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Intermolecular Electrophilic O-Amination of Alcohols†

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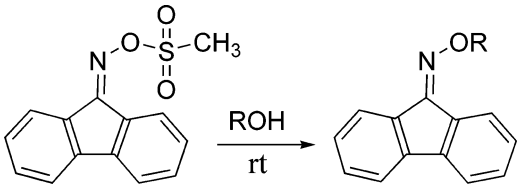
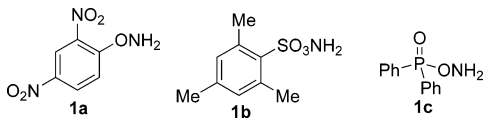
Received September 14, 2006



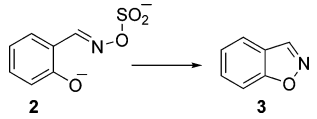
We report the first examples of an intermolecular electrophilic O-amination of aliphatic alcohols. Thus, the new reagents, fluorenone oxime tosylate, **5a**, or mesylate, **5b**, permit O-amination of diverse alcohols in the presence of NaH under mild conditions. By following the formation of the resulting oxime ethers, **6**, the reaction was shown to be sensitive to steric effects in the alcohol. Furthermore, the presence of an aromatic ring or of a double bond in the alcohol molecule (benzyl, allyl) was found to increase the reaction rate.

The oldest route to amine derivatives is nucleophilic displacement on carbon by nitrogen nucleophiles. Yet, over the past few years, reagents possessing good leaving groups on N have been developed for electrophilic amination;[1] foremost among them are hydroxylamine sulfonic acid derivatives, for instance, **1a,b**.[2,3] These compounds react primarily with stabilized carbanions or with amines, which displace the good leaving group on N. Though the yields in such reactions are often low, higher yields can been achieved, as in the amination of stabilized carbanions by *O*-diphenylphosphinyl hydroxylamine **1c**.[3]



Previous studies have indicated that such reactions most likely involve S_N2 displacement on nitrogen by a carbanion. However, since carbanions easily abstract protons attached to nitrogen, resulting in the decomposition of the aminating species, the yield of the aminated product often remains low. For a successful amination, it is therefore desirable to have an aminating agent that lacks a hydrogen on the nitrogen. This has led to the use, among others, of vinyl azides,[5] (phenylthio)methyl azide,[6] and diphenyl phosphorazidate[7] in the amination of aromatic, heteroaromatic, and even alkyl-lithiated carbanions or Grignard species.

By contrast to amination on carbon or nitrogen,[2−4] amination on oxygen is less explored. Thus *O*-sulfonylhydroxylamines[3a] do not aminate alcohols. Rapoport et al.[8] have shown that phenolates can react in an amine exchange reaction with **1a** to produce various *O*-arylhydroxylamines. A nice example of an attack by a phenolate on the N of an *O*-oxime sulfonate (**2**) leading to benzisoxazole **3** has been reported by Kemp and Woodward.[9] Similarly, some time ago, we reported the first examples of intramolecular N−N bond formation in the synthesis of pyrazolines.[10] Though the conversion of **2** to **3** was an example of an intramolecular reaction with a favorable formation of a five-membered ring, this result, as well as those by Rapoport, encouraged us to attempt to find a reagent for the electrophilic intermolecular amination of aliphatic alcohols. Herein, we report the first reagents of type **5** that serve to convert simple alcohols into *O*-alkylhydroxylamine derivatives.



Though an aldehyde oxime *O*-sulfonate was used in the formation of the O−N bond in **3**, our own studies and the literature[11] indicated that such aldehyde oxime species usually lead to the facile elimination of sulfate with the formation of a nitrile. Furthermore, many ketoxime sulfonates under basic conditions can undergo the Neber[12] or the Beckmann[4,13] rearrangement. Hence, we initially chose fluorenone oxime derivatives, **4**, the rationale being not only because they possess a good sulfate leaving group, as in Woodward's example, but mainly because attack by an O-nucleophile on N may proceed via addition to the N=C, facilitated by the formation of an intermediate 6π-electron-stabilized fluorene anion.[14] Furthermore, fluorenone oxime derivatives should be stable, easily isolable compounds, and the absence of α protons obviates the possibility of a Neber rearrangement.

