Preparation and Thermal Decomposition of *N,N'*-Diacyl-*N,N'*-Dialkoxyhydrazines: Synthetic Applications and Mechanistic Insights

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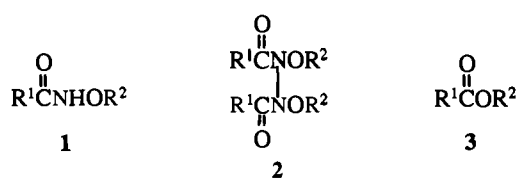
Abstract: Oxidation of various *O*-alkyl hydroxamates **1** where R^1 was a keto-methoxime, benzoyl, aryl, or alkyl group with ceric ammonium nitrate (CAN) or nickel peroxide ($NiO_2 \cdot H_2O$) leads to the corresponding esters in high yield. This augurs well for the facile synthesis of highly hindered esters. Dimers of type **2** were identified as intermediates in these oxidations, and a combination of experimental and theoretical results suggest that these dimers decompose in a stepwise 1,1-elimination manner via intermediate nitrenes to furnish the esters and not via a stepwise 1,2-elimination sequence as previously thought.

Introduction

We have been interested in finding easily removable protecting groups for carboxylic acids for use in carbohydrate and peptide chemistry.[1] Included in the study were various *O*-alkyl hydroxamates **1** where R^1 was a keto-methoxime, benzoyl, aryl, or alkyl group which can be readily derived from the corresponding acids. It was hoped that oxidation of **1** under mild conditions would lead to deprotection and afford the original acid.

Among the oxidizing reagents considered were ceric ammonium nitrate (CAN) and nickel peroxide ($NiO_2 \cdot H_2O$). Treatment of **1** (R^1 = 1-adamantyl and R^2 = methyl) with CAN afforded the desired acid along with substantial amounts of the corresponding ester **3** (ratio 1.5:1.0). Nitrogen was evolved during the course of this reaction so it was envisioned that the ester **3** (and acid via hydrolysis of **3**) was formed via the intermediate hydrazine **2**. Support for the formation of the dimer **2** came during the CAN oxidation of **1** (R^1 = 1-adamantyl and R^2 = *t*-Bu) which gave the acid as the major product along with ester **3** and another isolable product identified as the hydrazine **2**. Furthermore, treatment of **1** (R^1 = phenyl and R^2 = *t*-Bu) with CAN or $NiO_2 \cdot H_2O$ afforded the dimer **2** in 90% and quantitative yields, respectively. Heating of neat **2** afforded the corresponding ester **3** quantitatively.



1 **2** **3**

That such an oxidative coupling reaction exists for *O*-alkyl hydroxamates **1** has previously been demonstrated by Cooley and co-workers[2] and by Crawford and Raap.[3] The oxidizing reagents lead tetraacetate (LTA) and ammonium hexachloroplumbate (ACP) were employed by Cooley to synthesize a variety of simple hydrazines **2** in moderate yield. However, with these oxidizing reagents it was only possible to prepare hydrazines in which R^1 and R^2 were simple aliphatic groups as attempts to prepare dimers in which R^1 was aryl failed due to decomposition during preparation.[2] Attempts were also made to study the decomposition of the derived hydrazines in solution under acid, basic, and iodine catalysis; however, no clear mechanistic picture was presented. Furthermore, decomposition under these conditions afforded many products, making the decomposition synthetically useless. However, if no attempt was made to isolate the intermediate hydrazine **2**, the corresponding esters **3** were often isolated in modest yield. Crawford and Raap[2] also demonstrated that the oxidation of several simple *N*-carbalkoxy-*O*-alkylhydroxylamines with silver oxide afforded hydrazines of type **2** in good yield. This method was not applicable to the synthesis of **2** in which R^1 and R^2 were alkyl or aryl.[2]

We wish to report that ceric ammonium nitrate (CAN) and in particular nickel peroxide ($NiO_2 \cdot H_2O$) are superior mild oxidizing reagents to those employed previously and can be utilized to afford in many cases quantitative yields of hydrazines **2**. Additionally, the mechanism of thermal decomposition of the dimers **2** was investigated experimentally as well as theoretically. This method of coupling followed by nitrogen elimination represents a simple method for the preparation of hindered esters in near quantitative yield.

Results and Discussion

A number of *O*-alkyl hydroxamates **1** in which the α-position contained keto-methoxime, benzoyl, aryl, or alkyl (primary, secondary, and tertiary) moieties were readily prepared from the corresponding carboxylic acids. The derivatives employed in this study along with the product(s) obtained by CAN and/or $NiO_2 \cdot H_2O$ oxidation are summarized in Table 1.

Employing cerium(IV) as the oxidant afforded hydrazines **2** in excellent yield when R^1 was methoxime, benzoyl, or aryl. However, those hydrazines containing bulky alkyl groups (**1d**−**g**) decomposed under the reaction conditions.

[⊗] Abstract published in *Advance ACS Abstracts*, April 15, 1995.

