Reaction of Oximes with Dimethyl Carbonate: A New Entry to 3-Methyl-4,5-disubstituted-4-oxazolin-2-ones

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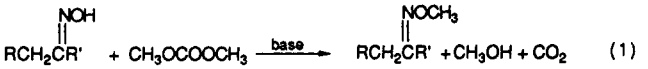
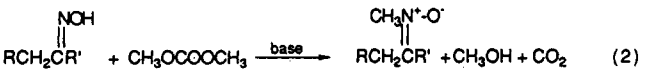
The reaction of ketone oximes with dimethyl carbonate (DMC) carried out in an autoclave at 180–190 °C and in the presence of K_2CO_3 yields 3-methyl-4,5-disubstituted-4-oxazolin-2-ones. The reaction can be applied to both aliphatic and aromatic ketone oximes, provided that a methylene group be present near the C=N bond. Nonoptimized yields range from 22 to 48%. The reaction seems to be a [3,3] sigmatropic rearrangement where DMC plays a key role in causing the initial N-methylation of the oximes.

Introduction

In order to explore other synthetic applications of dimethyl carbonate as an environmentally safe methylating agent,[1a–c] the reaction of oximes with dimethyl carbonate (DMC) was carried out. Contrary to our expectations, when ketone oximes bearing a methylene group reacted with DMC, the corresponding *O*-methyl derivatives (eq 1) were observed only in relatively low



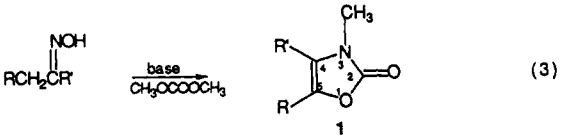
(1)



(2)

amounts, while the *N*-methyl derivatives (eq 2) were not detected at all.

Instead, the main reaction products were *N*-methyl-4,5-disubstituted-4-oxazolin-2-ones according to eq 3.



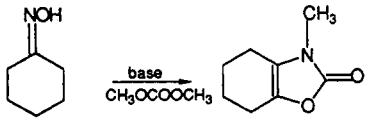
(3)

Results

When cyclohexanone oxime reacted (in a stainless steel autoclave for 435 min at 190 °C) with a 20 molar equiv excess of DMC (DMC also acts as the reaction solvent), in the presence of 2 molar equiv of K_2CO_3, the main product obtained was 3-methyl-4,5-cyclohexyl-4-oxazolin-2-one (eq 4).

The progress of the reaction for entry 1 of Table I is shown in detail in Figure 1. Cyclohexanone may originate from the hydrolysis of the oxime due to some water in the reaction mixture or coming from the reaction itself.

The reaction seems to be general and can be applied to both aliphatic (alicyclic and linear) and aromatic ketone



(4)

1a (isolated yield 48%)

oximes with a limitation: it is necessary that a methylene group be present. In fact, under the reaction conditions reported in Table I, benzophenone oxime gave after 410 min at 180 °C the oxime methyl ether and *N*-methylnitrone (the products were isolated by column chromatography: 56 and 24% yields, respectively); the acetophenone oxime gave after 240 min at 180 °C the corresponding *O*-methyl derivative (45%, GC analysis) together with other unidentified byproducts.

Moreover, when the oxime has two methylene groups near the C=N bond and one of these is benzylic, the reaction takes place regioselectively on the benzylic rather than the alkyl methylene (see entry 5, Table I).

The reaction proceeded similarly with diethyl carbonate; in this case, the respective 3-ethyl-4,5-disubstituted-4-oxazolin-2-ones were obtained (see Experimental Section). The results are reported in Table I.

Several methods are reported for the synthesis of 4,5-disustituted 4-oxazolin-2-ones. Among others are the following: (i) reaction of α-hydroxy ketones with ethyl carbamate[2a–c] or KNCO,[3] (ii) rearrangement of α,β-epoxyacyl azides,[4] and (iii) reactions of α-amino ketones with di-1-imidazolyl ketone.[5] 3-Alkyl derivatives of 4,5-disustituted 4-oxazolin-2-ones are usually obtained by alkylation with alkyl halides[2b–c,5] and dimethyl sulfate[5] or by reacting cyclic carbonates with alkylamines.[6a,b] Other more complicated and expensive methods have also been reported.[7a,b]

The reported new synthesis is more general because both aromatic and aliphatic 3-methyl-4,5-disustituted

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(2) (a) Filler, R.; Shyamsunder Rao, Y. *Adv. Heterocycl. Chem.* **1965**, *4*, 103–6. (b) Hakimelahi, G. H.; Boyce, C. B.; Kasmai, H. S. *Helv. Chim. Acta* **1977**, *60*, 342–47. (c) Gompper, R. *Chem. Ber.* **1956**, *89*, 1748–63.