† Dedicated to Prof. Albert Padwa on his 70th birthday.

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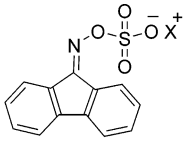
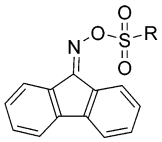
(14) Indeed, benzophenone oxime *O*-tosylate was also prepared, but its reaction with alcohol anions did not lead to *O*-alkyloxime ethers.

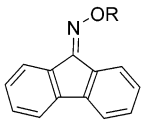
10.1021/jo061900m CCC: $37.00
Published on Web 12/21/2006



4a, X=Na or K
4b, X=NBu_4



5a, R= p-Tol
5b, R= Me
5c, R= CF_3



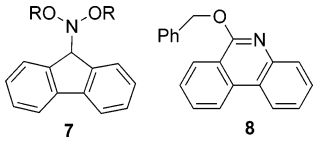
6a, R= Bn; **6b**, R= cyclopentyl
6c, R= n-Bu; **6d**, R= n-heptyl
6e, R= allyl; **6f**, R= 3-hexynyl
6g, ROH= **9**; **6h**, R= 3-butynyl

Isolation of the Na (or K) salt **4a** prepared from fluorenone and hydroxylamine-*O*-sulfonic acid (HOS) proved impractical because of its high solubility in water and the difficulty to remove excess HOS from the product. Hence, we prepared the tetrabutylammonium salt **4b** by reaction of HOS, fluorenone, and tetrabutylammonium hydroxide in a 3:1:2.25 ratio in methanol−water. Reaction of **4b** with the sodium salts of several alcohols (EtOH, BnOH, cyclopentanol) led to the consumption of the oxime sulfonate, but negligible amounts of O-aminated products, **6**, were detected; their presence was only confirmed by mass spectra. In order to avoid the presence of the negatively charged sulfonate group, as in **4**, we prepared the neutral fluorenone oxime *O*-tosylate **5a** (85% yield). The oxime tosylate **5a** was a stable solid, unaffected by 0.5 M HCl or 0.5 M NaOH at room temperature for 48 h.

Preliminary studies with **5a** were encouraging; heterogeneous reaction of oxime tosylate **5a**[15] with sodium benzyloxide, formed in situ from the alcohol and NaH in THF, led to O-amination with the formation of fluorenone oxime-*O*-alkyl ether, **6a**, at over an 80% yield at room temperature.[16] Lithium alcoholate gave slightly lower yield, and there was slight improvement in yield when THF−HMPA (1:1) or THF−DMSO (1:1) was used as the solvent. Following the reaction by HPLC initially proved to be advantageous. The disappearance of the starting oxime tosylate **5a** and the appearance of oxime ether **6a**, as well as of fluorenone oxime (the latter resulting from an attack of the alcoholate on the tosyl group), were monitored. Optimum reactant conditions for the reaction of oxime tosylate **5a** with benzyl alcohol were established as ROH:**5a**:NaH = 1:2:2 in a minimum of dry THF in a heterogeneous phase at room temperature. The reaction with benzyl alcohol was allowed to proceed for 6.5−7 h at room temperature and led to a 80% yield of benzyl ether **6a**, based on the alcohol as a limiting reagent and determined by HPLC integrations. The actual isolation of benzyl ether **6a** by column chromatography provided the compound in 84% yield. Thus, HPLC integration yields, despite the fact that the reaction was heterogeneous, are fairly representative of isolated yields. Theoretically possible double-amination products such as **7**, resulting from further addition of the alcoholate to the N=C, were not observed. Neither was a Beckmann rearrangement product.

