3-Chloro-5-iodo-2,6-pyrazinediamine (3). Pyrazinecarboxylic acid **2a**,[17] 9.45 g (50.0 mmol), was suspended in 250 mL of dry DMF under a nitrogen atmosphere and heated to 80 °C until a homogeneous solution was obtained. To the above solution was added 27.92 g (110.0 mmol) of iodine in 125 mL of DMF over the course of 0.5 h. At the end of the addition, the solution was kept at 80 °C for an additional 0.5 h before being cooled to room temperature. The reaction mixture was poured into 500 mL of stirred water; to the stirred solution was then added 1.0 L of saturated aqueous sodium thiosulfate. The aqueous solution was extracted with five 350-mL portions of ethyl acetate. The combined ethyl acetate washes were extracted: two times with 350-mL of $Na_2S_2O_3$ (saturated), two times with 350 mL of $NaHCO_3$ (saturated), and two times with 350 mL of water. The solution was dried with magnesium sulfate, and the solvent was removed under reduced pressure with a 35 °C water bath. The crude solid, 11.42 g, was dissolved in 70 mL of hot toluene, treated with decolorizing charcoal, and filtered hot, and the volume was reduced to 45 mL. Upon standing overnight at 5 °C, 8.75 g (65%) of yellow needles were obtained: mp 130 °C; TLC R_f 0.22 (A); ^{1}H NMR ($CDCl_3$) δ 4.69 (s); ^{13}C NMR (DMSO-d_6) δ 153.7, 150.1, 116.6, 78.8; MS (EI) 272 (M^+ + 2, 33), 270 (base). Anal. Calcd for $C_4H_4ClIN_4$: C, 17.76; H, 1.49; Cl, 13.10; N, 20.71. Found: C, 18.04; H, 1.54; Cl, 13.05; N, 20.80.

Preparation of 3-Chloro-5-(1-heptynyl)-2,6-pyrazinediamine (4a). Typical Procedure for Synthesis of Pyrazinylalkynes. In 150 mL of dry diethylamine[18] was dissolved 5.4 g (20.0 mmol) of iodide **3** under an inert atmosphere. To the stirred solution was added 0.35 g (0.5 mmol) of bis(triphenylphosphine)palladium dichloride,[19] followed by 3.13 mL (24.0 mmol) of 1-heptyne.[12] Copper(I) iodide, 0.047 g (0.25 mmol), was then added, and stirring was continued under nitrogen until all iodide **3** had been consumed as determined by TLC (~18 h). Solvent was removed under vacuum, and the crude product mixture dissolved in 500 mL of $CHCl_3$ and extracted with three 100-mL portions of H_2O. The chloroform extracts were then filtered through 300 mL of neutral alumina and reduced in volume. Flash chromatography yielded 3.61 g (76%) of material. It was then dissolved in 100 mL of hot toluene and filtered, and the volume was reduced to 30 mL. Upon standing at 5 °C, 2.99 g (63%) of product was obtained: mp 106–107 °C; TLC R_f 0.58 (B); ^{1}H NMR ($CDCl_3$) δ 4.8 (br, 4 H, NH_2), 2.46 (t, J = 10.5 Hz, 2 H), 1.62 (quintet, J = 10.5 Hz, 2 H), 1.33 (m, 4 H), 0.95 (t, J = 7 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 153.6, 148.6, 119.7, 112.0, 95.7, 75.2, 30.9, 28.1, 21.9, 19.4, 13.7; MS (CI) 239 (M^+ + 1, base). Anal. Calcd for $C_{11}H_{15}N_4Cl$: C, 55.34; H, 6.33; N, 23.45; Cl, 14.85. Found: C, 55.54; H, 6.35; N, 23.21; Cl, 14.90.

6-(3,5-Diamino-6-chloropyrazinyl)-6-hexynol (4b): mp 89–90 °C (from toluene); TLC R_f 0.2 (C); ^{1}H NMR ($CDCl_3$) δ 4.6 (br, 4 H, NH_2), 3.7 (s, 1 H, OH), 2.5 (t, J = 10.0 Hz, 2 H), 1.7 (m, 4 H); ^{13}C NMR (DMSO-d_6) δ 154.9, 149.7, 117.1, 109.0, 94.3, 76.2, 60.3, 31.8, 24.8, 18.9; MS (CI), 241 (M^+ + 1, base). Anal. Calcd for $C_{10}H_{13}N_4OCl$: C, 49.90; H, 5.44; N, 23.27; Cl, 14.72. Found: C, 50.19; H, 5.50; N, 22.90; Cl, 14.78.