(1) Barton, D. H. R.; Girijavallabhan, M.; Sammes, P. G.J. *Chem. Soc., Perkin. Trans. 1* **1972**, 929−932. de Oliveira Baptista, M. J. V.; Barrett, A. G. M.; Barton, D. H. R.; Girijavallabhan, M.; Jennings, R. C.; Kelly, J.; Papadimitriou, V. J.; Turner, J. V.; Usher, N. A. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1477−1500.

(2) Cooley, J. H.; Mosher, M. W.; Khan, M. A. *J. Am. Chem. Soc.* **1968**, *90*, 1867−1871.

(3) Crawford, R. J.; Raap, R. *J. Org. Chem.*, **1963**, *28*, 2419−2424.

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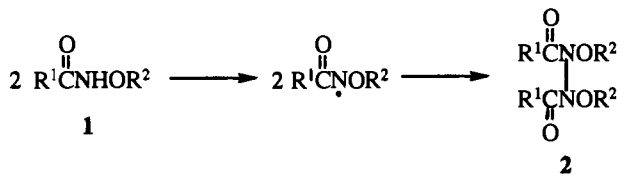
Table 1. Synthesis of *N,N'*-Diacyl-*N,N'*-Dialkoxyhydrazines **2**

substrate	R^1	R^2	method[a]	reaction conditions temp (°C)/ time (h)	yield of **2** (%)	yield of **3** (%)
1a	$PhC(NOCH_3)$	CH_3	CAN	25/4	94	–
1b	PhCO	CH_3	CAN	−20/3	100	–
1c	Ph	*t*-Bu	CAN	−20/3	90	–
1d	1-adamantyl	CH_3	CAN	−20/3	0	90[b]
1e	1-adamantyl	CH_{2Ph}	CAN	−20/3	0	85
1f	1-adamantyl	*t*-Bu	CAN	−20/3	30	60[c]
1g	*t*-Bu	CH_3	CAN	−20/4	0	90
1a	$PhC(NOCH_3)$	CH_3	$NiO_2{\cdot}H_2O$	25/12	100	–
1b	PhCO	CH_3	$NiO_2{\cdot}H_2O$	0/12	98	–
1h	Ph	CH_3	$NiO_2{\cdot}H_2O$	0/8	100	–
1i	$PhCH_2CH_2$	CH_3	$NiO_2{\cdot}H_2O$	0/12	100	–
1j	$PhCH_2CH_2$	CH_2Ph	$NiO_2{\cdot}H_2O$	0/12	90	–
1c	Ph	*t*-Bu	$NiO_2{\cdot}H_2O$	0/12	100	–
1k	cyclohexyl	CH_3	$NiO_2{\cdot}H_2O$	0/4	100	–
1g	*t*-Bu	CH_3	$NiO_2{\cdot}H_2O$	−20/6	93	7
1d	1-adamantyl	CH_3	$NiO_2{\cdot}H_2O$	0/16	0	95
1f	1-adamantyl	*t*-Bu	$NiO_2{\cdot}H_2O$	−20/32	70	12

[a] See Experimental Section for conditions. [b] Yield represents ester and acid (ratio 1.5:1.0). [c] Yield represents ester and acid (ratio 1.0:1.0).

Nickel peroxide proved to be a milder oxidizing reagent allowing hydrazines with all the aforementioned substituents to be isolated in many cases in quantitative yield (see Table 1). The coupling reaction requires greater reaction time as steric bulk increases. It failed for R^1 = 1-adamantyl, $R^2 = CH_3$ which is attributable to the rate of thermal decomposition being faster than the rate of the coupling reaction at ambient temperature. The dimer containing R^1 = 1-adamantyl and R^2 = *t*-Bu was formed in good yield over greater reaction time suggesting that the bulky groups in this hydrazine have twisted the conformation increasing the energy barrier to decomposition.

It was generally observed that the hydrazines **2** containing a methoxime, benzoyl or aryl group showed greater stability over those **2** simply substituted with alkyl groups. There is considerable evidence that oxidations employing CAN and $NiO_2{\cdot}H_2O$ involve free radical pathways.[4,5] It is therefore considered that the hydrazines **2** form from the dimerization of two nitrogen radical species.



The intermediate nitrogen radicals are presumably "captodative" in nature[6] and this perhaps explains the excellent yields of hydrazines obtained here when compared to those obtained for the $NiO_2{\cdot}H_2O$ oxidation of secondary amines.[5] Thermal decomposition of hydrazines **2** cleanly afforded the esters **3** in excellent yield as depicted in Table 2. Quantitative loss of nitrogen was confirmed by GCMS and mass balance experiments, *i.e.*, decomposition of a known amount of **2** resulted in the quantitative formation of ester **3** minus the weight required

(4) Doyle, M. P.; Zuidema, L. J.; Bade, T. R. *J. Org. Chem.* **1975**, *40*, 1454−1457. Trahanovsky, W. S.; Robbins, M. D.; Smick, D. *J. Am. Chem. Soc.* **1971**, *93*, 2086−2087. Bird, J. W.; Diaper, D. G. M. *Can. J. Chem.* **1969**, *47*, 145−150.