The structure of **6a** was established by ^{1}H and ^{13}C NMR and by mass spectra. In order to prove that no Beckmann rearrangement to **8** (an isomer of **6a**) had taken place, the structure of **6a** was verified by its independent synthesis from fluorenone and *O*-benzylhydroxylamine.

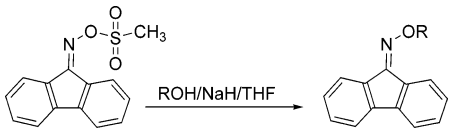
However, when tosylate displacement on **5a** was carried out with a secondary alcohol, namely, cyclopentanol, the reaction



7 **8**

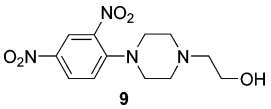
proceeded much more slowly, requiring 50−55 °C, and led to ether **6b** after 7 h in a 60% isolated yield. There was no significant improvement in the yield after 14 h, and the major side product detected after 14 h was fluorenone oxime. Surprisingly, even the primary alcohol, *n*-butanol, reacted very slowly with **5a** at room temperature and required heating to 50−60 °C to provide ether **6c** in 65% yield after 24 h (60% calculated by HPLC integrations).[15] There was no improvement in yield after 48 h of reaction time. In all reactions, fluorenone oxime was a byproduct.

Since reaction of some of the alcohols with tosylate **5a** required heating, we were searching for a more reactive substrate that could be employed at room temperature. To this end, we examined fluorenone oxime mesylate **5b**[17] and fluorenone oxime triflate **5c**[18] as O-amination substrates. The triflate **5c** reacted with the Na derivative of cyclopentanol at room temperature but furnished mainly fluorenone oxime, apparently by competitive attack at the sulfonyl group. The mesylate **5b** proved to be the most desirable substrate, reacting with most alcohols at room temperature to produce oxime ethers, **6**, with negligible formation of free oxime. Excess NaH should be avoided, as it reacts slowly with **5b** to form fluorenone.[19]



5b **6**

Table 1 records a few examples of O-amination of alcoholates, formed by treatment of each alcohol with 1.1 equiv of NaH in THF for 30 min and then allowing them to react with 1.1 equiv of mesylate **5b** in THF at 25 °C. The reactions of some representative primary and secondary alcohols were followed by TLC and stopped after disappearance of **5b**. The products **6**, isolated after evaporation, acidification, and chromatography, were pure by NMR. Alcohol **9** was chosen because its visually detectable chromophore can be useful as a universal standard reagent.[20]



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The general trend that emerges from our studies is that secondary alcohols react much more slowly than primary alcohols, and tertiary butanol did not react under these conditions, which is expected for steric reasons. The presence of an aromatic substituent, as in benzyl alcohol, as well as that of an

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(16) Unlike in the reaction with *n*-butanol, the yield of benzyl alcohol amination product **6a** was not much improved when the reaction was carried out at 50 °C.

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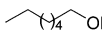
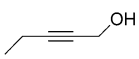
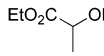
(19) While **5a** or **5c** reacted slowly with NaH in THF in the absence of alcohol to produce fluorenone oxime, **5b** was converted after 12 h to fluorenone (40%), apparently by hydride attack on N.

(20) For the application of analogous chromophores as universal standard reagents, see: Patchornik, A.; Hassner, A.; Kramer, M.; Gottlieb, H. E.; Cojocaru, M. *Heterocycles* **1999**, *51*, 1243.