3-Chloro-5-(6,6-diethoxy-1-hexynyl)-2,6-pyrazinediamine (4d): yellow oil; TLC R_f 0.8 (D); ^{1}H NMR (DMSO-d_6) δ 6.48 (s, NH_2, 2 H), 6.07 (s, NH_2, 2 H), 4.51 (t, J = 7 Hz, 1 H), 3.54 (m, 2 H), 3.43 (m, 2 H), 2.45 (t, J = 7 Hz, 2 H), 1.60 (m, 4 H), 1.10 (t, J = 7 Hz, 6 H). Anal. Calcd for $C_{14}H_{21}ClN_4O_2$: C, 53.76; H, 6.77; N, 17.91. Found: C, 53.59; H, 6.78; N, 17.77.

Preparation of 1-(3,5-Diamino-6-chloropyrazinyl)-1-heptanone (5a). Typical Alkyne Hydration Procedure. To **4a** (0.5 g, 2.10 mmol) dissolved in 50 mL of methanol was added 3.3 mL of 0.1 M sodium sulfide (0.33 mmol) and 2.0 mL of 10% hydrochloric acid (2.4 mmol); the mixture was heated to reflux temperature for 0.5 h. The cooled reaction suspension was filtered through Celite with methanol as eluent (2 × 80 mL). The solvent was removed in vacuo, and the oil was flash chromatographed on silica with $CHCl_3$; recrystallization from toluene yielded 0.48 g (89%) of product: mp 119–120 °C; TLC R_f 0.20 (B); ^{1}H NMR (DMSO-d_6) δ 8.38–7.12 (band, NH_2, 4 H), 2.82 (t, J = 7 Hz, 2 H), 1.54 (m, 2 H), 1.26 (m, 6 H), 0.89 (t, J = 8 Hz, 3 H); MS (EI) m/e 256 (M^+, 20), 186 (base). Anal. Calcd for $C_{11}H_{17}N_4OCl$: C, 51.46; H, 6.67; N, 21.82. Found: C, 51.63; H, 6.47; N, 21.81.

1-(3,5-Diamino-6-chloropyrazinyl)-6-hydroxy-1-hexanone (5b): mp 137–139 °C; TLC R_f 0.57 (E); ^{1}H NMR (DMSO-d_6) δ 8.24 (s, NH, 1 H), 7.73–6.92 (s, NH, 3 H), 3.76 (s, OH, 1 H), 3.37 (t, J = 7 Hz, 2 H), 2.85 (t, J = 7 Hz, 2 H), 1.53 (m, 2 H), 1.40 (m, 2 H), 1.30 (m, 2 H); ^{13}C NMR (DMSO-d_6) δ 198.6, 155.0, 153.4, 118.6, 118.4, 60.6, 36.3, 32.4, 25.4, 24.4; MS (CI) 259 (M^+ + 1, base). Anal. Calcd for $C_{10}H_{15}ClN_4O_2$: C, 46.43; H, 5.84; N, 21.66. Found: C, 46.03; H, 5.89; N, 21.36.

1-(3,5-Diamino-6-chloropyrazinyl)-6,6-dimethoxy-1-hexanone (5d): oil; TLC R_f 0.5 (D); ^{1}H NMR (DMSO-d_6) δ 8.19 (s, NH, 1 H), 7.33 (m, NH, 3 H), 4.30 (t, J = 8 Hz, 1 H), 3.22 (s, OCH_3, 6 H), 2.82 (t, J = 7.5 Hz, 2 H), 1.53 (m, 4 H), 1.28 (m, 2 H). Anal. Calcd for $C_{12}H_{19}ClN_4O_3$: C, 47.60; H, 6.33; N, 18.50. Found: C, 47.43; H, 6.11; N, 18.18.

