Preparation of the Racemic Minor Diastereomer of 3-Hydroxy-4-(trimethylammonio)pentanoic Acid Chloride (2). Minor diastereomer **4b** was quaternized with CH_3I and hydrolyzed in concentrated HCl to form racemic minor diastereomer **2** according to the procedure reported[10] for the preparation of racemic major diastereomer **2** from **4a**. Yields were essentially the same as those observed for the major diastereomer. For racemic minor diastereomer **2**: mp 190–192 °C dec (EtOH/Et_2O); ^1H NMR (D_2O) δ 4.93–4.40 (m, 1 H, C*H*OH), 3.46 (q, 1 H, C*H*CH_3), 3.1 (s, 9 H, $N(CH_3)_3$), 2.56 (d, 2 H, C*H*$_2CO_2H$), 1.37 (m, 3 H, CHC*H*$_3$); IR (KBr) 1718 (C=O) cm^{-1}.

Anal. Calcd for $C_8H_{18}NO_3Cl\cdot{}^1/_4H_2O$: C, 44.44; H, 8.62; N, 6.48. Found: C, 44.47; H, 8.66; N, 6.46.

This unusually hygroscopic salt was also analyzed as the tetraphenylborate derivative:[15] mp 156–160 °C dec (acetone/H_2O). Anal. Calcd for $C_{32}H_{38}NO_3B$: C, 77.57; H, 7.73; N, 2.83. Found: C, 77.53; H, 7.75; N, 2.83.

Preparation of the Four Stereoisomers of 3-Hydroxy-4-(trimethylammonio)pentanoic Acid Chloride (2a–d). Compounds **8a–d** were each hydrolyzed in 3 N HCl and purified by ion-exchange chromatography according to the procedure used above for the syntheses of **1a** and **1b** to provide 90% yields of 4-methylcarnitines **2a–d**, respectively. The hygroscopic products were crystallized from 1:1 EtOH/Et_2O to provide white solids. For enantiomers **2a** and **2b**, the 300-MHz ^1H NMR spectra were identical with that for the racemic major diastereomer of **2** (previously reported).[10] Additionally, for **2a**: mp 190–191 °C dec (EtOH/Et_2O); $[\alpha]^{23}_{D}$ −11.6° (*c* 0.870, H_2O). For **2b**: mp 188.5–190 °C dec (EtOH/Et_2O); $[\alpha]^{23}_{D}$ +11.6° (*c* 0.830, H_2O).

For enantiomers **2c** and **2d**, the 300-MHz ^1H NMR spectra were identical with that for the racemic minor diastereomer of **2** (given above). Additionally, for **2c**: mp 199.5–200.5 °C dec (EtOH/Et_2O); $[\alpha]^{22}_{D}$ +17.4° (*c* 1.07, H_2O). For **2d**: mp 204.5–205.5 °C dec (EtOH/Et_2O); $[\alpha]^{22}_{D}$ −16.9° (*c* 0.830, H_2O).

A Novel Route to 1-Vinyl-1,2,4-triazoles by the Fluoride-Catalyzed Peterson Reaction of 1-[Bis(trimethylsilyl)methyl]-1,2,4-triazole with Carbonyl Compounds

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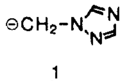
We recently found that the reaction of carbonyl compounds with (1,2,4-triazol-1-yl)methyl anion (**1**) generated from the fluoride-induced desilylation of 1-[(trimethylsilyl)methyl]-1,2,4-triazole (**2**) leads to 2-(1,2,4-triazol-1-yl)ethanols.[1] We now report that 1,2,4-triazol-1-yl(trimethylsilyl)methyl anion (**3**), generated from fluoride-induced desilylation of 1-[bis(trimethylsilyl)methyl]-1,2,4-triazole (**4**), reacts with carbonyl compounds **5** to give 1-vinyl-1,2,4-triazoles **7** in good yields.



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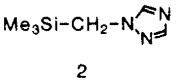

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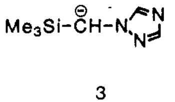