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(4) Lemmens, J. M.; Blommerde, W. W. J. M.; Thijs, L.; Zwanenburg, B. *J. Org. Chem.* **1984**, *49*, 2231–35.

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(6) (a) Filler, R.; Shyamsunder Rao, Y. *Adv. Heterocycl. Chem.* **1965**, *4*, 202–3. (b) Sheehan, J. C.; Guziec, F. S., Jr. *J. Am. Chem. Soc.* **1972**, *94*, 6561–62.

(7) (a) Shono, T.; Matsumura, Y.; Kanazawa, T. *Tetrahedron Letts.* **1983**, *24*, 4577–80. (b) Sasaki, Y.; Dixneuf, P. H. *J. Org. Chem.* **1987**, *52*, 4389–91.

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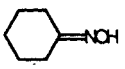
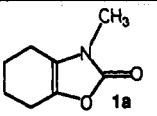
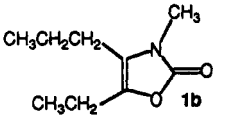
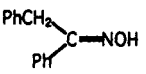
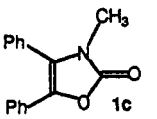
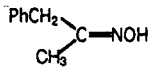
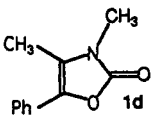
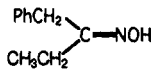
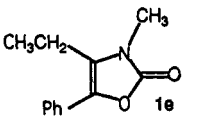
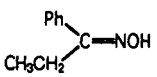
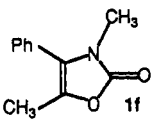
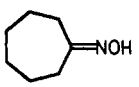
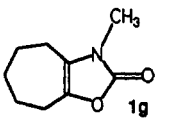
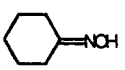
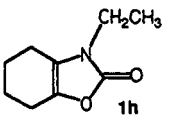
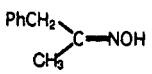
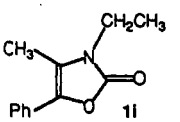
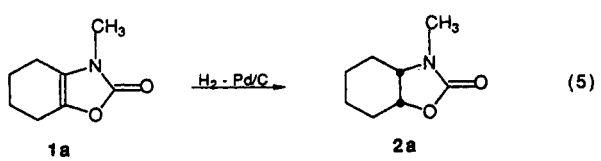
Table I. Reactions of Oximes with Dialkyl Carbonates[a]

entry	substrate	reactn temp, °C	reactn time, min	GC convn,[b] %	product	yield,[c] %
1		190	435	97	 **1a**	48
2	$(CH_3CH_2CH_2)_2CNOH$	180	300	100	 **1b**	22
3		180	465	95	 **1c**	37
4		180	480	97	 **1d**	31
5		180	480	98	 **1e**	37
6		180	480	95	 **1f**	28
7		180	210	100	 **1g**	22
8		190	505	100	 **1h**	31
9		180	330	98	 **1i**	35

[a] All reactions were carried out in autoclave. Entries 1–7: reactions with dimethyl carbonate (DMC). Entries 8 and 9: reactions with diethyl carbonate (DEC). Substrate, DMC (or DEC), and K_2CO_3 in 1:20:2 molar ratio, respectively. [b] Conversion is referred to substrate and determined by GC. [c] Yields based on isolated products by gravity column chromatography.

4-oxazolin-2-ones can be obtained in a one-step process. Yields in Table I were not optimized, and the solvent effect was not studied.

The compounds **1a–i** are quite stable,[8] but their C=C bond can be catalytically hydrogenated:[7a] for example (eq 5), the atmospheric pressure reduction of **1a** with H_2 using



1a **2a** (5)

Pd/C in isooctane at 90 °C gave after 300 min the corresponding *cis*-dihydro derivative **2a** in 84% yield (structure was confirmed by ^1H NMR and ^{13}C NMR spectra).

(8) Sheehan, J. C.; Guziec, F. S., Jr. *J. Org. Chem.* **1973**, *38*, 3034–40.