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Registry No. **2a**, 4878-36-8; **3**, 118476-03-2; **4a**, 118476-04-3; **4b**, 118476-05-4; **4c**, 118476-06-5; **4d**, 118476-07-6; **5a**, 118476-08-7; **5b**, 118476-09-8; **5c**, 118476-10-1; **5d**, 118476-11-2; **6a**, 118476-12-3; **6b**, 118476-14-5; **6c**, 118476-13-4; **6d**, 113195-44-1; **6e**, 118476-15-6; **6f**, 64146-61-8; **6g**, 14374-45-9; **6h**, 118476-16-7; **6i**, 118476-17-8; **7a**, 69561-06-4; **7c**, 53033-83-3; **7d**, 118476-18-9; **7f**, 69287-13-4; **7i** (methyl ester), 118476-19-0; $HC{\equiv}C(CH_2)_4CH_3$, 628-71-7; $HC{\equiv}C(CH_2)_3CH_2OH$, 928-90-5; $HC{\equiv}C(CH_2)_3CH(OCH_2)_2$, 98558-32-8; $HC{\equiv}C(CH_2)_3CH(OC_2H_5)_2$, 1720-35-0.

Supplementary Material Available: Tables containing NMR and analytical data for compounds **6** and **7** (3 pages). Ordering information is given on any current masthead page.

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(18) In some instances a 1:1 mixture of triethylamine to methylene chloride was used as solvent. This combination appears to lengthen the time course of the reaction over that with diethylamine.

(19) Greater amounts of this reagent simply accelerated the reaction. The indicated ratio of catalysts allowed the reactions to be complete within 24 h.

Synthesis of (1-Aryl-1-alkylethyl)alkoxyamines

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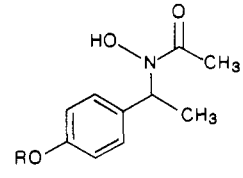
N-Hydroxy-*N*-(1-arylethyl)acetamides (**1**) have recently been shown to be potent orally active inhibitors of leukotriene biosynthesis.[1] As part of our investigations concerning the structure–activity relationships of these compounds,[1b] we examined analogs of structure **2**, which possess a second alkyl substituent in the benzylic position resulting in a tertiary carbon adjacent to nitrogen.



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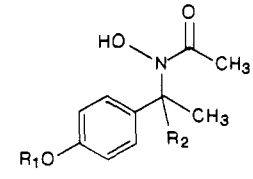

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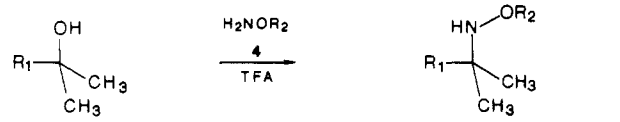
0022-3263/89/1954-1221$01.50/0

Table I. Reaction of 2-Aryl-2-propanols with Hydroxylamine Derivatives



3a: R_1 = *p*-BnOPh **4a**: R_2 = Bn **5a**: R_1 = *p*-BnOPh; R_2 = Bn
b: R_1 = *p*-BuOPh **b**: R_2 = BDPS **b**: R_1 = *p*-BnOPh; R_2 = BDPS
c: R_1 = 2-naphthyl **c**: R_2 = TMS **c**: R_1 = *p*-BnOPH, R_2 = H
d: R_1 = *p*-BuOPh; R_2 = Bn
e: R_1 = 2-naphthyl; R_2 = Bn

			product (yield,[e] %)	
entry	3	4	method A[a]	method B[b]
1	**3a**	**4a**	**5a** (83)	**5a** (79)[d]
2	**3a**	**4b**	**5b** (47)	**5c** (75)[d]
3	**3a**	**4c**		**5c** (63)
4	**3b**	**4a**	**5d** (86)	**5d** (80)[d]
5	**3c**	**4a**	**5e** (49)[c]	

[a] Method A: 2.0 equiv of H_2NOR_2, 1 equiv of TFA, benzene; room temperature. [b] Method B: 1 equiv of H_2NOR_2, 4 equiv of TFA, CH_2Cl_2. [c] Heated to reflux. [d] Isolated as CF_3CO_2H salt. [e] Isolated purified material.