(5) George, M. V.; Balachandran, K. S. *Chem. Rev.*, **1975**, *75*, 491−519, and references cited therein.

(6) *Substituent Effects in Radical Chemistry*; Viehe, H. G., Tanousek, Z., Merenyi, R. D., Eds.; Reidel: Dordrecht, Holland, **1986**. Beckwith, A. L. J. *Chem. Soc. Rev.* **1993**, 143−151.

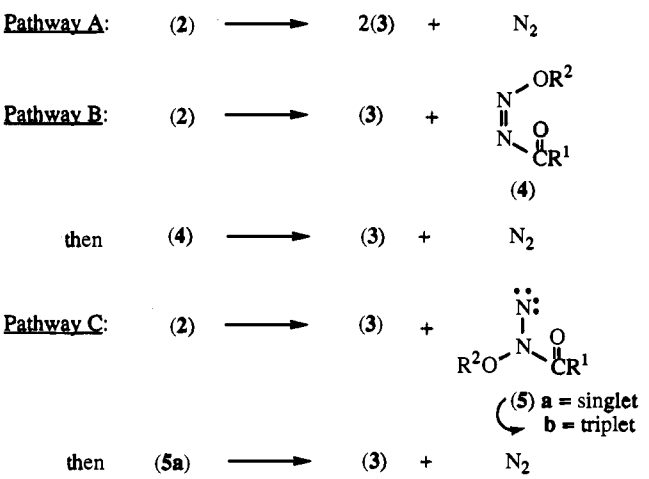
Table 2. Thermal Decomposition of Dimers **2**

substrate	R^1	R^2	reaction conditions[a] temp (°C)/time (h)	yield of **3** (%)
2a	$PhC(NOCH_3)$	CH_3	100−160/0.5	100
2b	PhCO	CH_3	30−40/6	90
2c	Ph	*t*-Bu	80−110/6	92
2f	1-adamantyl	*t*-Bu	40−65/6	87
2g	*t*-Bu	CH_3	25/12	100
2i	$PhCH_2CH_2$	CH_3	50−80/7	100
2j	$PhCH_2CH_2$	CH_2Ph	50−80/7	96
2k	cyclohexyl	CH_3	50−80/4	100

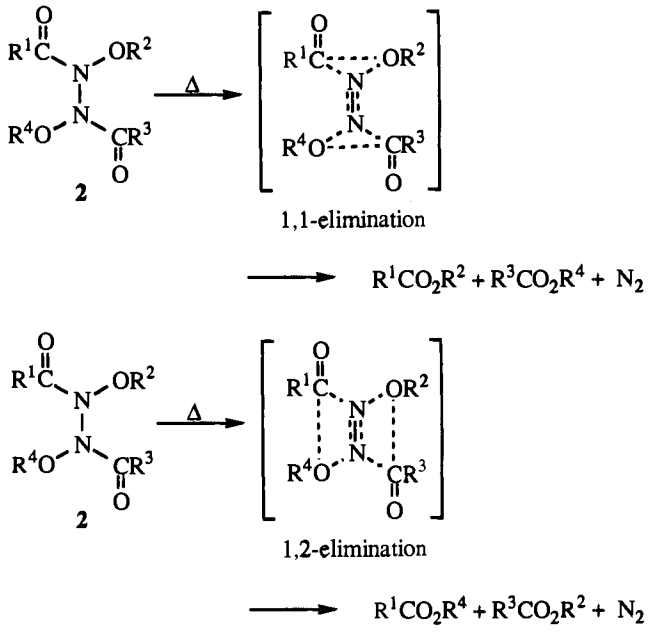
[a] See Experimental Section for conditions.

for nitrogen loss. Further observations were that the thermal decompositions were not accelerated by Lewis acids ($TiCl_4$, $SnCl_4$, $BF_3{\cdot}OEt_2$) or by the addition of mineral acids. Decomposition in the presence of TEMPO, $CDCl_3$, or CCl_4 resulted in no contamination. Addition of alcohols did however give rise to transesterification; however, "blank" experiments later revealed that the transesterification took place after the formation of the esters **3**. In principle this is a very simple and mild method for the construction of esters **3** containing hindered R^1 and R^2 functional groups.

As with all chemical reactions an understanding of the mechanism brings with it a greater opportunity to harness synthetically the use of such a process. In principle there are three different pathways for the thermal decomposition of hydrazines **2** which would explain the observed products. These are summarized by the following equations



Pathway A is simply a concerted mechanism in which one molecule of hydrazine **2** affords the ester **3** (2 molecules) and nitrogen . The net result of this pathway is the concerted breaking of four σ-bonds with formation of two new σ-bonds and two new π-bonds. Among the high symmetry-concerted decompositions (pathway A), the C_s and C_i pathways are symmetry forbidden, while the C_2 pathway is symmetry allowed. Although the forbiddenences of two routes does not necessarily mean that pathway A is high in energy, it is suggestive. Pathway B is a stepwise mechanism and first involves the decomposition of the hydrazine **2** to azine **4** and ester **3**, followed by further decomposition of azine **4** affording ester **3** and nitrogen. This pathway, a series of two first-order reactions was proposed previously based on several kinetic measurements even though the azine **4** was never observed spectroscopically.[2] Finally, pathway C is also a two-step mechanism and involves the intermediacy of a nitrene **5**. Initially, the nitrene would be formed in the singlet state which could decay to the triplet if the latter was lower in energy. Decomposition of the singlet nitrene affords the observed ester **3** and nitrogen.