Discussion

In order to investigate the reaction mechanism initially, *N*-methylcyclohexylnitrone (**3**), cyclohexanone *O*-methyloxime (**4**), and cyclohexanone *O*-(carboxymethyl)oxime (**5**) were independently prepared by classical methods (see Experimental Section) and treated under the reaction conditions reported in Table I (Scheme I). After 180 min reaction, *N*-methylcyclohexylnitrone was no longer detected (eq 6, Scheme I); the main reaction products were cyclohexanone (46%), *N*-cyclohexylidenemethylamine (13%), and cyclohexanone oxime (5%) (GC and GC/MS analyses); other unidentified high-boiling products were also formed, but no trace of **1a** was observed. Cyclohexanone *O*-methyloxime did not react at all (eq 7, Scheme I). Only cyclohexanone *O*-(carboxymethyl)oxime yielded **1a** (eq 8, Scheme I). In particular, after 340 min of reaction, conversion of **5** was 98%: products were **1a** (62%) and cyclohexanone (33%) (GC and GC/MS analyses).

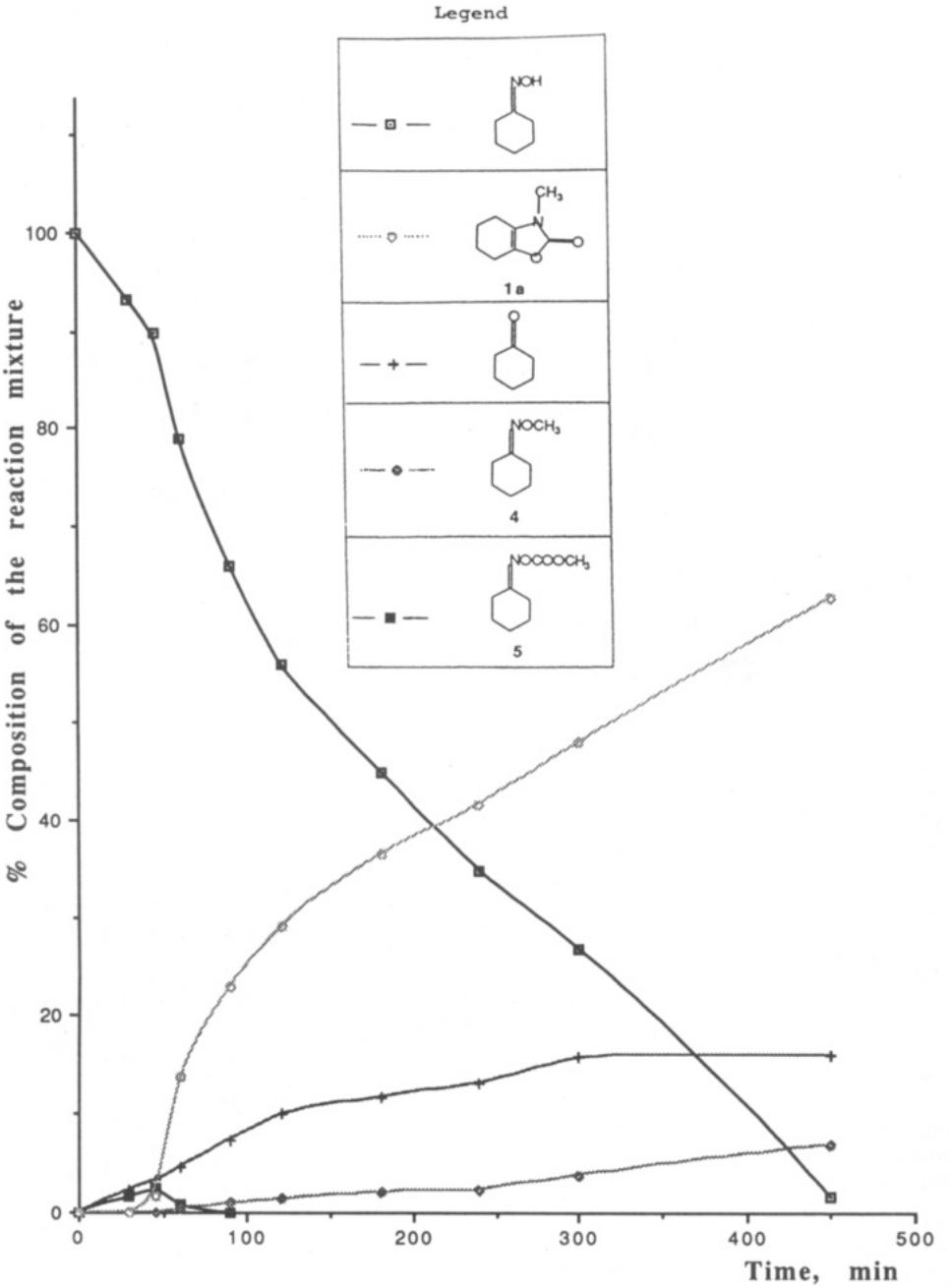


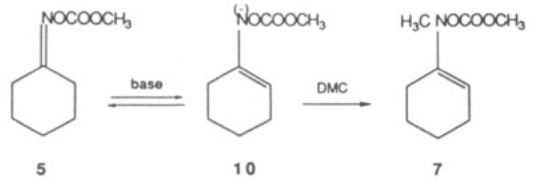
Figure 1. Progress of the reaction of cyclohexanone oxime with DMC at 190 °C by GC analyses using n-dodecane as internal standard. Few unidentified byproducts (ranging from 2 to 10%, in total) were detected.

Moreover, cyclohexanone oxime did not react in the absence of K_2CO_3.

Although few data are now available, the results to date suggest that a [3,3] sigmatropic rearrangement reaction might operate (Scheme II).