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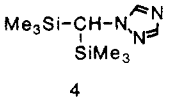
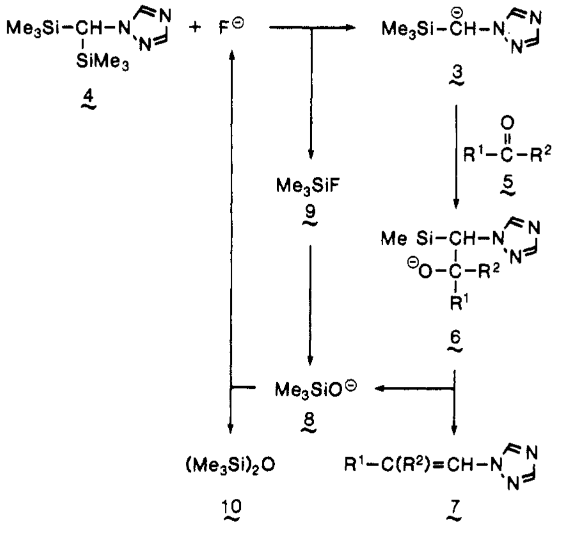


4

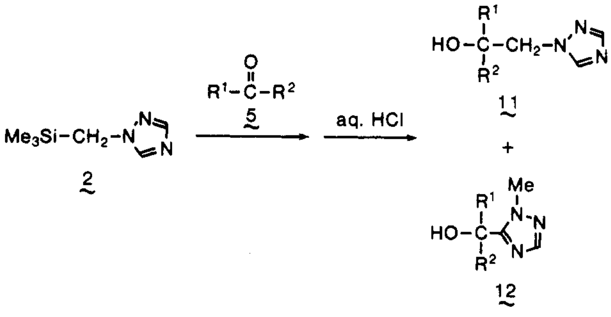
Results and Discussion

Preparation of 1-[Bis(trimethylsilyl)methyl]-1,2,4-triazole (4). Treatment of 1,2,4-triazole with bis(trimethylsilyl)chloromethane[2] in the presence of potassium carbonate in DMF at 60 °C gave **4** (61%) accompanied by **2** (4%), which could be removed by flash chromatography. The formation of **2** is considered to proceed via **4**, which undergoes nucleophilic attack by the 1,2,4-triazol-1-yl anion under the reaction conditions to cause cleavage of the carbon–silicon bond. Prolongation of the reaction time to more than 40 h decreased the yield of **4** but increased the formation of **2**.

Scheme I



Scheme II



Fluoride-Catalyzed Reaction of 1-[Bis(trimethylsilyl)methyl]-1,2,4-triazole (4) with Carbonyl Compounds 5. 1-[Bis(trimethylsilyl)methyl]-1,2,4-triazole (**4**) reacted smoothly with carbonyl compounds **5** in the presence of a catalytic amount of tetrabutylammonium fluoride (TBAF) in THF at −20 °C to give the 1-vinyl-1,2,4-triazoles **7** in good yields. The results are summarized in the Table I. Although 1 equiv of base is generally necessary for silicon elimination of a β-silylethanol,[3] the formation of **7** proceeded with a catalytic amount of TBAF. This catalytic Peterson reaction can be explained by the process shown in the Scheme I. Fluoride anion induced desilylation of **4** generates the anion **3** by addition to the carbonyl compound **5**, leading to β-silylethoxide **6**. The subsequent elimination reaction of **6** affords the 1-vinyl-1,2,4-triazole **7** and the alkoxide **8**, which reacts with the fluorosilane **9** to regenerate fluoride anion. In other work, it has been reported that bis(trimethylsilyl)methyl isothiocyanate[4] undergoes a similar fluoride-catalyzed Pe-

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Table I. TBAF-Catalyzed Reaction of 1-[Bis(trimethylsilyl)methyl]-1,2,4-triazole (4) with Carbonyl Compounds 5

entry	carbonyl compd	time, h	products[a] (isomer ratio, % yield)
1	p-ClC$_6$H$_4$CHO	2	**7a** p-ClC$_6$H$_4$CH=CHT (1:1, 89)
2	C$_6$H$_5$COC$_6$H$_5$	4	**7b** (C$_6$H$_5$)$_2$C=CHT (89)
3	p-ClC$_6$H$_4$COCH$_3$	5	**7c** p-ClC$_6$H$_4$C(CH$_3$)=CHT (1:1, 80)
4	C$_6$H$_5$CH$_2$CH$_2$CHO	0.5	**7d** C$_6$H$_5$CH$_2$CH$_2$CH=CHT (3:2, 82)
5	cyclohexanone	4	**7e** c-C$_5$H$_{10}$C=CHT (40)
6[b]	β-tetralone	4	... (0)

[a] T = 1,2,4-triazol-1-yl. Isolated yields as a mixture of isomers whose ratio E/Z was determined by ^{1}H NMR spectra. No attempt was made to separate and determine the configuration of two components. [b] 98% β-tetralone was recovered.

terson reaction, whereas bis(trimethylsilyl)dichloromethane[5] does not.