TABLE 1. Relative Yields of O-Amination Products 6 by Reaction of 5 with ROH and NaH at Room Temperature

Entry	Comp. **6**	ROH	Time (h)	Yield (%)
1	**6a**		3	90
2*	**6b**		6	63
3	**6c**		6	68
4	**6d**		6	70
5	**6e**		3	90
6	**6g**	Alcohol **9**	4	80
7	**6h**		7	55
8	**6i**		7	60
9	**6j**		7	70
10	**6k**		8	58

[a] Heating at 55 °C.

olefinic double bond, as in allyl alcohol or 3-butene-1-ol, appears to enhance the reactivity compared to that in the presence of *n*-butanol, but acetylenic alcohols are slower to react. An α-carbethoxy group, as in lactate, does not interfere. Since cyclopentanol required heating even with mesylate **5b**, we also examined its reaction with the mesylate of 5,7-dinitrofluoren-9-one oxime, which was expected to involve a more stable fluorene anion intermediate, but the reaction was less clean and led to a mixture of products. Finally, we showed that hydrolysis of the oxime ethers proceeds well upon heating with 6 N HCl in acetic acid to provide *O*-alkylhydroxylamines; for example, *O*-benzylhydroxylamine was isolated in 60% yield as its hydrochloride, and *O*-allylhydroxylamine was isolated in 65% yield.

In conclusion, we have shown that O-amination of aliphatic alcohol anions is possible by using the electrophilic N reagents **5a** or, preferably, **5b** to produce oxime ethers, **6**, which can be hydrolyzed to *O*-alkylhydroxylamines. Such O-aminations might prove of interest in enzyme inhibition studies.

Experimental Section

General. All of the solvents were dried according to standard procedures. All of the fine chemicals were commercial and were used as such without further purification. NMR spectra were recorded on a 300 MHz instrument in $CDCl_3$ (unless otherwise stated), and chemical shifts are reported relative to TMS. Mass spectra were recorded on a Finnigan 4021 spectrometer. All new compounds, except where melting points are given, were isolated as oils. Flash chromatography was carried out on silica gel (60H). HPLC was performed using a UV detector set at 256 nm with a flow rate of 1 mL/min. HPLC separations were carried out on a C-18 column, using elution with a 3:7 water/acetonitrile solution. Melting points were determined in an open capillary.

Tetrabutylammonium 9-Fluorenone Oxime-*O*-sulfate (4b). To a stirred solution of 9-fluorenone (0.60 g, 3.3 mmol) in methanol (4 mL) were added hydroxylamine-*O*-sulfonic acid (HOS) (1.025 g, 9 mmol) and tetrabutylammonium hydroxide (4.5 mL, 6.8 mmol, 40% in water). After stirring the slurry for 15 min at room temperature, solvent was removed under reduced pressure, water was added, and the solid precipitate was filtered and washed with *tert*-butyl methyl ether to give 1.28 g (75%) of tetrabutylammonium 9-fluorenone oxime-*O*-sulfate (**5**) (solid, mp 133 °C). ^{1}H NMR δ_H: 8.45−7.85 (m, 2H), 7.55−7.40 (m, 6H), 3.41−3.20 (m, 8H), 1.50−1.32 (m, 16H), 0.96−0.85 (m, 12H). ^{13}C NMR δ_C: 153.9, 141.3, 140.4, 135.2, 131.2, 130.3, 130.2, 128.0, 127.6, 122.6, 119.6, 119.6, 109.0, 58.1, 23.6, 19.4, 13.4. LRMS (EI) *m*/*z* (%): 274 (MH^+) (100). FAB+ *m*/*z* (%): 242 (MH^+) (100).