Compound **5** is formed through a well-known transesterification reaction.[9]

The proposed enamino intermediate **7** may also be formed through an alternate pathway involving deprotonation of the oxime ester **5** to give a resonance-stabilized enamino anion **10** which then undergoes alkylation:[10]



Actually, methyliminium salts of oxime acetates have been already reported.[11] But, the intermediate **7** was not observed during reaction 4. Because cyclohexanone *O*-methyloxime is formed, also the N-methylation of the oxime might occur in accordance with the already observed competition between O- and N-methylation of the oximes.[12a-c] Indeed, such behavior occurs under our conditions with the benzophenone oxime (see earlier text).

Similarly, *N*-acetoxyenamines have been invoked as possible intermediates in base-promoted reactions of oxime

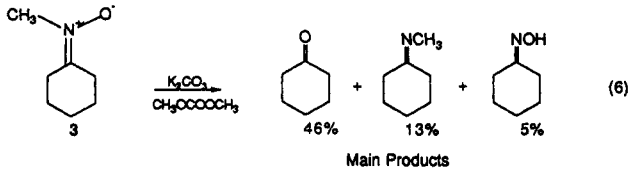
(9) Angeletti, E.; Tundo, P.; Venturello, P. *J. Org. Chem.* **1983**, *48*, 4106–8.

(10) The authors wish to thank a reviewer for suggesting the alternative mechanism described.

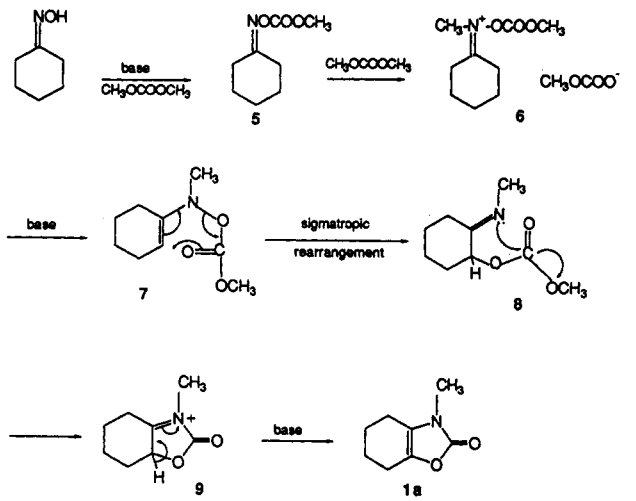
(11) House, H. O.; Richey, F. A., Jr. *J. Org. Chem.* **1969**, *34*, 1430.

(12) (a) Smith, P. A.; Robertson, J. E. *J. Am. Chem. Soc.* **1962**, *84*, 1197. (b) Smith, S. G.; Milligan, D. V. *J. Am. Chem. Soc.* **1968**, *90*, 2393–8. (c) Buehler, E. *J. Org. Chem.* **1967**, *32*, 261–5.

Scheme I



Scheme II



acetates[11] yielding a very fast sigmatropic rearrangement, although they have never been observed.