In the case of β-tetralone, which has the most enolizable carbonyl group, no product was obtained, and β-tetralone was recovered (97.5%, entry 6) due to formation of the enolate anion by proton transfer to the anion **3**.

Although the anion **3** reacted selectively with **5** to give **7**, anion **1**[1] generated from **2** acted as a base as well as a nucleophile to remove the proton at the 5-position of the triazole ring, which gave the 1,2,4-triazol-5-yl compound **12**, accompanied by the production of 1,2,4-triazol-1-yl compound **11**[6] (Scheme II). This could be attributed to the action of the silicon atom, which stabilizes the adjacent carbanion in anion **3** lowering the basicity of **3** below that of **1**.

Experimental Section

Melting points were determined on a Büchi apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Varian T-60 or EM-390 instrument with Me$_4$Si as an internal standard. A Hitachi 260-10 spectrophotometer was used to obtain IR spectra. Chromatography was performed on 230–400-mesh silica gel.

1-[Bis(trimethylsilyl)methyl]-1,2,4-triazole (4). A suspension of 1,2,4-triazole (2 g, 29 mmol), bis(trimethylsilyl)chloromethane[2] (6.2 g, 32 mmol), powdered K$_2$CO$_3$ (4.8 g, 35 mmol), and dry DMF (62 mL) was stirred at 60 °C for 40 h. The resulting mixture was poured into ice water and extracted with Et$_2$O. The organic layer was washed with water, dried (Na$_2$SO$_4$), and evaporated. The residue was chromatographed on silica gel. The fractions eluted with benzene–AcOEt (4:1) gave 3.99 g (61%) of **4**: mp 27–30 °C; bp 100–101 °C (6 mm); ^{1}H NMR (Me$_3$SO-d_6) δ 0.03 (s, 18 H, methyl), 3.79 (s, 1 H, methine), 7.86 (s, 1 H, 3-position of triazole), 8.23 (s, 1 H, 5-position of triazole); IR (neat) 2950, 1485, 1250, 1140, 1005, 845, 655 cm^{-1}. This material was converted to its oxalate: 82% yield from the free base; mp (oxalate) 113–122 °C [Et$_2$O–(i-Pr)$_2$O]. Anal. Calcd for C$_{11}$H$_{23}$O$_4$N$_3$Si$_2$: C, 41.61; H, 7.30; N, 13.24. Found: C, 41.48; H, 7.26; N, 13.35.

The fractions eluted with benzene–AcOEt (1:1) gave 195 mg (4%) of **2** as an oil, which was identified by ^{1}H NMR spectra.

General Procedure for TBAF-Catalyzed Reaction of 1-[Bis(trimethylsilyl)methyl]-1,2,4-triazole (4) with Carbonyl Compounds. To a solution of carbonyl compound (200 mg, 1.1–2.0 mmol) and **4** (1.2 mol equiv/mol of carbonyl compound) in dry THF (2.7 mL/mmol of carbonyl compound) under nitrogen atmosphere at −20 °C was added anhydrous TBAF (0.1 mol equiv/mol of carbonyl compound, 1 M in THF). The mixture was stirred at −20 °C for the period shown in Table I. The reaction mixture was poured into ice water and extracted with Et$_2$O. The organic layer was washed with water, dried (Na$_2$SO$_4$), and evaporated. The residue was purified by flash chromatography, and the results are summarized in Table I.

1-(4-Chlorophenyl)-2-(1,2,4-triazol-1-yl)ethylene (7a): 1:1 mixture of E and Z isomers as a semisolid; mp ~102.5 °C; IR (Nujol) 1655 ($\nu_{C=C}$) cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 6.43 (d, 0.5 H, J = 9.6 Hz, vinyl), 6.84–7.52 (m, 5.5 H, vinyl, phenyl), 7.90 (s, 0.5 H, 3-position of triazole), 7.95 (s, 0.5 H, 5-position of triazole), 7.98 (s, 0.5 H, 3-position of triazole), 8.24 (s, 0.5 H, 5-position of triazole). Anal. Calcd for C$_{10}$H$_8$ClN$_3$: C, 58.41; H, 3.92; Cl, 17.24; N, 20.43. Found: C, 58.40; H, 3.82; Cl, 17.33; N, 20.22.

1,1-Diphenyl-2-(1,2,4-triazol-1-yl)ethylene (7b): mp 65–67 °C [(i-Pr)$_2$O–petroleum ether]; IR (Nujol) 1645 ($\nu_{C=C}$) cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.08–7.48 (m, 12 H, vinyl, phenyl, 3-position of triazole), 7.89 (s, 1 H, 5-position of triazole). Anal. Calcd for C$_{16}$H$_{13}$N$_3$: C, 77.71; H, 5.30; N, 16.99. Found: C, 77.92; H, 5.18; N, 16.96.

