Chemistry of *N,N*-Bis(silyloxy)enamines. 3. *N,N*-Bis(silyloxy)enamines as *β*-C-Nucleophiles in Reaction with Acetals Mediated by Trimethylsilyl Trifluoromethanesulfonate[1]

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Introduction

Silylation of nitro compounds may afford silyl derivatives of two different types, namely, silyl nitronates and *N,N-b*is(silyloxy)*ena*mines (BENA). Whereas thoroughly studied transformations of silyl nitronates constitute a substantial part of the chemistry of aliphatic nitro compounds,[2] the reactivity of BENA remains scarcely investigated.[3] At the same time, these derivatives may become attractive intermediates in organic synthesis, especially in light of the convenience of their preparation and handling.[4]

Recently, we demonstrated that terminal BENA **1** behave as formal *β*-C-electrophiles in C,C-*cross*-coupling reactions with stabilized carbanions leading to corresponding oximes **3** through the intermediacy of conjugated nitroso alkenes **2** (Scheme 1).[5] Since the convenient conversion of oximes **3** into nitro compounds **4** has been reported,[6] the reaction sequence depicted in eq 1 could be considered as a simple way to introduce the nucleophile into the α-methyl group of starting nitro alkanes via their double silylation.

However, BENA **1** turned out to be "chemical chameleons". Under certain conditions, they could react at the *β*-carbon atom not only with nucleophiles, but also with electrophiles, furnishing corresponding nitro compounds **6** after protolysis of initially formed silyl nitronates **5** (Scheme 1, eq 2). Thus, it becomes feasible to incorporate the electrophile into α-methyl substituent of starting nitro compounds through their double silylation.

Herein we disclose the first C,C-*cross*-coupling reaction of BENA **1** with electrophiles generated from acetals giving rise to nitro compounds **6**.

Table 1. Synthesis of Nitro Compounds 6a−k from BENA 1a−c and Acetals 7a−g[a]

entry	1	7	time (h)	product[b]	yield[c] of **6** (%)
1	**1a**	**7a**	6	**6a**	77
2[d]	**1a**	**7a**	20	**6a**	
3	**1a**	**7b**	6	**6b**	74
4	**1a**	**7c**	0.25	**6c**	67
5	**1a**	**7c**[e]	1.5	**6c**	69
6	**1a**	**7d**	1	**6d**	53
7[f]	**1a**	**7e**	17	**6e**	42
8[f]	**1a**	**7e**[e]	17	**6e**	40
9	**1a**	**7f**	3	**6f**	70
10	**1a**	**7g**	6	**6g**	26
11	**1b**	**7a**	1	**6h**	59
12	**1b**	**7b**	1.5	**6i**	56
13	**1b**	**7d**	1	**6j**	62
14	**1c**	**7f**	6	**6k**	32

[a] All reactions were carried out in CH_2Cl_2 at −78 °C with the ratio **1**/**7**/TMSOTf/Py = 1:1.05:1.2:0.05 unless otherwise noted. [b] Mixture of diastereomers in ratio from 1:1 to 1.8:1 (see the Supporting Information for details). [c] Yield of isolated product. [d] Ratio **1**/**7**/TMSOTf/Py = 1:1.05:0.1:0.01 [e] *t*-BuMe_2Si-groups instead of Me_3Si-groups in BENA **1a**. [f] Ratio **1**/**7**/TMSOTf/Py = 1:1.05:1.7:0.5.

Results and Discussion

The reaction of BENA **1a−c** with acetals **7a−g** occurs smoothly in methylene chloride at −78 °C in the presence of stoichiometric amounts of trimethylsilyl trifluoromethanesulfonate (TMSOTf) (Scheme 2, Table 1) yielding corresponding nitro alkanes **6a−k**. To remove adventitious triflic acid, 5% of pyridine was added to the reaction mixture.

The proposed mechanism of the process is shown in Scheme 2. Acting as a Lewis acid, TMSOTf abstracts the alkoxy substituent from acetals **7** affording carboxonium ions **8**[7] which subsequently attack onto the BENA double bond, furnishing *N,N*-bis(silyloxy)immonium cations **9** existing in equilibrium with silyl nitronates **5a−k**.[8] According to Scheme 2, TMSOTf may be considered as a catalyst; however, the use of 10 mol % TMSOTf proved to be totally ineffective (see entry 2). After completion of the reaction (from 15 min to 17 h, see Table 1), the $BnNEt_3Cl$ (1.4 equiv) was added to shift the equilibrium to silyl nitronates **5a−k** by removal of the active Me_3Si group as chlorotrimethylsilane.