If all four substituents ($R^1 \rightarrow R^4$) are different, the two pathways can be classified as follows: (1) a 1,1-elimination pathway which would result in the formation of esters containing substituents R^1/R^2 and R^3/R^4 but not R^1/R^4 and R^3/R^2; (2) a 1,2-elimination pathway which would result in the formation of esters containing substituents R^1/R^4 and R^3/R^2 but not R^1/R^2 and R^3/R^4.

To distinguish between these two modes of decomposition an unsymmetrical hydrazine (**2l**, R^1 = cyclohexyl, R^2 = methyl, R^3 = benzyl and R^4 = phenethyl) was synthesized. Since the mixed coupling of nitrogen radicals might lead to a complex separation problem, we decided to use ionic chemistry instead. Thus the intermediate **1k** was converted by *N*-chlorosuccinimide into its *N*-chloro derivative. The intermediate **1j** was turned into its anion by using sodium hydride. This anion was then condensed with the *N*-chloro compound to furnish the desired **2l** in good (92%) yield. Decomposition of **2l** between 60−80 °C over 8 h resulted in quantitative formation of methyl cyclohexylcarboxylate and benzyl 3-phenylpropanoate in a ratio 1:1. Independently, cross-over experiments showed that there was no mixing during decomposition of equivalent amounts of **2j** and **2k**. These experimental results along with those discussed above clearly indicate that the thermal decomposition of hydrazines **2** proceed along a 1,1-elimination pathway and not as suggested previously,[1] *i.e.*, via pathway B.

Pathway C involved the nitrene as an intermediate and we have attempted to trap this nitrene in a variety of ways. Nitrenes are well known to undergo insertion reactions with alkenes.[7] Decomposition of a number of hydrazines in neat cyclohexene or styrene resulted only in the quantitative formation of ester **3** with no insertion. Additionally, decomposition of dimers **2a** and **2k** in the presence of a large excess of other well known nitrene traps (DMSO, nitrosobenzene, DEAD, and dimethylfumarate)[8] yielded only the corresponding esters and nitrogen with no trapping products. Furthermore, there was no formation of tetrazene from dimerization of a species like **5**.

Thus, the experimental results appear to support pathway A, which from simple theoretical considerations would appear to be least likely. To aid in understanding if this conclusion is warranted, we have examined the reaction theoretically. The reaction profiles for pathway A and pathway C are shown in Figure 1. Since these profiles were constructed with a semiempirical Hamiltonian (see Experimental Section), their absolute magnitudes may not be particularly accurate. However, their relative magnitudes clearly show that the concerted elimination (pathway A) is strongly disfavored over the stepwise elimination (pathway C).

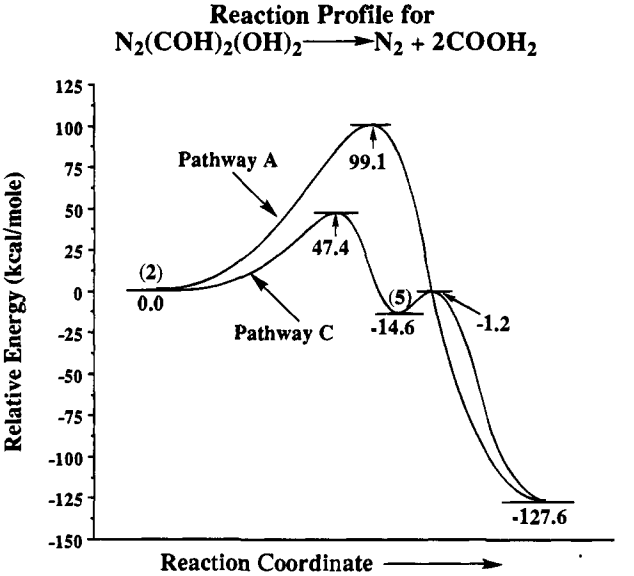


Figure 1. The reaction profiles for the decomposition of $N_2(COH)_2(OH)_2$ were computed from AM1 parameters by the MOPAC program in the CAChe modeling systems. All species and transition states were fully optimized. The nitrene **5** is formed on the low energy pathway (C), but its barrier to further reactions is so small that trapping it will prove difficult.

Because the second barrier in the stepwise elimination is smaller than the exothermicity of the first step, it would be very difficult to trap the nitrene **5** before it continued over this barrier making the final product. Ab initio calculations (MP2/6-31G*//HF/6-31G*) on the "stable" species in Figure 1 suggest that the nitrene (in its singlet ground state) is somewhat less stable (10 kcal mol^{-1}) than indicated and that the products are somewhat more stable (6 kcal mol^{-1}) than indicated by the AM1 energies on Figure 1. Thus at the ab initio level the second barrier may be even smaller.