2-(4-Chlorophenyl)-1-(1,2,4-triazol-1-yl)-1-propene (7c): 1:1 mixture of E and Z isomers as an oil; IR (neat) 1650 ($\nu_{C=C}$) cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 2.18 (d, 1.5 H, J = 1.7 Hz, methyl), 2.28 (d, 1.5 H, J = 1.4 Hz, methyl), 6.83–7.43 (m, 5 H, vinyl, phenyl), 7.51 (s, 0.5 H, 3-position of triazole), 7.89 (s, 0.5 H, 5-position of triazole), 8.04 (s, 0.5 H, 3-position of triazole), 8.24 (s, 0.5 H, 5-position of triazole). Anal. Calcd for C$_{11}$H$_{10}$ClN$_3$: C, 60.14; H, 4.59; Cl, 16.14; N, 19.13. Found: C, 60.13; H, 4.80; Cl, 16.14; N, 18.92.

4-Phenyl-1-(1,2,4-triazol-1-yl)-1-butene (7d): 3:2 mixture of E and Z isomers as an oil; IR (neat) 1670 ($\nu_{C=C}$) cm^{-1}; ^{1}H NMR (Me$_2$SO-d_6) δ 2.30–2.89 (m, 4 H, methylene), 5.32–5.64 (m, 0.4 H, vinyl), 6.13–6.46 (m, 0.6 H, vinyl), 6.92–7.36 (m, 6 H, vinyl, phenyl), 8.06 (s, 0.6 H, 3-position of triazole), 8.12 (s, 0.4 H, 3-position of triazole), 8.64 (s, 0.4 H, 5-position of triazole), 8.71 (s, 0.6 H, 5-position of triazole). Anal. Calcd for C$_{12}$H$_{13}$N$_3$: C, 72.34; H, 6.58; N, 21.09. Found: C, 71.97; H, 6.50; N, 20.76.

(1,2,4-Triazol-1-yl)cyclohexylidenemethane (7e): mp 50.5–52.5 °C (petroleum ether); IR (Nujol) 1670 ($\nu_{C=C}$) cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 1.39–1.82 (m, 6 H methylene), 2.07–2.42 (m, 4 H, allyl), 4.56 (s, 1 H, vinyl), 7.96 (s, 1 H, 3-position of triazole), 8.03 (s, 1 H, 5-position of triazole). Anal. Calcd for C$_9$H$_{13}$N$_3$: C, 66.23; H, 8.03; N, 25.74. Found: C, 66.51; H, 7.98; N, 25.64.

Registry No. **2**, 103817-03-4; **4**, 107743-46-4; **4**·oxalate, 107743-47-5; **5**(R^1 = 4-ClC$_6$H$_4$,R^2 = H), 104-88-1; **5**(R^1 = R^2 = Ph), 119-61-9; **5**(R^1 = 4-ClC$_6$H$_4$, R^2 = Me), 99-91-2; **5**(R^1 = Ph(CH$_2$)$_2$,R^2 = H), 104-53-0; **5**(R^1 = R^2 = c-C$_5$H$_9$), 108-94-1; (E)-**7a**, 107743-48-6; (Z)-**7a**, 107743-49-7; **7b**, 84595-58-4; (E)-**7c**, 107743-50-0; (Z)-**7c**, 107743-51-1; (E)-**7d**, 107743-52-2; (Z)-**7d**, 107743-53-3; **7e**, 107743-54-4; **11**(R^1 = R^2 = Ph), 76674-04-9; **12**(R^1 = R^2 = Ph), 103817-08-9; TBAF, 429-41-4; (Me$_3$Si)$_2$CHCl, 5926-35-2; 1,2,4-triazole, 288-88-0.

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[6] For example, 1-[(trimethylsilyl)methyl]-1,2,4-triazole (**2**) reacted with benzophenone (**5**, R^1 = R^2 = Ph) in the presence of a catalytic amount of TBAF to give 2-(1,2,4-triazol-1-yl)ethanol (**11**, R^1 = R^2 = Ph; 21%) and (1-methyl-1,2,4-triazole-5-yl)methanol (**12**, R^1 = R^2 = Ph; 46%) after acid-catalyzed hydrolysis.

Preparation of 3-Substituted 4-Methylfurans: 3-Iodo-4-methyl- and 3-Formyl-4-methylfuran

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The furan ring occurs frequently in sesquiterpenes. However, among the many syntheses available,[1] only a few

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