To effect hydrolysis of silyl nitronates **5** into nitro compounds **6**, we first tested the $AcOH/NEt_3$ quenching system. This proved to be unsuccessful, presumably owing to intramolecular hydrogen bond stabilization of initially formed nitronic acid **10**. Notably, addition of

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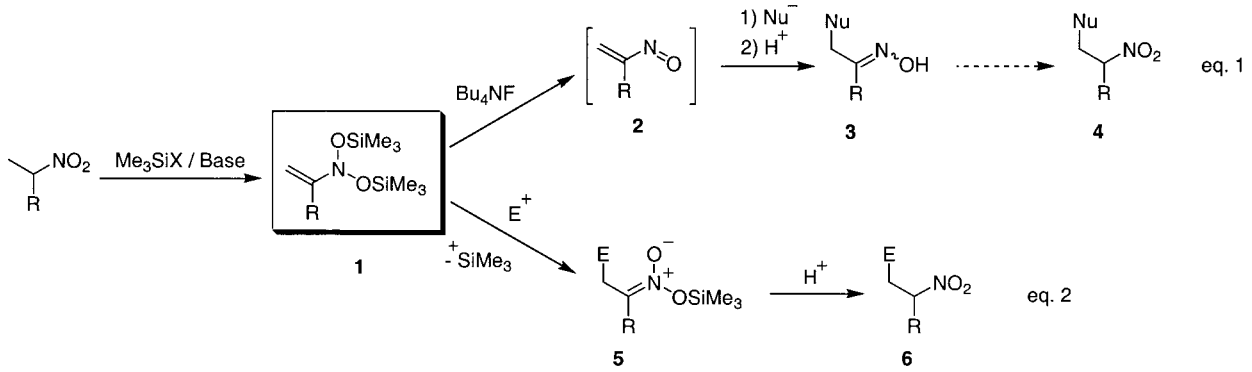
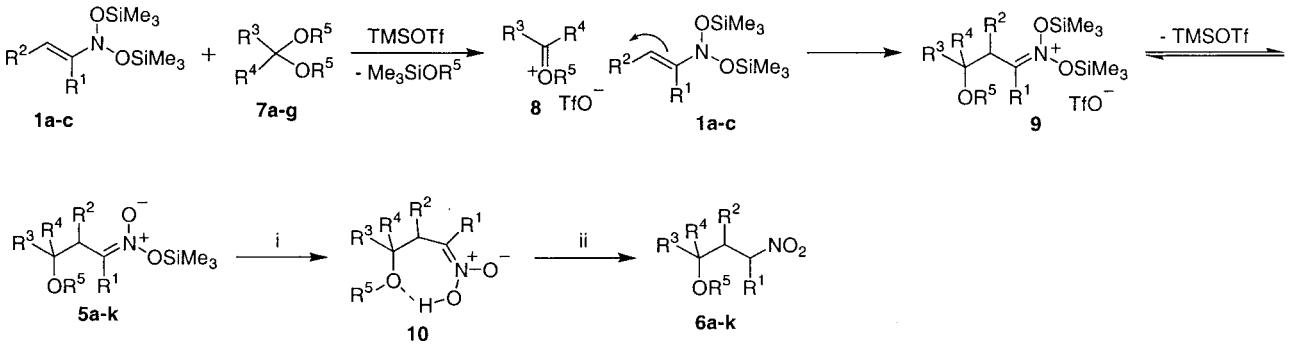
Scheme 1



Scheme 2



i: 1) 1.4 eq $BnNEt_3Cl$ in CH_2Cl_2
2) 2 eq AcOH / 2.2 eq NEt_3 in CH_2Cl_2

ii: 2 eq AcOH in MeOH

1a: R^1 = Me, R^2 = H
1b: $R^1 = MeO_2C(CH_2)_2$, R^2 = H
1c: R^1 = Me, $R^2 = CO_2Me$