Concluding Remarks

A combination of experimental and theoretical results suggest that dimers of type **2** decompose in a stepwise 1,1-elimination manner via intermediate nitrenes to furnish high yields of esters. There seems to be little steric congestion in the case of ester formation. This augurs well for the facile synthesis of sensitive highly hindered esters. The work also suggests that the coupling reactions of tetrasubstituted hydrazines in general may be of preparative interest. It is of significance that the excellent synthesis of benzyne from 1-*N*-aminobenzotriazole also involves the elimination of two molecules of nitrogen.[9] Nitrogen elimination also plays an important role in the formation of very hindered olefins.[10]

Experimental Section

Theoretical Methods. The reaction profiles were calculated from the AM1 parameterizations[11a] of the MOPAC Program[11b] with the

(7) Lwowski, W. *Reactive Intermediates*, Jones, M., Moss, R. A., Eds.; Wiley: New York, 1981; Vol. 2, pp 315−334. Lwowski, W. *Angew. Chem. Int. Ed. Engl.* **1967**, *6*, 897−906; Abramovitch, R. A.; Davis, B. A. *Chem. Rev.* **1964**, *64*, 149−185.

(8) Lwowski, W., Ed. *Nitrenes*; Interscience Publishers: New York, 1970.

(9) Campbell, C. D.; Rees, C. W. *J. Chem. Soc. (C)* **1969**, 748−751.

(10) Back, T. G.; Barton, D. H. R.; Britten-Kelly, M. R.; Guziec, F. S.; *J. Chem. Soc. Perkin Trans. 1*, **1976**, 2079−2089.

CAChe molecular modeling software.[11c] The geometry of stable species was optimized at the HF/6-31G* level of theory and the MP2 energy of the equilibrium geometry calculated. All calculations, with the exception of the open-shell MP2 calculation which was performed using Gaussian 92,[12a] were performed using the GAMESS-UK software package.[12b]

Materials and Instrumentation. Solvents were used as purchased or dried and purified by standard methods. Melting points were determined with a Kofler hot-stage melting point apparatus and are uncorrected. Boiling points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 881 spectrophotometer and referenced to a polystyrene standard while the UV/vis spectra were measured with a Beckman Model DU-7 spectrometer. Proton (chemical shifts referenced to TMS at δ 0.00) and ^{13}C (referenced to $CDCl_3$ at δ 77.00) NMR spectra were measured at ambient temperature on a Varian XL-200 or a Gemini-200 spectrometer operating at 200 and 50 MHz, respectively, using 5-mm tubes. Proton and carbon-13 spectral data are presented as follows: multiplicity (br = broad, s = singlet, d = doublet, m = multiplet, integration). GC-MS analyses were performed on a Hewlett-Packard 5790A series gas chromatograph equipped with a quadrupole mass-selective detector. Microanalyses were performed by Atlantic Microlab Inc., Norcross, GA.

General Procedure for Preparation of Hydroxamates 1a–k. To a mixture of *O*-alkyl hydroxylamine hydrochloride (12 mmol) in pyridine (10 mL) at 0 °C under argon was added dropwise a solution of the appropriate acid chloride (10 mmol)[13] in anhydrous THF. The mixture was allowed to warm to ambient temperature and stirring continued overnight, after which time the mixture was filtered and the volatiles removed in vacuo. The residue was dissolved in methylene chloride (50 mL) and the solution washed with aqueous saturated sodium hydrogen bicarbonate (2 × 25 mL) and water (25 mL). Desiccation over magnesium sulfate and removal of the solvent in vacuo afforded crude **1**. In the case of crystalline compounds, the residue was recrystallized from diethyl ether. In the case of oils, the residue was purified by flash chromatography, (hexane/EtOAc, 1:1). Yields, 80–95%. The authenticity and purity of known derivatives **1** were checked by comparison with physical and spectroscopic data published in the literature. **1c**,[14] **1h**,[15] **1i**,[16] **1k**.[17]

***O*-Methyl-2-phenyl-2-methoximinoacetohydroxamic Acid (1a).** Isolated as a colorless oil (72%): IR (neat cm^{-1}) 3273, 2926, 1653, 1221, 1102, 1035, 993, 946, 722, 691, 610; ^1H NMR δ 9.13 (br s, 1H), 7.54–7.63 (m, 2H), 7.30–7.40 (m, 3H), 3.95–4.0 (d, 3H), 3.75 (s, 3H); ^{13}C NMR showed **1a** to be a mixture of methoxime isomers; MS *m/z* (rel inten) 208 (35). Anal. Calcd for $C_{10}H_{12}N_2O_3$: C, 57.68; H, 5.81; N, 13.46. Found: C, 57.41; H, 5.85; N, 13.31.

***O*-Methyl-2-phenyl-2-oxoacetohydroxamic Acid (1b).** Recrystallized from CH_2Cl_2/hexanes, 1:1, (78%): mp 89–90 °C; IR (KBr cm^{-1}) 1650; ^1H NMR δ 9.70 (br s, 1H), 8.26–8.35 (m, 2H), 7.50–7.64 (m, 3H), 3.90 (s, 3H); MS *m/z* (rel inten) 179 (27). Anal. Calcd for $C_9H_9NO_3$: C, 60.33; H, 5.06; N, 7.82. Found: C, 60.42; H, 5.12; N, 7.89.

