Pergamon

Tetrahedron Letters 41 (2000) 795–796

TETRAHEDRON LETTERS

A facile one-pot conversion of non-enolizable aldehydes to diazirines

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Received 14 October 1999; revised 16 November 1999; accepted 17 November 1999

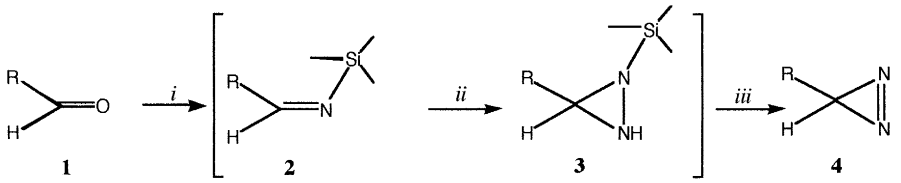
Abstract

A general route to monoalkyl diazirines from non-enolizable aldehydes through *N*-trimethylsilyl diaziridines is described.

Keywords: carbene sources; diazirines; aldehydes; *N*-trimethylsilyl imines.

Diazirines are valuable precursors of carbenes. A variety of preparations have been reported for the syntheses of dialkyl diazirines from ketones,[1] but fewer options are available for mono alkyl diazirines derived from aldehydes.[2] This is particularly true in the case of aryl aldehydes. One of the reasons for this difficulty is the instability of the intermediate diaziridines. To overcome this problem the most widely used general synthetic preparation, discovered by Schmitz in the early sixties,[2a] requires a large excess of the aldehyde to prepare a diaziridine triazolidine intermediate.[3] Knowles discovered that these species hydrolyze rapidly when R=aryl resulting in poor yields of 3-aryl-3-*H* diazirines.

Herein, we report a new approach to diazirines whereby stabilization of the intermediate diaziridine is achieved by substitution of one of the reactive hydrogens with a trimethylsilyl group (Scheme 1).



a : R = 3-noradamantyl; **b** : R = 1-adamantyl; **c** : R = t-Bu ; **d** : R = Ph

Scheme 1. (i) LiHMDS, THF, ice bath; (ii) NH_2OSO_3H; (iii) *t*-BuOCl

We found that if aldehydes **1** are converted first to the *N*-(trimethylsilyl) imines **2** by reaction with lithium bis(trimethylsilyl)amide,[4] then addition of the hydroxylamine-*O*-sulfonic acid in the presence of base affords the corresponding *N*-trimethylsilyl diaziridines **3** which are sufficiently stable, for our

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0040-4039/00/$ - see front matter
PII: S0040-4039(99)02213-3

purposes, to the reaction conditions. Transformation of these intermediates to alkyldiazirines **4** was achieved by oxidation with *tert*-butylhypochlorite or *N*-chlorosuccinimide.

This three-step, one-pot synthesis, is best performed on non-enolizable substrates. Relatively good yields with tertiary alkyl aldehydes were realized when the reaction was carried out at 0°C. In the case of benzaldehyde **1d** we found that the corresponding *N*-trimethylsilyldiaziridine **3d** was less stable than its alkyl counterparts and required cooling to about –30°C. We observed partial decomposition of phenyldiazirine **4d** during purification on a silica gel column. However, the 12% yield of the pure product realized in this case was comparable with the best previously reported two-step procedures (13%).[2b]

The following experimental procedure is typical: To a stirred solution of 3-noradamantanecarbaldehyde[5] **1a** (0.150 g, 1 mmol) in dry THF under argon (1.5 mL) cooled in an ice bath, 1 M lithium bis(trimethylsilyl) amide solution in THF (2 mL) was added dropwise via syringe. After the addition was complete the mixture was stirred for 0.5 h at 0°C, cooled to −30°C and a solution of hydroxylamine-*O*-sulfonic acid (0.126 g, 1 mmol) in dry diglyme (1 mL) was added dropwise. The mixture was stirred at 0°C for 1 h, then a solution of freshly prepared *tert*-butylhypochlorite[6] (0.11 mL, 1 mmol) in *tert*-butanol (0.12 mL) was added dropwise. (**CAUTION!** When *tert*-butylhypochlorite was added in one portion explosive decomposition of a 10 mmol scale reaction mixture occurred!) The mixture was stirred for another 1 h in the ice bath,[7] poured into water (15 mL), extracted with pentane,[8] washed with water, dried over sodium sulfate, concentrated with a rotory evaporator at room temperature and purified by column chromatography on silica gel with pentane. Evaporation of the solvent afforded (3-noradamantyl)diazirine **4a** (0.11 g, 67%).[9]

Acknowledgements

We thank the National Science Foundation for generous support of this work through Grant CHE-9613861.

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7. In the case of benzaldehyde **1d** hydroxylamine-*O*-sulfonic acid was added to the mixture at −50°C, the mixture was stirred at −30°C for 2 h, then *tert*-butylhypochlorite was added dropwise, the mixture was allowed to reach 0°C and stirred for 0.5 h.
8. For the reaction with pivalaldehyde **1c** (7 mmol) *N*-chlorosuccinimide (8 mmol, 18 h at 0–5°C) was used as the oxidant instead of *tert*-butylhypochlorite. The mixture was extracted with decane, washed with water, and dried over sodium sulfate. A slow stream of dry argon was bubbled through the decane solution, and the gas was passed through a 0°C trap to remove most of the solvent and hexamethyldisiloxane. Volatiles were collected in a −78°C trap. Final purification of *tert*-butyldiazirine[2c] **4c** was achieved by preparative GC. Yield 41%.
9. Diazirines **4a**,**b** are colorless liquids: Compound **4a**, yield 67%. ^{1}H NMR ($CDCl_3$) δ 0.96 (s, 1H), 1.41–1.65 (m, 10H), 2.17 (m, 2H), 2.24 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 26.8, 34.9, 37.0, 41.3, 43.8, 46.0, 47.9, IR 1582 cm^{-1}. UV (pentane) λ_{max} 340 nm. HRMS: 134.1090 (M^+-N_2); calcd: 134.1096 for $C_{10}H_{14}$. Compound **4b**, yield 45%. ^{1}H NMR ($CDCl_3$) δ 0.41 (s, 1H), 1.29 (m, 6H), 1.51 (m, 3H), 1.60 (m, 3H), 1.86 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 28.32, 29.79, 31.80, 36.94, 39.64. IR 1588 cm^{-1}. UV (pentane) λ_{max} 340, 352 nm. HRMS: 176.1304 (M^+); calcd: 176.1317 for $C_{11}H_{16}N_2$; Compound **4d**, yield 12%.