7a: R^3 = Ph, R^4 = H, R^5 = Me
b: R^3 = *p*-Cl-C_6H_4-, R^4 = H, R^5 = Me
c: R^3 = *p*-MeO-C_6H_4-, R^4 = H, R^5 = Me
d: R^3 = (*E*) MeCH=CH, R^4 = H, R^5 = Me
e: R^3, R^5 = Et, R^4 = H
f: R^3 = MeO, R^4 = H, R^5 = Me
g: R^3, R^4, R^5 = Me

6a: R^1, R^5 = Me, R^2, R^4 = H, R^3 = Ph
b: R^1, R^5 = Me, R^2, R^4 = H, R^3 = *p*-Cl-C_6H_4-
c: R^1, R^5 = Me, R^2, R^4 = H, R^3 = *p*-MeO-C_6H_4-
d: R^1, R^5 = Me, R^2, R^4 = H, R^3 = (*E*) MeCH=CH
e: R^1 = Me, R^2, R^4 = H, R^3, R^5 = Et
f: R^1, R^5 = Me, R^2, R^4 = H, R^3 = MeO
g: R^1, R^3, R^4, R^5 = Me, R^2 = H
h: $R^1 = MeO_2C(CH_2)_2$, R^2, R^4 = H, R^3 = Ph, R^5 = Me
i: $R^1 = MeO_2C(CH_2)_2$, R^2, R^4 = H, R^3 = *p*-Cl-C_6H_4-, R^5 = Me
j: $R^1 = MeO_2C(CH_2)_2$, R^2, R^4 = H, R^3 = (*E*) MeCH=CH, R^5 = Me
k: R^1, R^5 = Me, $R^2 = CO_2Me$, R^3 = MeO, R^4 = H

methanol disrupting the intramolecular hydrogen bond allowed the isolation of the desired nitro compounds **6a**−**k** (for detailed discussion about mechanistic problems see the Supporting Information).

The range of acetals reacting with BENA **1a**−**c** is rather wide (see Scheme 2). The rate of reaction increases in the following order of aldehyde acetals: propionic aldehyde < benzaldehyde < *p*-anisaldehyde, thereby suggesting formation of carboxonium ion on the rate-determining step.[9]

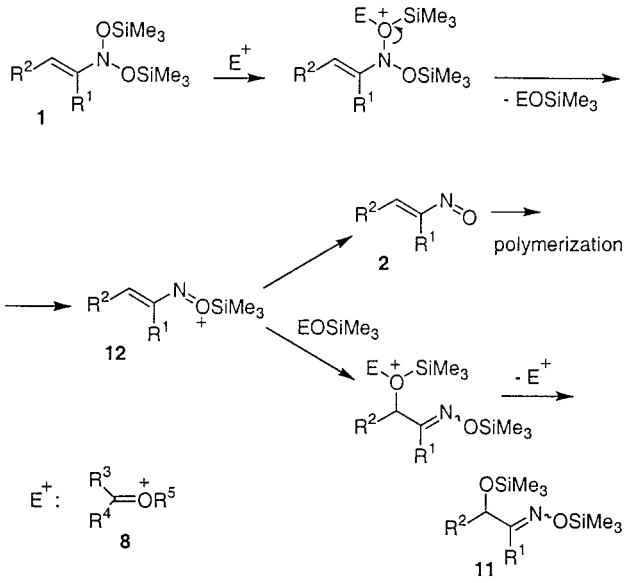
Employment of propionic aldehyde diethyl acetal **7e** in the reaction with BENA **1a** gives rise to considerable amount of α-silyloxyoxime **11**. We suppose that it is associated with attack of cation **8** (R^3, R^5 = Et, R^4 = H) onto the oxygen atom of BENA followed by heterolytic cleavage of the N−O bond (Scheme 3).[10] Generation of silylnitrosonium cation **12** could lead either to α-silyloxyoxime **11** or to conjugated nitroso alkene **2** prone to polymerization. Indeed, formation of α-silyloxyoxime **11** is typical for interaction of BENA with conventional Lewis acids (e.g., $TiCl_4$, $BF_3{\cdot}OEt_2$) as well as strong protic acids (e.g., TfOH).[3] While BENA are stable toward TMSOTf at − 78 °C, they undergo rearrangement into α-silyloxyoximes **11** in moderate yields at elevated temperature. Unfortunately, utilization of BENA containing bulky *t*-$BuMe_2Si$ groups gave no increase in yields of final products **6** (Table 1, entry 4 vs 5 and entry 7 vs 8). Attempts to involve the BENA **1** possessing hydrogen at α-carbon atom (R^1 = H) into reaction with acetals failed, leading to complex mixtures of products. Such phenomenon may be tentatively ascribed to the enhanced reactivity of initially formed primary *N*,*N*-bis(silyloxy)-immonium ion **9** which reacts with BENA much more effectively than carboxonium ion **8**.