The synthesis of these analogues proved to be problematic. The addition of organometallics to aldoximes to give mono-*N*-alkyl-substituted hydroxylamines has been reported from our laboratories.[2] Similar to other work,[3] it was found that the additions of this type of reagent to ketoximes of methyl ketones have limited synthetic application, and therefore this methodology could not be utilized. Other precedented routes to trisubstituted methylhydroxylamines[4] such as the reduction of *tert*-alkylnitro compounds to hydroxylamines[5] did not seem applicable to our needs. Known methods for the formation of α,α-disubstituted benzylazides from tertiary alcohols or α-methylstyrene in the presence of sodium azide and acid[6] represented a potential strategy from which to develop a practical route to compounds of structure **2**. Hydroxylamines or derivatives, which are considerably more basic than azides, had not been reported to react under these conditions.[7]

We now report that a variety of O-protected hydroxylamines react smoothly with 1-aryl-1-methylethanols in the presence of trifluoroacetic acid to give hydroxylamine adducts. Two sets of reaction conditions were found that gave the desired products in good yield. Initially, in an attempt to maintain a concentration of free base as a nucleophilic species, an excess of hydroxylamine derivative was reacted with 1 equiv each of tertiary alcohol and trifluoroacetic acid (TFA) in benzene. This method proved successful with several O-protected hydroxylamines (Table I, method A). Elimination of water to give an arylalkene was an undesired side reaction, and for entry 3 this proved to be the major product under these conditions. The desired adduct could also be obtained by reacting the tertiary alcohol with 1 equiv of hydroxylamine derivative and a 4-fold excess of TFA in methylene chloride. These conditions produced little elimination product, and the hydroxylamine adduct could be conveniently isolated as the TFA salt (Table I, method B).

The use of *O*-(trimethylsilyl)hydroxylamine (**4c**) with excess TFA allowed direct isolation of the substituted hydroxylamine (entry 3). *O*-(*tert*-Butyldiphenylsilyl)-hydroxylamine[8] (**4b**) also proved useful in the coupling reaction. Similar to *O*-(trimethylsilyl)hydroxylamine the *tert*-butyldiphenylsilyl group was cleaved with excess TFA in methylene chloride. However, using conditions that employed an excess of hydroxylamine derivative in benzene, the *O*-(*tert*-butyldiphenylsilyl)hydroxylamine adduct could be isolated.

The arylalkene produced by elimination using an excess of free amine apparently is not converted to desired product even after prolonged reaction time under these conditions. However, this olefin can proceed to product by addition of excess TFA. Under both reaction conditions, the hydroxylamine species is efficiently alkylated by a putative carbonium ion intermediate. The stabilization of this intermediate by the *p*-alkoxyaryl substituents is nicely illustrated by the lower reaction temperatures required with these substrates (entries 1–4) relative to the naphthyl substituent (entry 5).

This methodology provides efficient access to *N*-(1-aryl-1-alkylethyl)hydroxylamines and *O*-benzyl- or *O*-silyl-protected derivatives.

Experimental Section

Melting points were determined on a Thomas-Hoover apparatus and are uncorrected. ^1H NMR spectra were measured with a GE QE300 NMR with Me_4Si as internal standard and are reported in δ. Mass spectra were recorded on a Kratos MS-50 spectrometer.

Analytical TLC analysis was performed on Merck F254 silica gel. Silica gel (Merck, 230–400 mesh ASTM) was used for flash column chromatography. Products were visualized by UV light. Benzene was distilled from calcium hydride, and methylene chloride was distilled from P_2O_5 before use. *O*-(Trimethylsilyl)hydroxylamine was obtained from Aldrich Chemical Co. and used without further purification. *O*-Benzylhydroxylamine hydrochloride (Aldrich) was converted to its free base by standard methods.[9]

Tertiary alcohols (**3**) were prepared by addition of methylmagnesium bromide or methyllithium to the methyl ketone. 2′-Acetonaphthone was obtained commercially (Aldrich); 4-butoxyacetophenone and 4-(benzyloxy)acetophenone were prepared from 4-hydroxyacetophenone as previously reported.[1b]