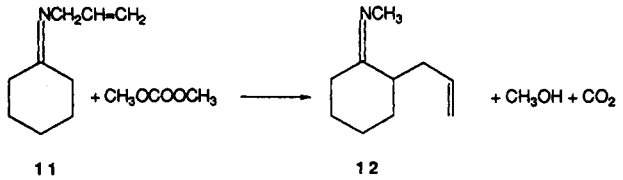
A six-centered intramolecular rearrangement has also been suggested in the preparation of *N,N*-diacetyl *O*-propionate from cyclohexanone oxime propionate.[13]

Indirect support of this mechanism may arise from the fact that, while cyclohexanone and cycloheptanone oximes gave the corresponding cyclic products **1a** and **1g** (see entries 1 and 7, Table I), cyclopentanone oxime yielded a complex reaction mixture where no trace of the corresponding **1** was found. It is well known that sigmatropic rearrangements are characterized by a highly ordered transition state,[14a-b] so that the required geometry might not be achieved if the rearrangement should involve a more strained C=C bond as it occurs in the rigid cyclopentene ring.

In regard to cyclization **8** → **1a**, a comparable reaction concerning 4-imino ketones generated from sigmatropic rearrangements of *O*-phenyl-[15a-e] and *O*-vinyloximes[16] has been reported. Particularly in the case of *O*-vinyloximes, cyclization occurred by an intramolecular nucleophilic attack of the imine group on the carbonyl, resulting in the formation of pyrroles. In our case, the same nucleophilic attack in the 2-(methylimino)cyclohexyl methyl carbonate (**8**) may produce **1a**. The reaction is surely assisted by the presence of the leaving group CH_3O^-. Noticeably, after sigmatropic rearrangement of *O*-(2-pyridyl)oximes, cyclization does not occur because of the lack of a leaving group.[17]

In summary, reaction 3 represents a new one-step synthetic method for the construction of an oxazolinone ring. The key step should be the initial N-methylation of the *O*-carbonate derivative of the oxime which, in turn, produces the enamine intermediate **7**; then, sigmatropic rearrangement of **7** involving the C=O bond (in the 5 position) might take place by cleavage of the 3,4 N–O bond. Central N–O bonds in hetero-Cope systems are reported to facilitate such rearrangements.[18,19] Our isomerization **7** → **8**, having intermediate features between the aza-[20a-c] and retro-[21a,b] Claisen rearrangements, may be classified as a 1-aza-1′,3′-dioxa-Cope rearrangement.[18]

Additional support of the suggested mechanism is the observation that when the *N*-cyclohexylideneallylamine (**11**) was reacted with DMC under the conditions reported in Table I, the following reaction took place:



Likewise, reaction occurs via N-methylation of **11** by DMC, followed by a classic aza-Claisen rearrangement.[22]

Experimental Section

General. All compounds were ACS grade and were employed without further purification. Melting points were determined on a Buchi 535 melting point apparatus and are uncorrected.

^{1}H NMR spectra were recorded on Varian EM 390 (90 MHz, compounds **4**, **5**, **1b**, **2a**) and Brucker (200 MHz, compounds **1a**, **1c–i**) spectrometers using $CDCl_3$ with TMS as the internal standard. ^{13}C NMR were recorded on a Brucker (200 MHz) spectrometer in $CDCl_3$ which was used as the internal standard. GC analyses were performed on a Varian GC 3300 using a fused silica capillary column (30 m × 0.25 mm) with DB5 as liquid phase (film thickness 0.25 μm). GC/MS analyses were performed on a HP 5971 mass detector coupled to a HP 5890 gas chromatograph fitted with a 30 m × 0.25 mm DB5 capillary column.

(13) Vivekananda Bhatt, M.; Gundu Rao, C.; Rengaraju, S. *J. Chem. Soc., Chem. Commun.* **1976**, 103.

(14) (a) Brown, A.; Dewar, M. J. S.; Schoeller, W. *J. Am. Chem. Soc.* **1970**, *92*, 5516. (b) Shea, K. J.; Phillips, R. B. *J. Am. Chem. Soc.* **1980**, *102*, 3156.

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(16) Sheradsky, T. *Tetrahedron Lett.* **1970**, *1*, 25.

(17) Sheradsky, T.; Galemnick, G. *J. Org. Chem.* **1971**, *36*, 1061.

(18) Blechert, S. *Synthesis* **1989**, *71*.

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(22) The structure of the *N*-[2-(2-propenyl)cyclohexylidene]methylamine (**12**) was confirmed by GC/MS. Starting from 8.0 g of **11**, the hydrolysis of the reaction mixture yielded 2-(2-propenyl)cyclohexanone, 3.93 g (48% yield, 92% pure by GC) of distilled product (bp = 39–42 °C, 0.08 mmHg) was obtained.