Presence of stoichiometric amounts of TMSOTf in reaction mixture could be further exploited to achieve silylation of silylnitronates **5**. As exemplified in Scheme 4, BENA **13** could be formed simply by adding the triethylamine to the reaction mixture obtained from reaction of acetal **7c** with BENA **1a**. Subsequent addition of trimethylorthoformate and TMSOTf furnishes after workup nitro compound **14** in 20% overall yield. Thus,

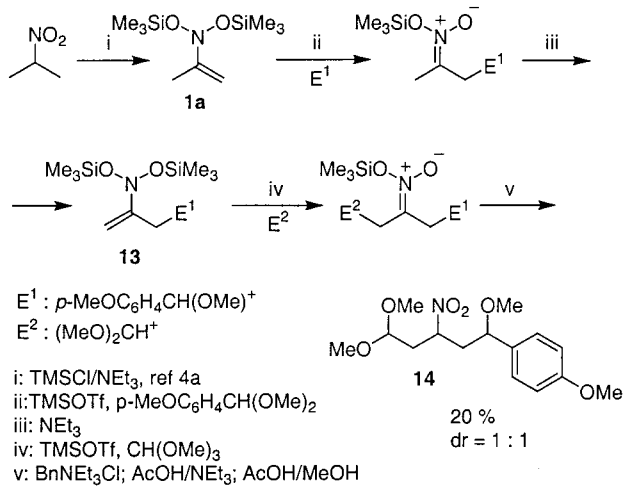
(9) For relative reactivity of acetals in reaction with vinyl ethers, see: von der Brüggen, U.; Lammers, R.; Mayr, H. *J. Org. Chem.* **1988**, *53*, 2920.

(10) $ROSiMe_3$ could react with carboxonium cations: (a) Tsunoda, T.; Suzuki, M.; Noyori, R. *Tetrahedron Lett.* **1980**, *21*, 1357. (b) Haynes, R. K.; Lam, K.-P.; Wu, K.-Y.; Williams, I. D.; Yeung, L.-L. *Tetrahedron* **1999**, *55*, 89.

Scheme 3



Scheme 4



this reaction sequence demonstrates the possibility to achieve functionalization of easily available 2-nitropropane via sequential coupling of BENA **1a** with two different electrophiles in a one-pot procedure.

In summary, we demonstrated that, depending on reagents used, the products of double silylation of aliphatic nitro compounds may behave either as β-C-electrophiles or β-C-nucleophiles, thereby allowing diverse functionalization of β-carbon atom of starting nitro compounds. The possible applications of the reactions between BENA and electrophiles in organic synthesis need yet to be elaborated. Nevertheless, the process described herein represents realization of a general principle in electrophile/nucleophile combination in which incipient positive charge is stabilized by conjugation with silicon (or tin) bearing functionality (in analogy to the well-known TMSOTf-catalyzed reaction of acetals with silyl enol ethers[11]).

Applications of the reaction of acetals with BENA in the synthesis of polyfunctional compounds will be reported in due course.

(11) Murata, S.; Suzuki, M.; Noyori, R. *J. Am. Chem. Soc.* **1980**, *102*, 3248.

Experimental Section

N,*N*-bis(silyloxy)enamines **1a**,**b**[4a] and **1c**[4b] were synthesized according to literature procedures. All reactions were carried out in an atmosphere of dry Ar. CH_2Cl_2 was distilled from CaH_2 prior to use.