***O*-(*tert*-Butyldiphenylsilyl)hydroxylamine (4b).** To a stirred suspension of hydroxylamine hydrochloride (5.0 g, 71.9 mmol) in methylene chloride (100 mL) was added triethylamine (16.02 g, 158.3 mmol). The mixture was allowed to stir for 1 h at room temperature under argon. *tert*-Butylchlorodiphenylsilane (21.76 g, 79.15 mmol) was added neat via syringe, and the reaction mixture was allowed to stir overnight at room temperature. The mixture was then concentrated to dryness, and THF (100 mL) was added to the residue. Triethylamine hydrochloride was removed by filtration, and the resulting THF solution was concentrated. During concentration more precipitate formed; the residue was resuspended in ether and refiltered. The ether solution was concentrated, and hexane (150 mL) was added to the residue, which had begun to crystalize. The solid was collected to afford 8.8 g (45%) of **4b** as a white crystalline solid: mp (Et_2O/hexane) 87–89 °C; ^1H NMR (300 MHz) (DMSO-d_6) δ 1.01 (s, 9 H), 6.14 (b s, 2 H), 7.35–7.47 (m, 6 H), 7.69 (m, 4 H); IR ($CDCl_3$) 3330, 3080, 2940, 1580, 1430, 1110cm^{-1}; MS *m/e* 289 (M + NH_4)$^+$, 272 (M + H)$^+$, 211. Anal. Calcd for $C_{16}H_{21}NOSi$: C,

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70.80; H, 7.80; N, 5.16. Found: C, 70.79; H, 7.85; N, 5.11.

General Procedure for Reaction of Hydroxylamine Derivatives and 2-Aryl-2-propanols. *O*-Benzyl-*N*-[1-methyl-1-[4-(benzyloxy)phenyl]ethyl]hydroxylamine (5a). Method A. 1-Methyl-1-[4-(benzyloxy)phenyl]ethanol (**3a**) (0.1 g, 0.41 mmol) and *O*-benzylhydroxylamine (**4a**) (0.1 g, 0.82 mmol) were dissolved in benzene (2 mL) and stirred under an argon atmosphere. To the reaction flask was added TFA (0.047 g, 0.41 mmol) via syringe, and the reaction mixture was allowed to stir at room temperature for 48 h. The reaction mixture was concentrated, and the residue was dissolved in Et_2O (50 mL). The organic layer was washed with saturated $NaHCO_3$ (25 mL) and brine (25 mL), dried over $MgSO_4$, filtered, and concentrated to afford a slightly yellow oil. Purification by column chromatography (silica gel, 3:1 hexane/ether) afforded 0.118 g (83%) of **5a** as a clear oil that solidified on prolonged standing to give a white power: mp 67–69 °C; ^1H NMR (300 MHz) (DMSO-d_6) δ 1.35 (s, 6 H), 4.53 (s, 2 H), 5.08 (s, 2 H), 6.85 (s, 1 H), 6.93 (m, 2 H), 7.19–7.48 (m, 12 H); IR ($CDCl_3$) 3060, 3030, 2980, 1610, 1510, 1460, 1010 cm^{-1}; MS *m/e* 348 $(M + H)^+$, 225, 164, 91. Anal. Calcd for $C_{23}H_{25}NO_2$: C, 79.51; H, 7.25; N, 4.03. Found: C, 79.70; H, 7.39; N, 4.01.

Method B. 1-Methyl-1-[4-(benzyloxy)phenyl]ethanol (**3a**) (0.2 g, 0.83 mmol) and *O*-benzylhydroxylamine (**4a**) (0.102 g, 0.83 mmol) were dissolved in methylene chloride (3 mL) and stirred under an argon atmosphere at 0 °C. To the reaction flask was added TFA (0.377 g, 3.31 mmol) via syringe, and the reaction mixture was allowed to stir at 0 °C for 1 h. The reaction mixture was concentrated, and the residue was partitioned between EtOAc (60 mL) and H_2O (30 mL). The organic layer was separated, dried ($MgSO_4$), and concentrated. The semicrystalline residue was triturated with Et_2O/hexane to afford 0.21 g of the trifluoroacetic acid salt of **5a** as a white powder. An additional 0.068 g precipitated from the filtrate to give a total of 0.28 g (79%): mp (EtOAc/hexane) 140–142 °C; ^1H NMR (300 MHz) (DMSO-d_6) δ 1.48 (s, 6 H), 4.70 (s, 2 H), 5.11 (s, 2 H), 6.85 (s, 2 H), 6.99 (m, 2 H), 7.20–7.50 (m, 12 H). Anal. Calcd for $C_{25}H_{26}F_3NO_4$: C, 65.07; H, 5.68; N, 3.04. Found: C, 65.09; H, 5.67; N, 3.02.