4-Heptanone, benzyl phenyl ketone, benzyl methyl ketone, benzyl ethyl ketone, propiophenone, benzophenone, acetophenone, and cycloheptanone oximes were prepared from their parent ketones using classical methods reported in the literature.[23]

***N*-Methylcyclohexylnitrone (3).** A mixture of cyclohexanone (3.0 g, 0.036 mol), *N*-methylhydroxylamine hydrochloride (3.82 g, 0.046 mol), K_2CO_3 (6.33 g, 0.046 mol), and *t*-BuOH (120 mL as solvent) was refluxed[12b] for 8 h. The mixture was then filtered and the solvent evaporated under vacuum. The yellow-brown residue was distilled (bp = 115–120 °C, 0.3 mmHg) yielding 1.85 g of **3** (80% pure by GC, the structure was confirmed by GC/MS) as a pale yellow liquid which slowly turned brown and decomposed on standing. Mass spectrum (70 eV) *m/z* (relative intensity): 127 (M^+, 78), 111 (28), 110 (33), 99 (21), 98 (74), 82 (45), 81 (52), 68 (100), 55 (60).

Cyclohexanone *O*-Methyloxime (4). To a solution of cyclohexanone (5.0 g, 0.051 mol), *O*-methylhydroxylamine hydrochloride (6.6 g, 0.079 mol), EtOH (95%, 50 mL), and H_2O (4 mL) was carefully added NaOH (10.0 g, 0.25 mL) while cooling. The mixture was then refluxed for 30 min. After the mixture was cooled to rt, water (20 mL) was added. The product was then extracted with diethyl ether (50 mL), dried over anhydrous Na_2SO_4, and after solvent removal, distilled using a Vigreux column (bp = 56–61 °C, 20 mmHg), obtaining 2.2 g of **4** (34% yield, 99% pure by GC). ^1H NMR ($CDCl_3$) δ: 1.4–2.7 (m, 10 H, 5 CH_2), 3.83 (s, 3H, CH_3).

Cyclohexanone *O*-Methyloxime (5). Methyl chloroformate (3.75 mL, 0.048 mol) was added dropwise, at rt, under stirring, to a solution of cyclohexanone oxime (5 g, 0.044 mol) and NEt_3 (4.46 g, 0.044 mol) in CH_2Cl_2 (150 mL). After 3 h, diethyl ether (50 mL) was added, and the Et_3NHCl was filtered. The solvent was removed under vacuum and the yellow residue distilled to give **5** as a colorless liquid product (4.32 g, 98.5% pure by GC, 57% yield, bp = 88–90 °C, 0.3 mmHg) that slowly crystallized on standing. ^1H NMR ($CDCl_3$) δ: 1.36–2.66 (m, 10 H, 5 CH_2), 3.85 (s, 3 H, CH_3).

Reactions Carried out in Autoclave. General Procedure. All reactions were carried out by loading a stainless steel (AISI 316) autoclave with a mixture of oxime, DMC, and K_2CO_3 in a 1:20:2 molar ratio, respectively. The autoclave was equipped with a purging valve through which, at room temperature, air was removed before each reaction by purging with a N_2 stream. The autoclave was heated in an electric oven to the desired operating temperature (180–190 °C), while the reaction mixture was kept under magnetic stirring. A thermocouple and a needle valve were fixed onto the autoclave head. The former was dipped into the reaction mixture, and the latter was connected to a 1/8-in. stainless steel suction-pipe which, in turn, was immersed into the reaction mixture. In this way it was possible to extract samples (analyzed by GC) during the course of the reaction.

Products **1a–i** were obtained from the corresponding oximes following the above-reported general procedure, under the conditions described in Table I. All products were isolated by gravity column chromatography (gradient elution) performed on Merck silica gel (Kieselgel 60). Compounds **1a** and **1h** were eluted using 0–80% (v/v) of diethyl ether in petroleum ether. Compounds **1b–g** were eluted using 0–70% (v/v) of diethyl ether in petroleum ether (bp = 40–70 °C). Compound **1i** was eluted using 0–55% of diethyl ether in petroleum ether.