General Procedure for Coupling of BENA 1 with Acetals 7. To a solution of TMSOTf (113 μL, 0.6 mmol) and Py (2 μL, 0.025 mmol) in CH_2Cl_2 (0.5 mL) at −78 °C were successively added acetal **7** (0.53 mmol) in CH_2Cl_2 (0.5 mL) and BENA **1** (0.5 mmol) in CH_2Cl_2 (1 mL). After being stirred at −78 °C for the time indicated in Table 1, the reaction mixture was quenched with a solution of $BnNEt_3Cl$ (160 mg, 0.7 mmol) in CH_2Cl_2 (1 mL), kept for another 5 min, and treated with the mixture of AcOH (57 μL, 1 mmol) and NEt_3 (153 μL, 1.1 mmol) dissolved in CH_2Cl_2 (1 mL) followed by addition of AcOH (57 μL, 1 mmol) in MeOH (1 mL). Then the cooling bath was removed, and the reaction mixture was allowed to warm to room temperature and kept for an additional 1 h. For the workup, the mixture was poured into H_2O (10 mL)/Et_2O (20 mL). The organic phase was separated, and the aqueous phase was extracted with Et_2O (3 by 10 mL), and the combined organic extracts were washed with brine (10 mL), dried (Na_2SO_4), and concentrated in vacuo. Product **6** was purified by flash chromatography on silica gel. Analytically pure sample was obtained after short-path vacuum distillation.

For coupling of compound **1a** with acetone dimethylketal **7g**, the reverse order of addition of **1a** and **7g** was found to be superior; see the Supporting Information for details.

For the synthesis of **6k**, the reaction should be quenched with Bu_4NOAc followed by addition of TBAF/AcOH in MeOH; see the Supporting Information for details.

In most cases, diastereoisomers were separated by flash column chromatography on silica gel and are denoted as upper and lower according to R_f. In cases where separation by flash chromatography was unsuccessful, the compounds are characterized as mixtures with only distinction as major and minor isomers.

The following products were prepared:

(1-Methoxy-3-nitrobutyl)benzene (6a) (1:1 isomer mixture): ^{1}H NMR upper isomer δ 1.54 (d, J = 7.0 Hz, 3H), 1.99 (ddd, J = 3.4, 10.4, 15.1 Hz, 1H), 2.29 (ddd, J = 3.0, 10.4, 15.1 Hz, 1H), 3.20 (s, 3H), 4.08 (dd, J = 3.0, 10.4 Hz, 1H), 4.91−5.03 (m, 1H), 7.23−7.41 (m, 5H); lower isomer δ 1.54 (d, J = 6.7 Hz, 3H), 1.93 (dt, J = 5.4, 14.1 Hz, 1H), 2.59 (dt, J = 8.1, 14.1 Hz, 1H), 3.15 (s, 3H), 4.15 (dd, J = 5.4, 8.1 Hz, 1H), 4.62 (h, J = 6.7 Hz, 1H), 7.23−7.42 (m, 5H); ^{13}C NMR upper isomer δ 20.0, 43.7, 56.9, 79.9, 80.4, 128.6, 126.2, 128.0, 140.7; lower isomer δ 19.3, 43.0, 56.6, 80.6, 80.8, 126.6, 128.7, 128.2, 140.4.

1-Chloro-4-(1-methoxy-3-nitrobutyl)benzene (6b) (1:1 isomer mixture): ^{1}H NMR upper isomer δ 1.56 (d, J = 6.6 Hz, 3H), 1.95 (ddd, J = 2.9, 10.3, 14.7 Hz, 1H), 2.26 (ddd, J = 2.2, 10.3, 14.7 Hz, 1H), 3.20 (s, 3H), 4.07 (dd, J = 2.9, 10.3 Hz, 1H), 4.90−5.03 (m, 1H), 7.21 (d, J = 8.1 Hz, 2H), 7.34 (d, J = 8.1 Hz, 2H); lower isomer δ 1.56 (d, J = 7.1 Hz, 3H), 1.91 (dt, J = 5.2, 14.7 Hz, 1H), 2.57 (dt, J = 7.1, 14.7 Hz, 1H), 3.16 (s, 3H), 4.14 (dd, J = 5.2, 7.1 Hz, 1H), 4.60 (h, J = 7.1 Hz, 1H), 7.24 (d, J = 8.1 Hz, 2H), 7.36 (d, J = 8.1 Hz, 2H); ^{13}C NMR upper isomer δ 20.0, 43.7, 57.0, 79.2, 80.3, 127.6, 128.87, 133.7, 139.3; lower isomer δ 19.3, 42.8, 56.7, 80.0, 80.7, 127.9, 128.93, 134.0, 138.9.