General Procedure for Formation of Oxime Ethers, 6 (Table 1), from Corresponding Alcohols and 5b, with Fluoren-9-one *O*-Benzyl Oxime (6a) as an Example. Benzyl alcohol (0.22 g, 2 mmol) and NaH (0.08 g, 2 mmol, 60% in mineral oil) were stirred in dry THF (15 mL) for 30 min at room temperature. The solution of fluoren-9-one *O*-methanesulfonyl oxime **5b**, mp 150 °C (0.55 g, 2 mmol) in THF (30 mL), was added to the reaction mixture and stirred for 3 h at room temperature. The reaction was followed by TLC. Solvent was evaporated under reduced pressure, and the residue was extracted with ethyl acetate (50 mL), washed with water, and dried (Na_2SO_4). Oxime ether **6a** was purified by silica-gel column chromatography (eluant 1:20 ethyl acetate in *n*-hexane) (yield 0.51 g, 90%, mp 55 °C). ^{1}H NMR δ_H: 8.40−8.37 (m, 1H), 7.89−7.85 (m, 1H), 7.68−7.57 (m, 4H), 7.47−7.39 (m, 5H), 7.35−7.33 (m, 2H), 5.54 (s, 2H, CH_2O). ^{13}C NMR δ_C: 152.5, 141.3, 140.2, 137.5, 135.6, 130.9, 130.6, 129.8, 129.3, 128.5, 128.4, 128.4, 128.1, 128.1, 128.0, 127.8, 121.7, 119.9, 119.8, 77.8. LRMS (CI, CH_4) *m*/*z* (%): 286 (MH^+) (100). HRMS *m*/*z*: calcd for $C_{20}H_{15}NO$, 285.115; found, 286.125 (MH^+). Anal. Calcd for $C_{20}H_{15}NO$: C, 84.19; H, 5.30; N, 4.91. Found: C, 84.25; H, 5.33; N, 4.81.

The identical product (**6a**) was obtained in 95% yield by reaction of 180 mg of 9-fluorenone with 285 mg (1.8 equiv) of *O*-benzylhydroxylamine hydrochloride in EtOH−water and NaOH.

Fluoren-9-one *O*-Cyclopentyl Oxime (6b). ^{1}H NMR δ_H: 8.37−8.32 (m, 1H), 7.85−7.78 (m, 1H), 7.68−7.62 (m, 4H), 7.34−7.28 (m, 2H), 5.04−4.93 (m, 1H, C*H*−O), 2.15−1.65 (m, 8H). ^{13}C NMR δ_C: 151.7, 141.1, 139.9, 135.7, 130.5, 129.8, 129.4, 128.8, 128.0, 127.6, 121.4, 119.7, 119.6, 87.1, 32.3, 32.3, 23.8, 23.8. LRMS (CI, CH_4) *m*/*z* (%): 264 (MH^+) (100), 196 ($M-C_5H_8$) (35). HRMS *m*/*z*: calcd for $C_{18}H_{17}NO$, 264.138; found, 264.138.

Fluoren-9-one *O*-Butyl Oxime (6c). ^{1}H NMR δ_H: 8.20−8.17 (m, 1H), 7.68−7.65 (m, 1H), 7.67−7.47 (m, 2H), 7.29−7.15 (m, 4H), 4.31 (t, J = 7 Hz, 2H, O−CH_2CH$_2$), 1.78−1.69 (m, 2H), 1.45 (m, 2H), 0.90 (t, J = 7 Hz, 3H, CH$_2$CH_3). ^{13}C NMR δ_C: 159.1, 141.2, 140.1, 135.7, 130.7, 130.3, 129.6, 129.1, 128.1, 127.8, 121.5, 119.8, 119.7, 75.7, 31.3, 19.2, 13.9. LRMS (CI, NH_3) *m*/*z* (%): 252 (MH^+) (100). HRMS *m*/*z*: calcd for $C_{17}H_{17}NO$, 251.131; found, 251.131.

Fluoren-9-one *O*-Heptyl Oxime (6d). ^{1}H NMR δ_H: 8.38−8.30 (m, 1H), 7.75−7.71 (m, 1H), 7.60−7.51 (m, 2H), 7.45−7.30 (m, 4H), 4.40 (t, J = 7 Hz, 2H, O−CH_2CH$_2$), 1.85−1.78 (m, 2H), 1.60−1.21 (m, 10H), 0.9 (t, J = 7 Hz, 3H, CH$_2$CH_3). ^{13}C NMR δ_C: 151.7, 141.2, 140.0, 135.7, 130.6, 129.5, 129.0, 128.0, 127.76, 121.4, 119.7, 119.7, 76.0, 31.8, 29.2, 29.1, 26.0, 22.6, 14.0. LRMS (CI, NH_3) *m*/*z* (%): 294 (MH^+) (100). HRMS *m*/*z*: calcd for $C_{20}H_{30}NO$, 293.178; found, 294.185 (MH^+).