3-Methyl-4,5-cyclohexyl-4-oxazolin-2-one (1a). Starting from 6.0 g of cyclohexanone oxime, 3.9 g of **1a** was isolated (97.5% pure by GC, 48% yield). The product was recrystallized from n-hexane to give pale yellow needles (mp = 76.0–76.5 °C). ^1H NMR ($CDCl_3$) δ: 1.78–1.81 (m, 4H, $2CH_2$), 2.31–2.37 (m, 4H, $2CH_2$), 3.17 (s, 3H, NCH_3). ^{13}C NMR decoupled ($CDCl_3$) δ: 19.23 (CH_2), 20.89 (CH_2), 21.87 (CH_2), 22.28 (CH_2), 27.71 (CH_3), 120.92 (C=C), 134.43 (C=C), 156.19 (CO). Mass spectrum (70 eV) *m/z* (relative intensity): 153 (M^+, 73), 125 (50), 97 (40), 68 (100), 55 (10). IR (KBr) 1776, 1762, 1755, 1716 cm^{-1}. Anal. Calcd for $C_8H_{11}NO_2$: C, 62.73; H, 7.24; N, 9.14. Found: C, 62.88; H, 7.41; N, 9.18.

3-Methyl-4-ethyl-5-propyl-4-oxazolin-2-one (1b). Starting from 2.0 g of 4-heptanone, 0.58 g of **1b** was isolated (98% pure by GC, yield 22%); the product is a pale yellow liquid (bp = 283–285 °C, 760 mmHg). ^1H NMR ($CDCl_3$) δ: 0.98 (t, 3H, CH_3), 1.20 (t, 3H, CH_3), 1.60 (q, 2H, CH_2), 2.00–2.67 (m, 4H, $2CH_2$), 3.20 (s, 3H, NCH_3). Mass spectrum (70 eV), *m/z* (relative intensity): 169 (M^+, 46), 154 (100), 140 (51), 113 (10), 84 (28), 68 (12), 57 (12).

3-Methyl-4,5-diphenyl-4-oxazolin-2-one (1c). Starting from 4.0 g of benzyl phenyl ketone oxime, 1.76 g of **1c** was isolated (99% pure by GC, 37% yield); the product was recrystallized from n-hexane/$CHCl_3$ to give pale yellow needles (mp = 95.5–97.0 °C) (Lit.[2b] mp = 94–96 °C). ^1H NMR ($CDCl_3$) δ: 3.07 (s, 3H, NCH_3), 7.18–7.54 (m, 10H, 2Ph). Mass spectrum (70 eV) *m/z* (relative intensity): 251 (M^+, 93), 194 (2), 165 (11), 118 (100), 77 (25), 51 (7). Anal. Calcd for $C_{16}H_{13}NO_2$: C, 76.47; H, 5.21; N, 5.57. Found: C, 76.24; H, 5.45; N, 5.63.

3-Methyl-4-methyl-5-phenyl-4-oxazolin-2-one (1d). Starting from 4.0 g of benzyl methyl ketone oxime, 1.57 g of **1d** was isolated (98% pure by GC, 31% yield); the product was recrystallized from n-hexane/$CHCl_3$ to give white needles (mp = 121.5–122.5 °C) (lit.[5] mp = 115–117 °C). ^1H NMR ($CDCl_3$) δ: 2.28 (s, 3H, CH_3), 3.23 (s, 3H, NCH_3), 7.22–7.51 (m, 5H, Ph). Mass spectrum (70 eV) *m/z* (relative intensity): 189 (M^+, 87), 130 (7), 105 (10), 77 (15) 56 (100), 51 (7). Anal. Calcd for $C_{11}H_{11}NO_2$: C, 69.84; H, 5.82; N, 7.41. Found: C, 69.65; H, 5.85; N, 7.36.

3-Methyl-4-ethyl-5-phenyl-4-oxazolin-2-one (1e). Starting from 4.0 g of benzyl ethyl ketone oxime, 1.84 g of **1e** was isolated (98.5% pure by GC, 37% yield); the product was recrystallized from n-hexane/$CHCl_3$ to give white needles (mp = 78.0–79.5 °C). ^1H NMR ($CDCl_3$) δ: 1.29 (t, 3H, CH_3), 2.66 (q, 2H, CH_2), 3.25 (s, 3H, NCH_3), 7.24–7.49 (m, 5H, Ph). Mass spectrum (70 eV) *m/z* (relative intensity): 203 (M^+, 100), 188 (40), 160 (4), 146 (3), 105 (58), 77 (23), 70 (64), 51 (9). Anal. Calcd for $C_{12}H_{13}NO_2$: C, 70.94; H, 6.40; N, 6.89. Found: C, 70.61; H, 6.41; N, 6.83.