***O*-Methyl-1-adamantylhydroxamic Acid (1d).** Recrystallized from ether (91%): mp 156–157 °C; IR (KBr cm^{-1}) 3242, 2907, 1636, 1030, 920; ^1H NMR δ 8.70 (br s, 1H), 3.71 (s, 3H), 1.94–2.05 (m, 3H), 1.81–1.88 (m, 6H), 1.65–1.72 (m, 6H); ^{13}C NMR δ 175.65, 64.10, 40.03, 38.70, 36.38, 27.89; MS *m/z* (rel inten) 209 (14). Anal. Calcd for $C_{12}H_{19}NO_2$: C, 68.86; H, 9.15; N, 6.69. Found: C, 68.73; H, 9.17; N, 6.70.

***O*-Benzyl-1-adamantylhydroxamic Acid (1e).** Recrystallized from ether (92%): mp 129–130 °C; IR (KBr cm^{-1}) 3193, 2903, 1634, 1012, 923, 694; ^1H NMR δ 8.30 (br s, 1H), 7.30–7.42 (m, 5H), 4.88 (s, 2H), 1.94–2.05 (m, 3H), 1.79–1.84 (m, 6H), 1.65–1.72 (m, 6H); ^{13}C NMR δ 175.47, 135.34, 129.39, 128.69, 128.53, 77.87, 40.12, 38.75, 36.35, 27.87; MS *m/z* (rel inten) 285 (42). Anal. Calcd for $C_{18}H_{23}NO_2$: C, 75.75; H, 8.12; N, 4.91. Found: C, 75.54; H, 8.14; N, 4.91.

***O*-*tert*-Butyl-1-adamantylhydroxamic acid (1f).** Isolated as a colorless oil (89%): IR (neat cm^{-1}) 3250, 2976, 2907, 1644, 1016, 929, 858, 677, 631; ^1H NMR δ 7.95 (br s, 1H), 1.98–2.11 (m, 3H), 1.88–1.94 (m, 6H), 1.70–1.76 (m, 6H), 1.26 (s, 9H); ^{13}C NMR δ 176.58, 81.75, 40.40, 38.98, 36.38, 27.92, 26.23; MS *m/z* (rel inten) 177 (38), 135 (100), 120 (98), 107 (8), 93 (20), 79 (28).

General Procedure for Preparation of Hydrazines 2a–c and 2f–k. CAN Method. To a solution of **1** (1 mmol) in anhydrous THF (10 mL) at −20 °C (25 °C in case of **1a**) under argon was added CAN (0.60 g, 1.1 mmol). Stirring was continued for the time indicated in Table 1 while the temperature was allowed to slowly attain 10 °C, after which time the mixture was diluted with ether (20 mL), washed quickly with cold water (20 mL), dried ($MgSO_4$), and concentrated in vacuo at ≈15 °C affording crude **2**. In the case of crystalline compounds, the residue was recrystallized from cold hexane. The hydrazine **2a** was isolated by flash chromatography (hexane/EtOAc, 1:1).

$NiO_2 \cdot H_2O$ Method. To a solution of **1** (1 mmol) in anhydrous THF (10 mL) at 0 °C (or −20 °C in the case of **1f** and **1g**) was added nickel peroxide hydrate (0.206 g, 1.9 mmol, 0.40 g in case of **1f**). Stirring was continued for the time indicated in Table 1 while the temperature was allowed to slowly attain ambient temperature, after which time the mixture was filtered through Celite 545, washed with cold ether (3 × 40 mL), and concentrated in vacuo at ≈15 °C. In the case of crystalline compounds, the residue was recrystallized from cold hexane. Oils were purified by flash chromatography, (hexane/EtOAc, 1:1). Yields are as depicted in Table 1.

Hydrazine 2a. Flash chromatography afforded both methoxime isomers. The first eluted as a crystalline compound, recrystallized from hexanes: mp 101–103 °C; IR (KBr cm^{-1}) 3150, 3094, 2930, 1724, 1697, 1046, 994, 792, 771; ^1H NMR δ 7.75–7.85 (m, 4H), 7.35–7.46 (m, 6H), 4.06 (s, 6H), 3.78 (s, 6H); ^{13}C NMR δ 163.34, 151.35, 130.54, 129.86, 128.85, 126.42, 64.10, 62.98; MS *m/z* (rel inten) 193 (100), 168 (38), 134 (82), 119 (100), 103 (49), 77 (37). Anal. Calcd for $C_{20}H_{22}N_4O_6$: C, 57.96; H, 5.35; N, 13.52. Found: C, 57.93; H, 5.37; N, 13.53. The second eluted as colorless oil: IR (neat cm^{-1}) 3047, 2969, 2930, 1708, 1582, 1026, 940, 771, 733, 689; ^1H NMR δ 7.65–7.82 (m, 2H), 7.35–7.45 (m, 3H), 4.03 (s, 3H), 3.70–3.90 (br d, 3H); MS *m/z* (rel inten) 193 (100), 168 (38), 134 (82), 119 (100), 103 (49), 77 (37).

