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1,3-Dipolar Addition of Oximes to Olefins. Conversion of Aldoximes to Nitriles under Mild Conditions

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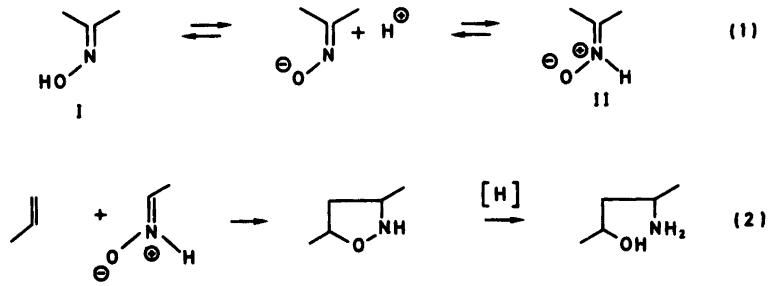
Under certain conditions Oximes react directly with olefins in a 1,3-dipolar fashion to produce isoxazolidines. *N*-Unsubstituted isoxazolidines can also be produced by reacting some nitrones with olefins and subsequent removal of the *N*-substituent. Aldoximes are converted to nitriles under mild conditions by dimethyl succinimidylsulfonium chloride and triethylamine.

1,3-Dipolar addition of alkyl[1] and silyl nitronates,[2] nitrile oxides[3] and nitrones[1cd,4] to olefins and acetylenes has found considerable application in synthetic methodology. The isoxazolidines, 2-isoxazolines, or isoxazoles formed are valuable intermediates for the synthesis of a number of heterocycles, cyclopentenones, aminols, carbohydrates, amino acids, and hydroxy and carbonyl functionalized hydrocarbons, *e.g.* aldols. The latter derivatives are of interest because the isoxazoline route offers a valuable alternative to the classical Claisen or aldol reactions.[2ehi,3giq] The present work deals with another aspect of nitrone chemistry. The oximes occur as the hydroxy tautomer I but are undoubtedly present in minor amounts as the considerably more acidic tautomer II, the nitrone form (1). The oximes do not normally show any inclination to participate in 1,3-dipolar addition. However, if we transiently could force the equilibrium towards the tautomer II, the easily accessible oximes could be used as attractive agents for functionalizing olefins and acetylenes according to (2) eventually leading to 1,3-amino alcohols by reductive cleavage of the intermediate isoxazolidines. This work describes our efforts to make use of oximes in the desired way.

It occurred to us that transoximation, as practiced by liberation of carbonyl compounds from their oximes by treatment with formalin, could proceed *via* a nitrone stage (3). Furthermore, it is known that formaldoxime is prone to polymerize and this process could pass a nitrone stage (4) which conceivably could be trapped by an olefin present as suggested by (5, 6).

Vasella *et al.*[4k-m] have accomplished basically the same reaction by locking the nitrone as a cyclic alkoxy alkyl nitrone by reacting a γ- or δ-hydroxy oxime from a sugar with a carbonyl



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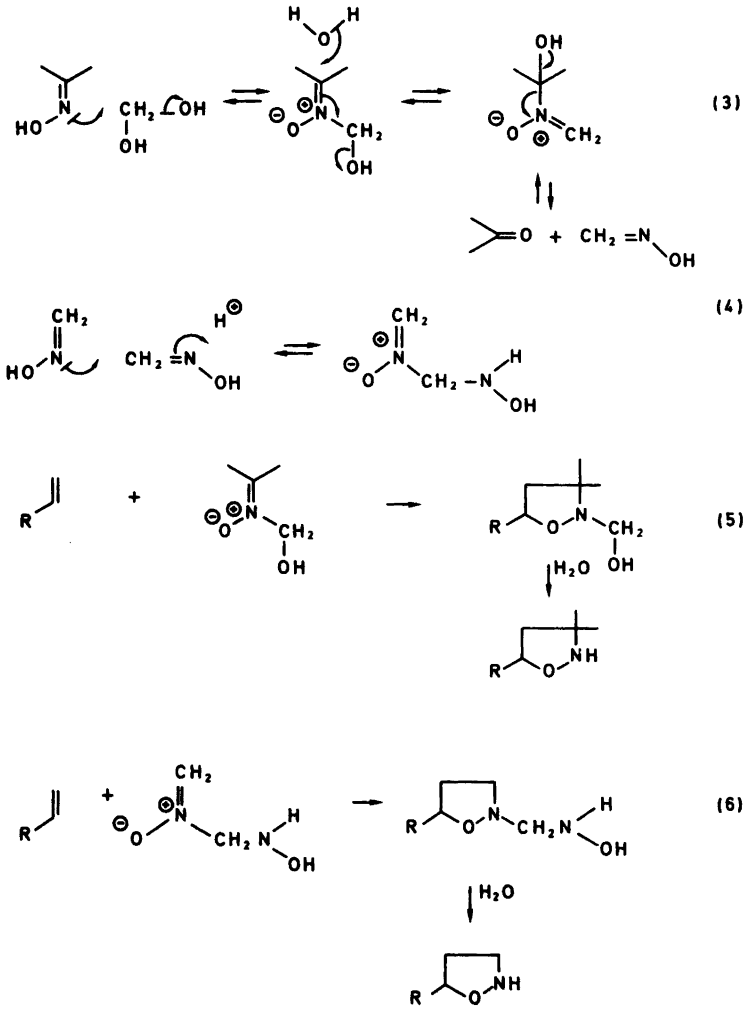
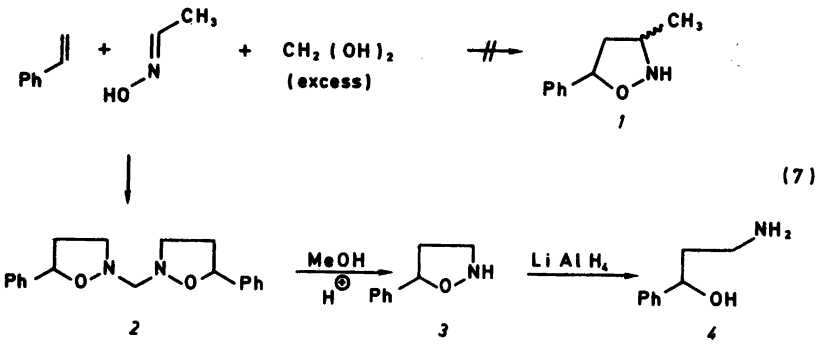