1-Methoxy-4-(1-methoxy-3-nitrobutyl)benzene (6c) (1:1 isomer mixture): ^{1}H NMR upper isomer δ 1.54 (d, J = 6.6 Hz, 3H), 2.00 (ddd, J = 3.9, 10.5, 15.1 Hz, 1H), 2.26 (ddd, J = 3.3, 9.9, 15.1 Hz, 1H), 3.17 (s, 3H), 3.80 (s, 3H), 4.03 (dd, J = 3.3, 10.5 Hz, 1H), 4.85−5.02 (m, 1H), 6.89 (d, J = 8.5 Hz, 2H), 7.18 (d, J = 8.5 Hz, 2H); lower isomer δ 1.54 (d, J = 7.2 Hz, 3H), 1.90 (dt, J = 5.9, 14.4 Hz, 1H), 2.59 (dt, J = 7.9, 14.4 Hz, 1H), 3.13 (s, 3H), 3.81 (s, 3H), 4.09 (dd, J = 5.9, 7.9 Hz, 1H), 4.57 (h, J = 7.2 Hz, 1H), 6.90 (d, J = 8.5 Hz, 2H), 7.20 (d, J = 8.5 Hz, 2H); ^{13}C NMR upper isomer δ 20.0, 43.7, 55.2, 56.6, 79.4, 80.5, 114.0, 127.5, 132.6, 159.4; lower isomer δ 19.4, 42.9, 55.2, 56.3, 80.1, 80.8, 114.1, 127.9, 132.2, 159.5.

4-Methoxy-6-nitro-2-heptene (6d) (1.2:1 isomer mixture): ^{1}H NMR δ 1.54 (d, J = 6.6 Hz, 3H) and 1.55 (d, J = 6.6 Hz, 3H), 1.67−1.87 (m, 8H), 2.17 (ddd, J = 3.6, 9.8, 14.8 Hz, 1H, minor), 2.39 (dt, J = 7.9, 15.6 Hz, 1H, major), 3.20 (s, 3H, major), 3.22 (s, 3H, minor), 3.35−3.58 (m, 2H), 4.66 (h, J = 6.6, 1H, major),

4.77−4.92 (m, 1H, minor), 5.16−5.32 (m, 2H), 5.59−5.79 (m, 2H); ^{13}C NMR δ 17.6, 17.7, 19.4, 20.0, 40.5, 41.3, 55.9, 56.1, 78.5, 79.1, 80.2, 80.6, 129.9, 130.0, 130.1, 130.7.

4-Ethoxy-2-nitrohexane (6e) (1.8:1 isomer mixture): ^{1}H NMR δ 0.88 (t, J = 7.4 Hz, minor) and 0.90 (t, J = 7.4 Hz, major) (3H), 1.15 (t, J = 6.6 Hz, major) and 1.18 (t, J = 6.6 Hz, minor) (3H), 1.40−1.64 (m) and 1.69 (ddd, J = 2.9, 10.3, 14.7 Hz, minor) and 1.79 (ddd, J = 4.4, 6.6, 14.7 Hz, major) (6H), 2.16 (ddd, J = 2.9, 10.3, 14.7 Hz, minor) and 2.27 (ddd, J = 6.6, 8.8, 14.7 Hz, major) (1H), 3.10−3.19 (m) and 3.21−3.43 (m) (2H), 3.47−3.66 (m, 1 H), 4.69 (h, J = 6.6 Hz, major) and 4.81−4.93 (m, minor) (1H); ^{13}C NMR major isomer δ 9.1, 15.3, 19.4, 26.2, 38.9, 64.2, 77.2, 81.1; minor isomer δ 8.9, 15.5, 20.3, 26.4, 39.8, 65.0, 76.5, 80.7.

1,1-Dimethoxy-3-nitrobutane (6f): ^{1}H NMR δ 1.49 (d, J = 6.9 Hz, 3H), 1.87 (ddd, J = 4.6, 6.2, 14.4 Hz, 1H), 2.34 (ddd, J = 4.9, 8.9, 14.4 Hz, 1H), 3.26 (s, 3H), 3.28 (s, 3H), 4.32 (dd, J = 4.9, 6.2 Hz, 1H), 4.63 (m, 1H); ^{13}C NMR δ 19.9, 37.9, 53.6, 54.1, 79.7, 101.8.