3-Methyl-4-phenyl-5-methyl-4-oxazolin-2-one (1f). Starting from 4.0 g of propiophenone oxime, 1.42 g of **1f** was isolated (98% pure by GC, 28% yield); the product was recrystallized from n-hexane/$CHCl_3$ to give a pale yellow solid (mp = 81.0–82.5 °C). ^1H NMR ($CDCl_3$) δ: 2.11 (s, 3H, CH_3), 3.10 (s, 3H, NCH_3), 7.26–7.51 (m, 3H, Ph). Mass spectrum (70 eV) *m/z* (relative intensity): 189 (M^+, 73), 160 (3), 146 (3), 118 (100), 103 (8), 77 (19), 51 (6). Anal. Calcd for $C_{11}H_{11}NO_2$: C, 69.84; H, 5.82; N, 7.41. Found: C, 69.61; H, 5.79; N, 7.34.

3-Methyl-4,5-cycloheptyl-4-oxazolin-2-one (1g). Starting from 4.0 g of cycloheptanone oxime, 1.16 g of **1g** was isolated (97.5% pure by GC, 22% yield); the product was recrystallized from n-hexane/$CHCl_3$ to give a pale yellow solid (mp = 42.5–44.0 °C). ^1H NMR ($CDCl_3$) δ: 1.60–1.83 (m, 6H, $3CH_2$), 2.35–2.54 (m, 4H, $2CH_2$), 3.09 (s, 3H, NCH_3). Mass spectrum (70 eV) *m/z* (relative intensity): 167 (M^+, 100), 139 (10), 138 (24), 126 (19), 125 (16), 113 (80), 94 (12), 82 (23), 68 (25), 55 (40). Anal. Calcd for $C_9H_{13}NO_2$: C, 64.63; H, 7.84; N, 8.38. Found: C, 64.62; H, 7.65; N, 8.15.

3-Ethyl-4,5-cyclohexyl-4-oxazolin-2-one (1h). Starting from 2.0 g of cyclohexanone oxime, 0.92 g of **1h** was isolated (98% pure by GC, 31% yield). The product was a brownish liquid at rt. ^1H NMR ($CDCl_3$) δ: 1.24 (t, 3H, NCH_3), 1.77–1.83 (m, 4H, $2CH_2$) 2.31–2.38 (m, 4H, $2CH_2$), 3.54 (q, 2H, NCH_2). Mass spectrum (70 eV) *m/z* (relative intensity): 167 (M^+, 100), 139 (52), 111 (49), 96 (43), 82 (55), 67 (14), 55 (14), 54 (16).

3-Ethyl-4-methyl-5-phenyl-4-oxazolin-2-one (1i). Starting from 2.0 g of benzyl methyl ketone oxime, 0.95 g of **1i** was isolated (99% pure by GC, 35% yield); the product was recrystallized from n-hexane/$CHCl_3$ to give a pale yellow solid (mp = 66.0–67.0 °C). ^1H NMR ($CDCl_3$) δ: 1.31 (t, 3H, NCH_3), 2.29 (s, 3H, CH_3), 3.69 (q, 2H, NCH_2), 7.24–7.49 (m, 5H, Ph). Mass spectrum (70 eV) *m/z* (relative intensity): 203 (M^+, 100), 175 (12), 149 (5), 130 (4), 105 (27), 77 (18), 70 (33), 51 (5). Anal. Calcd for $C_{12}H_{13}NO_2$: C, 70.94; H, 6.40; N, 6.89. Found: C, 71.06; H, 6.45; N, 6.92.

Hydrogenation of 1a to 3-Methyl-4,5-cyclohexyl-4,5-*cis*-dihydro-4-oxazolin-2-one (2a). A mixture of **1a** (0.5 g, 3.3 mmol), isooctane (10 mL), and Pd/C (5% wt, 0.075 g, 0.0352 Pd mmol) was stirred into a thermostated reactor at 90 °C, while a continuous flow of H_2 was bubbled below the liquid surface at atmospheric pressure. The reaction was completed in 5 h. Pd/C was filtered, and solvent was evaporated under vacuum. The

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product **2a** (0.42 g, 84% yield) was obtained. ^{1}H NMR ($CDCl_3$) δ: 1.24–1.84 (m, 8H, $4CH_2$), 2.83 (s, 3H, NCH_3), 3.60 (q, 1H, CH), 4.50 (q, 1H, CH). ^{13}C NMR decoupled ($CDCl_3$) δ: 19.01 (CH_2), 19.19 (CH_2), 24.78 (CH_2), 26.51 (CH_2), 28.26 (CH_3), 55.84 (CH), 72.77 (CH), 158.81 (CO). Mass spectrum (70 eV) *m/z* (relative intensity): 155 (M^+, 49), 112 (100), 99 (8), 68 (10), 57 (5).

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