Fluoren-9-one *O*-Allyl Oxime (6e). ^{1}H NMR δ_H: 8.27−8.25 (m, 1H), 7.74−7.71 (m, 1H), 7.57−7.48 (m, 2H), 7.34−7.17 (m, 4H), 6.21−6.13 (m, 1H, C*H*═CH$_2$), 5.43−5.24 (m, 2H, CH═CH_2), 4.88−4.86 (m, 2H, OCH_2). ^{13}C NMR δ_C: 152.3, 141.3, 140.2, 135.6, 134.6, 133.9, 130.9, 129.8, 129.3, 128.1, 127.8, 121.6, 119.9, 119.8, 118.0, 76.6. HRMS *m*/*z*: calcd for $C_{16}H_{13}NO$, 235.100; found, 235.100 (M^+) (100).

Fluoren-9-one *O*-{2-[4-(2,4-Dinitrophenyl)piperazin-1-yl]-ethyl} Oxime (6g). Solid, mp 57 °C. ^{1}H NMR δ_H: 8.72−8.65 (m, 1H), 8.01−8.3 (m, 2H), 7.71−7.60 (m, 3H), 7.42−7.30 (m, 4H), 7.10−7.02 (m, 1H), 4.61−4.55 (m, 2H), 3.41−3.30 (m, 4H), 2.95−2.75 (m, 6H). ^{13}C NMR δ_C: 152.4, 149.2, 141.3, 140.1, 138.1,

137.9, 135.4, 131.0, 130.4, 129.9, 129.0, 128.1, 127.9, 123.7, 121.5, 119.9, 119.1, 73.5, 56.8, 52.7, 50.6. MS (CI, CH_4) *m*/*z* (%): 474 (MH^+) (9), 444 (M−NO) (5), 180 (M−$C_{13}H_8N$) (100). HRMS *m*/*z*: calcd for $C_{25}H_{23}N_5O_5$, 474.170; found, 474.168.

Fluoren-9-one *O*-But-3-ynyl Oxime (6h). ^{1}H NMR δ_H: 8.36−8.33 (m, 1H), 7.80−7.77 (m, 1H), 7.67−7.60 (m, 2H), 7.44−7.29 (m, 4H), 4.54 (t, J = 7 Hz, 2H), 4.25 (s, 1H), 2.83−2.77 (m, 2H). ^{13}C NMR δ_C: 152.7, 141.4, 140.3, 135.5, 131.0, 130.9, 129.9, 129.4, 128.2, 127.8, 121.7, 119.9, 119.8, 80.8, 73.2, 63.8, 19.5. HRMS (CI, CH_4) *m*/*z* (%): calcd for $C_{17}H_{13}NO$, 247.100; found, 247.102 (M^+) (49), 248.113 (M^++1) (16), 217.071 (M^+−NO) (100).

Fluoren-9-one *O*-Pent-2-ynyl Oxime (6i). ^{1}H NMR δ_H: 8.39−8.36 (m, 1H), 7.85−7.82 (m, 1H), 7.64−7.58 (m, 2H), 7.46−7.27 (m, 4H), 4.05 (s, 2H), 2.33 (q, J = 7 Hz, 2H), 1.23 (t, J = 7 Hz, 3H). ^{13}C NMR δ_C: 152.8, 141.4, 140.3, 135.5, 131.0, 130.6, 129.9, 129.6, 128.2, 127.8, 121.9, 119.9, 119.8, 89.2, 75.1, 64.0, 13.7, 12.7. HRMS (CI, CH_4) *m*/*z* (%): calcd for $C_{18}H_{15}NO$, 261.115; found, 261.114 (M^+) (100), 262.126 (M^++1) (36).