2-Methoxy-2-methyl-4-nitropentane (6g): ^{1}H NMR δ 1.15 (s, 3H), 1.20 (s, 3H), 1.55 (d, J = 6.6 Hz, 3H), 1.74 (dd, J = 3.3, 15.1 Hz, 1H), 2.43 (dd, J = 8.2, 15.1 Hz, 1H), 3.14 (s, 3H), 4.75−4.90 (m, 1H); ^{13}C NMR δ 21.6, 24.1, 24.9, 45.1, 49.3, 73.4, 80.0.

6-Methoxy-4-nitro-6-phenylhexanoic acid methyl ester (6h) (1.2:1 isomer mixture): ^{1}H NMR upper isomer (minor) δ 2.02 (ddd, J = 3.1, 10.4, 14.7 Hz, 1H), 2.09−2.42 (m, 5H), 3.19 (s, 3H), 3.68 (s, 3H), 4.04 (dd, J = 3.1, 10.4 Hz, 1H), 4.88−5.01 (m, 1H), 7.22−7.40 (m, 5H); lower isomer (major) δ 1.98 (dt, J = 5.5, 14.6 Hz, 1H), 2.12−2.40 (m, 4H), 2.56 (dt, J = 8.6, 14.7 Hz, 1H), 3.15 (s, 3H), 3.66 (s, 3H), 4.17 (dd, J = 5.5, 8.6 Hz, 1H), 4.53−4.65 (m, 1H), 7.22−7.40 (m, 5H); ^{13}C NMR upper isomer δ 29.2, 30.0, 42.4, 51.8, 56.9, 79.7, 84.6, 126.2, 128.67, 128.1, 140.6, 172.1; lower isomer δ 28.6, 29.8, 41.7, 51.8, 56.6, 80.8, 85.0, 126.6, 128.72, 128.3, 140.3, 172.2.

6-(4-Chlorophenyl)-6-methoxy-4-nitrohexanoic acid methyl ester (6i) (1.2:1 isomers mixture): ^{1}H NMR upper isomer (minor) δ 1.99 (ddd, J = 3.1, 10.4, 14.9 Hz, 1H), 2.06−2.46 (m, 5H), 3.19 (s, 3H), 3.69 (s, 3H), 4.02 (dd, J = 2.8, 10.4 Hz, 1H), 4.88−5.04 (m, 1H), 7.21 (d, J = 8.7 Hz, 2H), 7.34 (d, J = 8.7 Hz, 2H); lower isomer (major) δ 1.95 (dt, J = 5.0, 14.6 Hz, 1H), 2.10−2.43 (m, 4H), 2.54 (dt, J = 8.7, 14.6 Hz, 1H), 3.15 (s, 3H), 3.68 (s, 3H), 4.16 (dd, J = 5.0, 8.7 Hz, 1H), 4.50−4.68 (m, 1H), 7.24 (d, J = 8.7 Hz, 2H), 7.36 (d, J = 8.7 Hz, 2H); ^{13}C NMR upper isomer δ 29.0, 29.8, 42.2, 51.9, 56.9, 78.9, 84.3, 127.5, 128.8, 133.7, 139.0, 172.1; lower isomer δ 28.5, 29.6, 41.6, 51.9, 56.7, 80.1 84.8, 127.9, 128.9, 133.9, 138.7, 172.2.

6-Methoxy-4-nitro-7-nonenoic acid methyl ester (6j) (1.4:1 isomer mixture): ^{1}H NMR δ 1.60−1.90 (m) and 2.02−2.44 (m) (9H), 3.18 (s, major) and 3.19 (s, minor) (3H), 3.23−3.54 (m, 1H), 3.68 (s, 3H), 4.54−4.67 (m, major) and 4.74−4.88 (m, minor) (1H), 5.15−5.29 (m, 1H), 5.58−5.77 (m, 1H); ^{13}C NMR δ 17.6, 17.7, 28.7, 29.2, 29.9, 30.0, 39.3, 39.9, 51.8, 51.9, 55.9, 56.1, 78.4, 79.3, 84.3, 84.7, 129.8, 129.9, 130.2, 130.9, 172.2, 172.3.