compound in the presence of an olefin. Optically active isoxazolidines are liberated by acid hydrolysis.

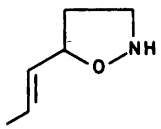
As reactants in our reaction we first chose acetaldoxime and styrene which were refluxed with an excess of 40 % aqueous formaldehyde for 4 h. The workup showed only traces of the anticipated product *1*. Another compound, *2*, was formed in a good yield (7). The formation of *2* can be rationalized by eqn (3) under the supposition that the intermediate α-methyl substituted nitrone reacts slower than the methylene nitrone with the dipolarophile. The 5-phenyl isoxazolidine *3* was set free by acid hydrolysis. Reduction of *3* with $LiAlH_4$ gave 1-phenyl-3-aminopropanol *4*. The same products were obtained when formaldoxime was reacted directly with styrene or when acetone oxime was used together with formalin. *1* was not formed when acetaldoxime was reacted with styrene in the presence of excess of acetaldehyde. Reaction of pentadiene and butadiene with formalin and acetone oxime followed by methanolysis gave *5* and *6*, respectively, in analogy with the formation of the phenyl derivative *3*. The yields of *5* and *6* were *ca.* 30–40 %. *5* was obtained as a mixture of *cis* and *trans* isomers and some addition of methanol to the double bond of *6* occurred at the methanolysis stage.

A literature search revealed that similar



(7)

work had indeed been carried out a few years earlier.[5–8] When formaldoxime was reacted with methyl acrylate, *7* was formed together with small amounts of *8*.[5] Similarly, benzophenone oxime gave *9* with methyl vinylketone[6] (8, 9). *7*



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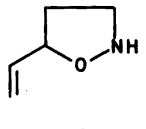
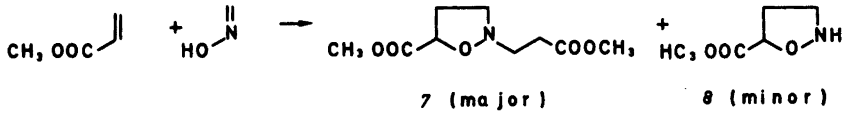


6

and *9* are most likely formed by Michael addition of the oxime to the olefin and subsequent 1,3-dipolar addition (10). This mechanism was supported by our finding that heating of two moles of methyl acrylate, acrylonitrile, or methyl vinyl ketone with one mole of an oxime for a few hours at 80–90 °C gave the isoxazolidines *10a–f*. No reaction occurred with 1-hexene. It is stated in the literature[3a] that monosubstituted olefins with few exceptions[9–11] give exclusively 5-substituted derivatives. We found by closer inspection of the ^{1}H NMR spectra of the products from reaction (10) that considerable amounts (10–35 %) of the 4-substituted isomers *11a–11f* were formed. It was not possible to separate them by distillation (partial dec.) or by TLC but *10a* (major) was separated from *11a* by HPLC. Electron donating substituents on the nitrone in combination with electron withdrawing substituents on the olefin (dipolarophile) tend to increase the amount of 4-substitution.[11] Attempted distillation of *10d* at *ca.* 150 °C, 0.1 mmHg caused nearly complete fragmentation of the isoxazolidine into cyclohexanone oxime and methyl acrylate, demonstrating that the 1,3-dipolar and the Michael additions are reversible as indicated in (10); see Ref. 1b for earlier observations of reversibility.

