iminium salts by silver nitrate.[2] Treatment of III, which is cyclic α-aminonitrile, with silver nitrate or silver perchlorate in absolute ethanol gave *t*-butyl-(3,3-diethoxypropyl)ammonium nitrate (VIa) or perchlorate (VIb) instead of the expected 1-*t*-butyl-1-azetinium nitrate or perchlorate (IV). The structure of VI was determined by means of elementary analysis, infrared spectrum and NMR spectrum.



In this reaction, silver cyanide was obtained almost quantitatively, which suggests the formation of azetinium salt (IV) as an intermediate. However, IV is highly strained and reacts easily with ethanol affording VI, presumably *via* 1-*t*-butyl-2-ethoxyazetidinium nitrate (Va) or perchlorate (Vb) as shown above. This mechanism is strongly supported by the fact that 1-phenyl-2-methoxy-3,3-dimethylazetidine is unstable and reacts with methanol to give anilinoacetal.[3] We found that 1-*t*-butyl-2-cyanoaziridine gave only adduct with silver perchlorate,[4] probably due to the difference of ring strain between azetidines and aziridines. Attempts to isolate IV by using aprotic solvents such as acetonitrile or methylene chloride were unsuccessful and gave only resinous product in spite of the formation of silver cyanide.

Experimental

1-*t*-Butylazetidine-2-carboxamide (II). A mixture of methyl 1-*t*-butylazetidine-2-carboxylate (8.6 g), liquid ammonia (50 m*l*) and aqueous methanol (1 : 1, 5 m*l*) was stirred in a sealed tube at room temperature for a week. Ammonia was evaporated by standing overnight at room temperature. Methanol and water were removed by vacuum distillation to give an oily residue which crystallized on standing for several hours. Recrystallized from *n*-hexane. Mp 80—81°C. Yield, 7.5 g (94%).

Found: C, 61.61; H, 10.02; N, 18.21%. Calcd for $C_8H_{16}ON_2$: C, 61.50; H, 10.32; N, 17.93%.

Picrate: mp 186.5—187.5°C.

Found: C, 43.91; H, 5.25; N, 18.11%. Calcd for $C_{14}H_{19}O_8N_5$: C, 43.64; H, 4.97; N, 18.18%.

1-*t*-Butyl-2-cyanoazetidine (III). To a solution of triphenylphosphine dibromide (prepared from 27.5 g of triphenylphosphine, 16.8 g of bromine and 21.2 g of triethylamine) in acetonitrile (120 m*l*) was added a solution of amide (II) in acetonitrile (30 m*l*). After heating for 20 min, acetonitrile was removed in a vacuum and the residue was extracted with petroleum ether, dried over anhydrous sodium sulfate and the solvent was removed by distillation. The residual oil was distilled under reduced pressure. Bp 55—56.5°C/2.5 mmHg. Yield, 8.6 g (71%). NMR ($CDCl_3$, τ): 8.98 (9H, singlet), 7.38—7.92 (2H, multiplet), 6.72—6.92 (2H, multiplet), 6.02 (1H, triplet).

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[1] R. M. Rodebaugh and N. H. Cromwell, *J. Heterocycl. Chem.*, **5**, 309 (1968).

[2] H. G. Reiber and T. D. Stewart, *J. Amer. Chem. Soc.*, **62**, 3026 (1940).

[3] F. Nerdel, P. Weyerstahl and K. Zabel, *Chem. Ber.*, **102**, 1606 (1969).

[4] K. Ichimura, Ph. D. Thesis, Tokyo Institute of Technology (1968).

Found: C, 69.57; H, 9.98; N, 20.00%. Calcd for $C_8H_{14}N_2$: C, 69.52; H, 10.21; N, 20.27%.

Picrate: mp 158—159°C (decomp.).

Found: C, 46.01; H, 4.43; N, 19.05%. Calcd for $C_{14}H_{17}O_7N_5$: C, 45.78; H, 4.69; N, 19.07%.

Perchlorate: mp 170—171°C (decomp.).

Found: C, 40.23; H, 6.04; N, 11.81%. Calcd for $C_8H_{15}O_4N_2Cl$: C, 40.26; H, 6.34; N, 11.74%.

Reaction of III with Silver Nitrate in Ethanol. To a suspension of silver nitrate (2.84 g) in 15 m*l* of ethanol, was added dropwise a solution of III in ethanol (5 m*l*). After stirring for 3 hr at room temperature, silver cyanide was filtered off, the filtrate was concentrated in a vacuum and absolute ether was added to give 2.9 g of VIa. Recrystallized from ethyl acetate–ligroin; mp 71.5—73°C.

Found: C, 49.36; H, 9.65; N, 10.71%. Calcd for $C_{11}H_{26}O_5N_2$: C, 49.60; H, 9.84; N, 10.52%. IR (KBr): 2700—2300, 2030, 1575 cm^{-1} (NH_2^+), 1405, 1370, 830 cm^{-1} (NO_3^-), 1135, 1110, 1075 cm^{-1} (C–O–C). NMR ($CDCl_3$, τ): 8.81 (6H, triplet), 8.60 (9H, singlet), 7.92 (2H, quartet), 6.87 (2H, broad singlet), 6.25—6.60 (4H, multiplet), 5.37 (1H, triplet), 1.55 (2H, broad singlet).

Reaction of III with Silver Perchlorate in Ethanol. The procedure was the same as described above. Starting from 2.76 g of III, 4.7 g of VIb was obtained; mp 89.5—90°C (ethyl acetate–ligroin).

Found: C, 43.64; H, 8.35; N, 4.85%. Calcd for $C_{11}H_{26}O_6NCl$: C, 43.49; H, 8.63; N, 4.61%.