2-Dimethoxymethyl-3-nitrobutyric acid methyl ester (6k) (1:1 isomer mixture): ^{1}H NMR upper isomer δ 1.57 (d, J = 7.5 Hz, 3H), 3.35 (s, 3H), 3.39 (s, 3H), 3.56 (t, J = 7.5 Hz, 1H), 3.74 (s, 3H), 4.65 (d, J = 7.5 Hz, 1H), 4.80 (quin, J = 7.5 Hz, 1H); lower isomer δ 1.66 (d, J = 6.6 Hz, 3H), 3.34 (t, J = 6.6 Hz, 1H), 3.42 (s, 3H), 3.43 (s, 3H), 3.73 (s, 3H), 4.67 (d, J = 6.6 Hz, 1H), 4.95 (quin, J = 6.6 Hz, 1H); ^{13}C NMR upper isomer δ 16.7, 52.2, 52.7, 54.7, 55.0, 81.0, 103.2, 169.2; lower isomer δ 17.6, 52.4, 52.5, 55.6, 55.9, 80.8, 103.6, 169.3.

Synthesis of 14. To a solution of TMSOTf (207 μL, 1.1 mmol) and Py (4 μL, 0.05 mmol) in CH_2Cl_2 (1 mL) at −78 °C were successively added acetal **7c** (182 mg, 1 mmol) in CH_2Cl_2 (1 mL) and BENA **1a** (1 mmol) in CH_2Cl_2 (2 mL). After the mixture was stirred for 15 min, NEt_3 (153 μL, 1.1 mmol) was injected. After 2.5 h at −78 °C, $HC(OMe)_3$ (131 μL, 1.2 mmol) and TMSOTf (207 μL, 1.1 mmol) were successively added and the resulting solution was kept 4.5 h at −78 °C. The reaction mixture was quenched with $BnNEt_3Cl$ (160 mg, 0.7 mmol) in CH_2Cl_2 (2 mL), kept for another 5 min, and treated with the mixture of AcOH (114 μL, 2 mmol) and NEt_3 (0.31 mL, 2.2 mmol) dissolved in CH_2Cl_2 (2 mL) followed by addition of AcOH (114 μL, 1 mmol) in MeOH (2 mL). Then the cooling bath was removed, and the reaction mixture was allowed to warm to room temperature and kept for additional 1 h. The H_2O/Et_2O workup as above gave crude product that was purified by flash chromatography to give 62.5 mg of **14** as clear colorless oil, 20% yield.

1-Methoxy-4-(1,5,5-trimethoxy-3-nitropentyl)benzene (14) (1:1 isomer mixture): ^{1}H NMR upper isomer δ 1.88−2.12 (m, 2H), 2.20 (ddd, J = 2.6, 10.2, 14.8 Hz, 1H), 2.36 (ddd, J = 4.9, 9.9, 14.8 Hz, 1H), 3.18 (s, 3H), 3.32 (s, 3H), 3.35 (s, 3H), 3.81 (s, 3H), 3.98 (dd, J = 2.6, 10.5 Hz, 1H), 4.38 (t, J = 4.9 Hz, 1H), 5.03 (tt, J = 3.6, 10.2 Hz, 1H), 6.90 (d, J = 8.5 Hz, 2H), 7.18 (d, J = 8.5 Hz, 2H); lower isomer δ 1.90−2.07 (m, 2H), 2.35 (ddd, J = 4.8, 9.6, 14.3 Hz, 1H), 2.53 (dt, J = 8.5, 14.3 Hz, 1H), 3.12 (s, 3H), 3.30 (s, 3H), 3.32 (s, 3H), 3.81 (s, 3H), 4.08 (dd, J = 5.9, 8.5 Hz, 1H), 4.33 (dd, J = 4.8, 6.3 Hz, 1H), 4.55−4.68 (m, 1H), 6.90 (d, J = 8.5 Hz, 2H), 7.20 (d, J = 8.5 Hz, 2H); ^{13}C NMR upper isomer δ 37.3, 42.9, 53.8, 53.9, 55.3, 56.7, 79.2, 81.9, 101.9, 114.06, 127.5, 132.6, 159.4; lower isomer δ 36.8, 42.0, 53.91, 53.95, 55.3, 56.4, 80.3, 82.3, 101.8, 114.10, 127.9, 132.1, 159.6.

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Supporting Information Available: ^{14}N NMR and IR spectra, chromatography and microanalyses data, as well as boiling points, for compounds **6a**−**k**, **14**. This material is available free of charge via the Internet at http://pubs.acs.org.

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