A disadvantage of reaction (10) is that *N*-substituted derivatives are formed, a circumstance which motivated us to examine other reaction conditions. As predicted by (3) excess of formalin in reaction (8) should block the first Michael addition step and favour the formation of *8* or *12*. This was indeed borne out in practice.



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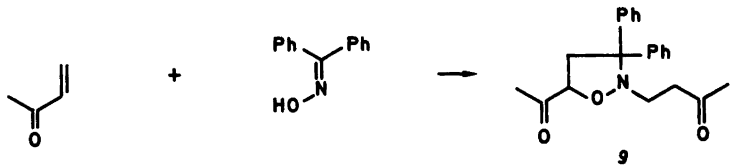

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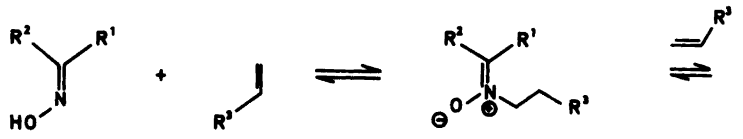

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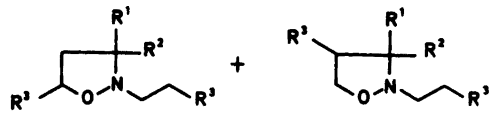


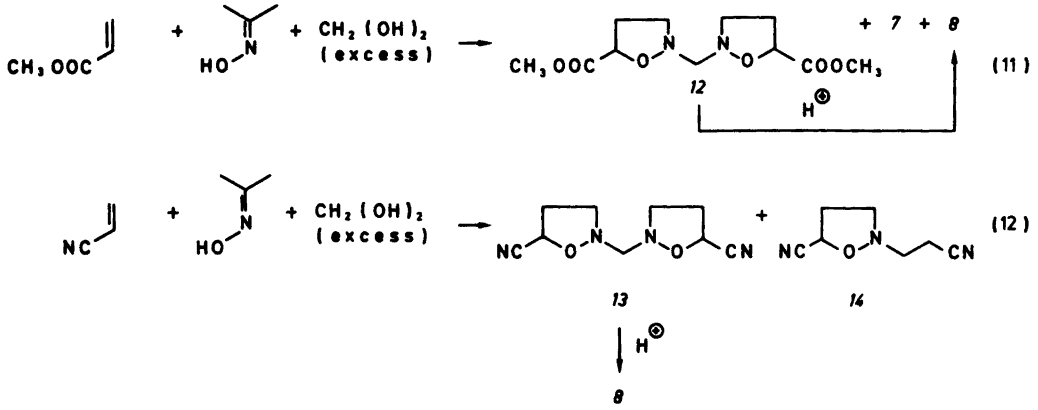
(major) (minor)

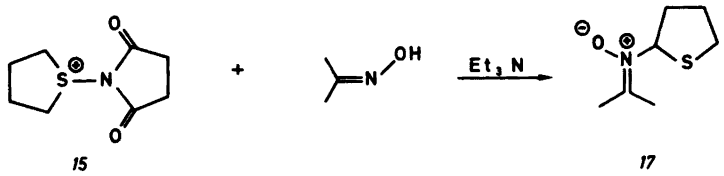
10a $R^1=R^2=CH_3$; $R^3=COOCH_3$ *11a*
10b $R^1=H$, $R^2=CH_3$; $R^3=COOCH_3$ *11b*
10c $R^1=H$, $R^2=C_6H_5$; $R^3=COOCH_3$ *11c*
10d R^1; $R^2=(CH_2)_5$; $R^3=COOCH_3$ *11d*
10e $R^1=R^2=CH_3$; $R^3=CN$ *11e*
10f R^1, $R^2=(CH_2)_5$; $R^3=CN$ *11f*

We found that *12* became the major product, whereas *7* and *8* were formed only to a minor extent (11) in analogy with the formation of compound *3*.

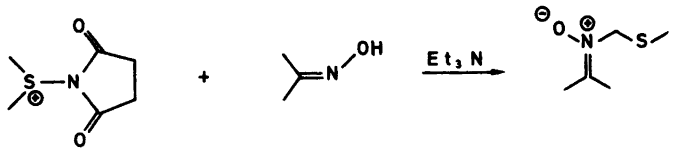
Subsequent hydrolysis of 12 in methanolic hydrogen chloride gave the desired 5-methoxycarbonylisoxazolidine *8*. *8* was also obtained by a slightly different route (12). Acrylonitrile reacted in the presence of excess of formalin with acetone oxime to *13* (major) and *14* (minor). *13* gave directly *8* by hydrolysis with methanolic hydrogen chloride.