***O*-(*tert*-Butyldiphenylsilyl)-*N*-[1-methyl-1-[4-(benzyloxy)phenyl]ethyl]hydroxylamine (5b)** was prepared by method A from 1-methyl-1-[4-(benzyloxy)phenyl]ethanol (**3a**) (0.5 g, 2.06 mmol), *O*-(*tert*-butyldiphenylsilyl)hydroxylamine (**4b**) (1.12 g, 4.13 mmol), and TFA (0.236 g, 2.07 mmol) in benzene (2 mL) as a slightly yellow oil. Purification by column chromatography (silica gel, 97:3 hexane/ether) afforded 0.46 g (45%) of **5b** as a colorless oil: ^1H NMR (300 MHz) (DMSO-d_6) δ 1.10 (s, 9 H), 1.21 (b s, 6 H), 5.06 (s, 2 H), 6.06 (s, 1 H), 6.85 (m, 2 H), 7.18–7.48 (m, 13 H), 7.62 (m, 4 H); IR ($CDCl_3$) 3110, 2950, 2860, 1605, 1510, 1240, 1110 cm^{-1}; MS *m/e* 496 $(M + H)^+$, 225. Anal. Calcd for $C_{32}H_{37}NO_2Si$: C, 77.53; H, 7.52; N, 2.83. Found: C, 77.53; H, 7.53; N, 2.30.

***N*-[1-Methyl-1-[4-(benzyloxy)phenyl]ethyl]hydroxylamine (5c)** was prepared by method B from 1-methyl-1-[4-(benzyloxy)phenyl]ethanol (**3a**) (0.6 g, 2.48 mmol), *O*-(trimethylsilyl)-hydroxylamine (**4c**) (0.39 g, 3.7 mmol), and TFA (1.13 g, 10 mmol) in methylene chloride (3 mL). Neutralization, workup, and concentration gave a white solid. Purification by column chromatography (silica gel, 97:3 CH_2Cl_2/MeOH) afforded 0.434 g (68%) of **5c** as a white solid: mp (EtOAc/hexane) 122–124 °C; ^1H NMR (300 MHz) (DMSO-d_6) δ 1.30 (s, 6 H), 5.07 (s, 2 H), 5.56 (b s, 1 H), 6.90 (m, 2 H), 6.95 (b s, 1 H), 7.28–7.47 (m, 7 H); IR ($CDCl_3$) 3060, 3030, 2980, 1610, 1510, 1460, 1010 cm^{-1}; MS *m/e* 275 $(M + NH_4)^+$, 258 $(M + H)^+$, 225. Anal. Calcd for $C_{16}H_{19}NO_2$: C, 74.68; H, 7.44; N, 5.44. Found: C, 74.82; H, 7.59; N, 5.42.

***O*-Benzyl-*N*-[1-methyl-1-(4-butoxyphenyl)ethyl]-hydroxylamine (5d)** was prepared by method A from 1-methyl-1-(4-butoxyphenyl)ethanol (**3b**) (0.2 g, 1.0 mmol), *O*-benzylhydroxylamine (**4a**) (0.246 g, 2.0 mmol), and TFA (0.144 g, 1.0 mmol) in benzene (5 mL) as a slightly yellow oil. Purification by column chromatography (silica gel, 3:1 hexane/ether) afforded 0.27 g (86%) of **5d** as a colorless oil: ^1H NMR (300 MHz) (DMSO-d_6) δ 0.93 (t, 3 H, J = 7.5 Hz), 1.35 (s, 6 H), 1.43 (m, 2 H), 1.68 (m, 2 H), 3.93 (t, 2 H, J = 7.5 Hz), 4.53 (s, 2 H), 6.58 (s, 2 H), 6.83 (m, 2 H), 7.19–7.39 (m, 5 H), 7.49 (m, 2 H); IR (neat) 2960, 2930, 2870, 1610, 1510, 1245, 1180 cm^{-1}; MS *m/e* 314 $(M + H)^+$, 191, 135. Anal. Calcd for $C_{20}H_{27}NO_2$: C, 76.64; H, 8.68; N, 4.47. Found: C, 76.25; H, 8.62; N, 4.65.