Fluoren-9-one *O*-(1-Methylallyl) Oxime (6j). ^{1}H NMR δ_H: 8.37 (d, J = 7.5 Hz, 1H), 7.69−7.63 (m, 2H), 7.50−7.27 (m, 5H), 6.21−6.09 (m, 1H, O−C*H*), 5.43 (d, J = 17 Hz, 1H), 5.28 (d, J = 10 Hz, 1H), 5.09−5.01 (m, 1H), 1.56 (d, J = 6 Hz, 3H). ^{13}C NMR δ_C: 152.0, 141.4, 140.2, 139.3, 130.8, 130.7, 129.7, 129.4, 129.3, 128.2, 127.8, 121.7, 119.9, 119.8, 116.0, 81.6, 19.8. HRMS (CI, CH_4) *m*/*z* (%): calcd for $C_{17}H_{15}NO$, 249.115; found, 249.116 (M^+) (100), 250.123 (M^++1) (74), 219.110 (M^+−NO) (61).

2-(Fluoren-9-ylidene aminooxy) Propionic Acid Ethyl Ester (6k). ^{1}H NMR δ_H: 8.44−8.41 (m, 1H), 7.78−7.75 (m, 1H), 7.64−7.58 (m, 2H), 7.43−7.27 (m, 4H), 5.05 (q, J = 6 Hz, 1H), 4.30 (q, J = 7 Hz, 2H), 1.73 (d, J = 6 Hz, 3H), 1.32 (d, J = 7 Hz, 3H). ^{13}C NMR δ_C: 172.2, 153.2, 141.5, 140.4, 135.4, 131.1, 130.5, 130.1, 129.7, 128.3, 127.8, 121.9, 119.9, 119.8, 79.1, 61.0, 17.3, 14.2. HRMS (CI, CH_4) *m*/*z* (%): calcd for $C_{18}H_{17}NO_3$, 295.129; found, 295.129 (M^+) (100), 296.139 (M^++1) (50), 222.091 (M^+−CO_2-Et) (40).

2-[4-(2,4-Dinitrophenyl)piperazin-1-yl] Ethanol (9). To a stirred solution of 1-(2-hydroxyethyl)piperazine (0.70 g, 5.4 mmol) in dichloromethane (4 mL) was added 2,4-dinitrofluorobenzene (0.3 mL, 2.36 mmol). After 15 min, the solvent was evaporated under reduced pressure. The residue was dissolved in ethyl acetate, washed with aqueous K_2CO_3 and water, and dried ($MgSO_4$). Removal of solvent gave 0.67 g (97%) of product, mp 92 °C. ^{1}H NMR δ_H: 8.5−8.6 (m, 1H), 8.23−8.26 (m, 1H), 6.93−7.10 (m, 1H), 3.53−3.70 (m, 2H), 3.41−3.30 (m, 4H), 2.82−2.7 (m, 4H), 2.65−2.63 (m, 2H). ^{13}C NMR δ_C: 149.2, 138.4, 138.2, 128.2, 123.6, 119.3, 57.8, 52.4, 59.2, 50.6. LRMS (CI, NH_3) *m*/*z* (%): 297 (M) (100), 267 (M−NO) (70), 237 (M−2NO) (35). HRMS *m*/*z*: calcd for $C_{12}H_{16}N_4O_5$, 297.119; found, 297.113 (M^+) (65).

Hydrolysis of Oxime Ethers 6a and 6e. To a solution of oxime ether (1 mmol) in 30 mL of hot glacial AcOH was added 6 N HCl (2 mL), and heating continued for 24 h. The solvent was removed under reduced pressure, and benzene was added to remove fluorenone and unreacted oxime ether. The solid was crystallized from EtOH to yield 60−65% of the corresponding *O*-alkylhydroxylamine hydrochloride salt, identical to the authentic material by NMR and mp.

Acknowledgment. Support of this research by the Marcus Center for Medicinal and Pharmaceutical Chemistry at Bar-Ilan University is gratefully acknowledged.

JO061900M