Hydrazine 2b. Isolated as colorless oil: IR (neat cm^{-1}) 3063, 2958, 2927, 1736, 1685, 1595, 1208, 1175, 978, 711, 684; ^1H NMR δ 8.05–8.18 (m, 4H), 7.44–7.70 (m, 6H), 3.89 (s, 6H); ^{13}C NMR δ 188.40, 166.30, 135.39, 131.90, 129.89, 129.12, 64.53; MS *m/z* (rel inten) 164 (10), 136 (12), 105 (100), 77 (70), 51 (26). A satisfactory microanalysis could not be obtained due to the thermal instability of this compound above 30 °C.

Hydrazine 2c. Recrystallized from hexanes: mp 98–100 °C; IR (KBr cm^{-1}) 3086, 3061, 2976, 1685, 1388, 1258, 1176, 910, 701, 621; ^1H NMR δ 7.10–7.80 (br m, 10H), 1.00–1.30 (br s, 18H); ^{13}C NMR δ 172.00, 133.95, 130.87, 128.86, 127.59, 83.52, 27.10, signals were broad due to rotational isomers. Anal. Calcd for $C_{22}H_{28}N_2O_4$: C, 68.72; H, 7.34; N, 7.29. Found: C, 68.76; H, 7.47; N, 7.27.

Hydrazine 2f. Isolated as colorless oil: IR (neat cm^{-1}) 2950, 1708, 1433, 1320, 1024, 846, 659; ^1H NMR δ 1.90–2.02 (m, 4H), 1.80–1.82 (m, 12H), 1.64–1.71 (m, 12H), 1.40 (s, 18H); ^{13}C NMR δ 177.09, 79.20, 41.02, 38.80, 36.55, 28.01, 27.85. A satisfactory microanalysis could not be obtained due to the thermal instability of this compound above 30 °C.

Hydrazine 2g. Isolated as colorless oil: IR (neat cm^{-1}) 2974, 2934, 2872, 1684, 1458, 1273, 1146, 989, 841, 606; ^1H NMR δ 3.81 (s, 6H), 1.31 (s, 18H); ^{13}C NMR δ 178.03, 61.56, 39.81, 26.71.

(11) (a) Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.*, **1985**, 107, 3902. (b) Stewart, J. J. P. The MOPAC Manual. (c) CAChe User's Guide, Tektronix Inc.

(12) (a) Gaussian 92, Revision F. Frisch, M. J.; Trucks, G. W.; Head-Gordon, M.; Gill, P. M. W.; Wong, M. W.; Foresman, J. B.; Johnson, B. G.; Schlegel, H. B.; Robb, M. A.; Replogle, E. S.; Gomperts, R.; Andres, J. L.; Raghavachari, K.; Binkley, J. S.; Gonzalez, C.; Martin, R. L.; Fox, D. J.; Defrees, D. J.; Baker, J.; Stewart, J. J. P., Pople, J. A., Gaussian Inc. Pittsburgh, PA, 1992. (b) Guest, M. F., Sherwood, P. *GAMESS-UK*, Revision B.0, S. E. R. C., Daresbury Laboratory, 1992.

(13) The acid chlorides were prepared by treatment of the parent acids in ether with oxalyl chloride via standard methods.

(14) Koenig, T.; Deinzer, M.; Hoobler, J. A. *J. Am. Chem. Soc.* **1971**, *93*, 938–944.

(15) Hearn, M. T. W.; Ward, A. D. *Aust. J. Chem.* **1969**, *22*, 161–173.

(16) Glover, S. A.; Goosen, A.; McCleland, C. W.; Schoonraad, J. L. *Tetrahedron*, **1987**, *43*, 2577–2592.

(17) Fisher, L. E.; Caroon, J. M.; Jahangir; Stabler, S. R.; Lundberg, S.; Muchowski, J. M. *J. Org. Chem.* **1993**, *58*, 3643–3647.

Hydrazine 2h. Isolated as colorless oil: IR (neat cm^{-1}) 3235, 3066, 2939, 1718, 1624, 1447, 1313, 998, 782, 699, 650; ^1H NMR δ 7.32–7.70 (m, 10H), 3.85 (s, 6H); ^{13}C NMR δ 169.89, 132.13, 128.48, 128.35, 128.19, 63.39; MS *m/z* (rel inten) 136 (69), 105 (100), 77 (73).

Hydrazine 2i. Isolated as colorless oil: IR (neat cm^{-1}) 3086, 2958, 3027, 2940, 1725, 1438, 1361, 1293, 1175, 1013, 933, 743; ^1H NMR δ 7.18–7.34 (m, 10H), 3.79 (s, 6H), 2.95–3.15 (m, 4H), 2.74–2.86 (m, 4H); ^{13}C NMR δ 173.45, 140.48, 128.57, 128.46, 126.36, 63.07, 34.93, 30.31.