Using method B, **5d** was prepared from 1-methyl-1-(4-butoxyphenyl)ethanol (**3b**) (0.1 g, 0.5 mmol), *O*-benzylhydroxylamine (**4a**) (0.084 g, 0.7 mmol), and TFA (0.216 g, 1.90 mmol) in methylene chloride (8 mL). The reaction mixture was concentrated, and the residue was purified by column chromatography (silica gel, 7:3 hexane/ether) to afford 0.18 g of the trifluoroacetic acid salt of **5d** as a white power (80%): mp (EtOAc/hexanes) 113–114 °C; ^1H NMR (300 MHz) ($CDCl_3$) δ 0.93 (t, 3 H, J = 7.5 Hz), 1.39 (m, 2 H), 1.64 (m, 2 H), 1.69 (s, 6 H), 3.68 (t, 2 H, J = 7.5 Hz), 4.67 (s, 2 H), 6.62 (b s, 1 H), 6.78 (m, 2 H), 7.23 (m, 2 H), 7.33 (m, 3 H), 7.47 (m, 2 H); IR ($CDCl_3$) 2960, 2875, 2760, 1675, 1520, 1260, 1190 cm^{-1}; MS *m/e* 331 $(M + NH4)^+$, 314 $(M + H)^+$, 225, 191, 91. Anal. Calcd for $C_{22}H_{28}F_3NO_4$: C, 61.82; H, 6.60; N, 3.28; F, 13.33. Found: C, 61.78; H, 6.76; N, 3.28; F, 13.83.

***O*-Benzyl-*N*-[1-methyl-1-(2-naphthyl)ethyl]hydroxylamine (5e)** was prepared by method A from 1-methyl-1-(2-naphthyl)ethanol (**3c**) (0.19 g, 1.0 mmol), *O*-benzylhydroxylamine (**4a**) (0.246 g, 2.0 mmol), and TFA (0.114 g, 1.0 mmol) in benzene (2 mL) as a slightly yellow oil. Purification by column chromatography (silica gel, 3:1 hexane/ether) afforded 0.143 g (49%) of **5e** as a colorless oil: ^1H NMR (300 MHz) (DMSO-d_6) δ 1.48 (s, 6 H), 4.55 (s, 2 H), 6.82 (s, 1 H) 7.16–7.31 (m, 5 H), 7.47 (m, 2 H), 7.75–7.95 (m, 5 H); MS *m/e* 496 $(M + H)^+$, 225. Anal. Calcd for $C_{20}H_{21}NO$: C, 82.44; H, 7.26; N, 4.81. Found: C, 82.51; H, 7.31; N, 4.82.

Registry No. **3a**, 94571-13-8; **3b**, 93308-49-7; **3c**, 20351-54-6; **4a**, 622-33-3; **4b**, 103587-51-5; **4c**, 22737-36-6; **5a**, 118684-93-8; **5a**·CF_3CO_2H, 118684-99-4; **5b**, 118684-94-9; **5c**, 118684-95-0; **5c**·CF_3CO_2H, 118684-98-3; **5d**, 115514-06-2; **5d**·CF_3CO_2H, 118684-97-2; **5e**, 118684-96-1; TFA, 76-05-1; hydroxylamine hydrochloride, 5470-11-1; *tert*-butylchlorodiphenylsilane, 58479-61-1.

Claisen Rearrangement of (*Z*)-3-Deoxy-3-*C*-[(hydroxymethyl)methylene]-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranose with Triethyl Orthopropionate[1]

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Recently, we reported the stereoselective quaternization at C-3 of some aldohexofuranoses by means of the ortho ester Claisen rearrangement of (*Z*)-3-deoxy-3-*C*-[(hydroxymethyl)methylene]-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-(1), -β-L-*lyxo*-, and -β-D-*arabino*-hexofuranose with triethyl orthoacetate.[2] These rearrangements proceed with high stereoselectivity to provide the corresponding 3-*C*-[(ethoxycarbonyl)methyl]-3-*C*-vinyl derivatives in moderate to high yields. For an extension of our interest in the Claisen rearrangement of carbohydrate-derived cyclic models, we describe herein the Claisen rearrangement of 1 with triethyl orthopropionate.

By heating 1 in triethyl orthopropionate at 135 °C in the presence of propanoic acid,[3] two products, **2S** and **2R**, were obtained in 65% and 16% yields, respectively, after recrystallization of the mixture followed by silica gel

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