Hydrazine 2j. Recrystallized from hexanes: mp 38–39 °C; IR (KBr cm^{-1}) 3088, 3063, 2937, 1724, 1362, 1207, 1177, 910, 750, 698; ^1H NMR δ 7.08–7.36 (m, 20H), 4.93 (s, 4H), 2.84–2.93 (m, 4H), 2.61–2.72 (m, 4H); ^{13}C NMR δ 173.53, 140.33, 134.82, 129.45, 129.14, 128.87, 128.58, 128.37, 126.35, 77.52, 34.76, 30.00. Anal. Calcd for $C_{32}H_{32}N_2O_4$: C, 75.56; H, 6.34; N, 5.51. Found: C, 75.37; H, 6.46; N, 5.26.

Hydrazine 2k. Recrystallized from hexanes: mp 53–54 °C; IR (KBr cm^{-1}) 2936, 2855, 2817, 1711, 1446, 1329, 1247, 1166, 1003, 938, 894, 799, 716; ^1H NMR δ 3.88 (s, 6H), 2.58–2.72 (m, 2H), 1.20–2.00 (m, 20H); ^{13}C NMR δ 176.71, 62.85, 41.23, 28.63, 25.55, 25.41. Anal. Calcd for $C_{16}H_{28}N_2O_4$: C, 61.51; H, 9.03; N, 8.97. Found: C, 61.53; H, 9.07; N, 8.96.

Hydrazine 2l. To a solution of *O*-methyl cyclohexanohydroxamate **1k** (0.785g, 5.0 mmol) in carbon tetrachloride (10 mL) at room temperature was added *N*-chlorosuccinimide (0.80g, 6.0 mmol). The mixture was heated under reflux for 6 h and cooled and hexane (10 mL) was added. The resulting solution was allowed to stand at −20 °C for 1 h after which time the mixture was filtered through Celite 545, washed with cold ether (3 × 30 mL), and concentrated in vacuo at ≈15 °C to afford pure *N*-chloro,*O*-methylcyclohexanohydroxamic acid quantitatively (0.95g) as a colorless oil. IR (neat cm^{-1}) 2936, 2858, 1719, 1445, 1312, 1242, 1104, 923, 688; ^1H NMR δ 3.81 (s, 3H), 2.66–2.82 (m, 1H), 1.20–1.90 (m, 10H); ^{13}C NMR δ 180.64, 62.60, 42.61, 29.18, 25.56, 25.47. To a solution of **1j** (0.255 g, 1.0 mmol) in anhydrous THF (20 mL) at 0 °C under argon was added sodium hydride (25 mg, 1.0 mmol). The mixture was stirred at 0 °C for 10 min after which time a solution of **1k** (0.194 g, 1.0 mmol) in anhydrous THF (10 mL) was added dropwise over 5 min. The mixture was stirred an additional 2 h and allowed to attain room temperature. The organics were filtered through Celite 545 and washed with ether (3 × 30 mL) and the combined organics concentrated in vacuo at ≈15 °C to afford crude **2l** (0.45 g). Purification was achieved by flash chromatography (hexane/EtOAc, 1:1) affording **2l** (0.41 g, 92%) as a colorless oil: IR (neat cm^{-1}) 3086, 3029, 2936, 2858, 1706, 1365, 1160, 993; ^1H NMR δ 7.10–7.42 (m, 10H), 5.00 (s, 2H), 3.80 (s, 3H), 2.87–2.98 (m, 2H), 2.55–2.75 (m, 3H), 1.21–1.96 (m, 10H); ^{13}C NMR showed **2l** to be two rotational isomers at ambient temperature. A satisfactory microanalysis could not be obtained due to the thermal instability of this compound.

Thermal Decomposition of Hydrazines (2a–c,f–g,i–k). The hydrazine **2** (0.1 mmol) was progressively heated in a closed NMR tube or in a closed flask according to the temperatures and reaction times indicated in Table 2. The esters **3** were purified by flash chromatography (hexane/EtOAc, 1:1) and characterized by comparison with authentic samples reported in the literature. **3b**,[18] **3c**,[19] **3d**,[20] **3g**,[21] **3h**,[18] **3i**,[19] **3j**,[22] **3k**.[18] Esters **3a,e,f** were identified by hydrolysis to their known acids.[21] Yields are tabulated in Tables 1 and 2.

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(18) Grasselli, J. G.; Ritchey, W. M. *CRC Atlas of Spectral Data and Physical Constants for Organic Compounds*, 2nd ed.; CRC Press: Boca Raton, FL, **1975**.

(19) Rossi, R. A.; de Rossi, R. H. *J. Org. Chem.*, **1974**, *39*, 855–856.

(20) Newkome, G. R.; Behera, R. K.; Moorefield, C. N.; Baker, G. R. *J. Org. Chem.* **1991**, *56*, 7162–7169.

(21) Lide, D. R.; Milne, G. W. A., Eds. *Handbook of Data on Organic Compounds*, 3rd ed.; CRC Press: Boca Raton, FL, **1994**.

(22) Aiapurua, J. M.; Palomo, C. *Synthesis* **1982**, 684–687.