N-*Methylthiomethyl nitrones*. The reactions of oximes and olefins with formalin have limitations since first they do not allow introduction of a substituent at C^3 of the isoxazolidines and second the intermediate nitrone requires a reactive olefin, such as styrene, acrylates, *etc.*, as dipolarophile. Hexane as olefinic component gave no isoxazoline. Use of dioxane as cosolvent in order to increase the solubility of the reactants had no effect. Therefore a route to *N*-methylthiomethylnitrones[12] from ketoximes was further investigated. It was anticipated that these nitrones should add in the usual way to various olefins and that the methylthiomethyl group could be removed again by acid hydrolysis. Two sulfides, tetrahydrothiophene and dimethyl sulfide, were

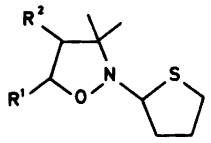




15 *17*

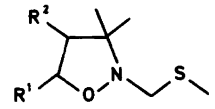


16 *18*



19a R^1 = $COOCH_3$, R^2 = H

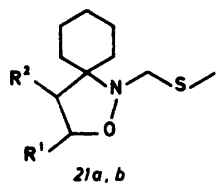
19b R^1 = H, R^2 = $COOCH_3$



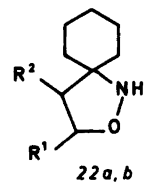
20a R^1 = $COOCH_3$, R^2 = H

20b R^1 = H, R^2 = $COOCH_3$

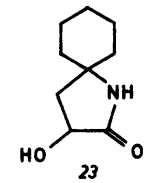
tested as reagents. They reacted instantanously in acetonitrile at 0 °C with *N*-chlorosuccinimide to the sulfonium salts *15* and *16*[13,14] which with acetone oxime and triethylamine gave the nitrones *17* and *18*. They were unstable and could not be purified by preparative TLC. Dipolar addition of crude *17* to methyl acrylate gave a low yield of *19ab*. The yield of *20ab* from *16* was considerably better and further experimentation was therefore carried out with the sulfonium salt



21a, b



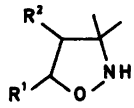
22a, b



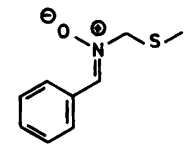
23

a : R^1 = $COOCH_3$, R^2 = H

b : R^1 = H, R^2 = $COOCH_3$



24a, b



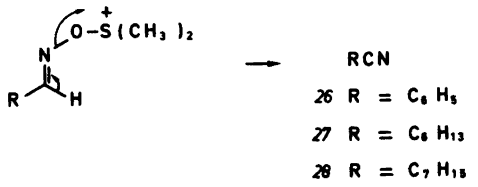
25

a : R^1 = $COOCH_3$, R^2 = H

b : R^1 = H, R^2 = $COOCH_3$

16. Cyclohexanone oxime gave similarly the isomeric mixture *21ab* which was hydrolyzed to *22ab* and hydrogenated to give the pyrrolidone *23* in a total yield of *ca.* 30 %. Hydrolysis of *20ab* in methanolic hydrogen chloride gave a mixture of *24ab*. The instability of *18* precluded addition to less reactive olefins, such as 1-hexene.

Conversion of aldoximes to nitriles. When benzaldoxime was treated with *16* and triethylamine at −20 °C, a disappointingly low yield of the nitrone *25* was obtained. Substantial amounts of benzonitrile and dimethylsulfoxide were formed instead. By carrying out the reaction at 0−20 °C benzonitrile was formed in 85 % yield. Aliphatic aldoximes gave the corresponding nitriles *27* and *28* in high yields (80−90 %). This



procedure constitutes a mild method for converting aldoximes til nitriles (13). Numerous procedures have been published for the dehydration of aldoximes to nitriles.[15]

EXPERIMENTAL

5-Phenylisoxazolidine, 3 and bis 2-(5-phenylisoxazolidinyl)methane, 2. Acetone oxime (5.1 g), formalin (17 g, 40 % aqueous solution) and styrene (7.2 g) were stirred for 4 h at 90 °C, cooled, and extracted with dichloromethane. Evaporation of the solvent gave 12.4 g of crude *2*. A small portion (600 mg) was purified by preparative TLC (SiO_2, ether−lightpetroleum, 4:1) giving a slightly yellow oil (450 mg). The yield of pure *2* is 82 %. ^{1}H NMR ($CDCl_3$): δ 1.9−3.0 (4H, m), 3.1−3.4 (4H, m), 3.98 (2H, s), 5.03 (2H, t, *J* 6 Hz), 7.2 (10H, br.s). The mass spectrum showed no M^+ peak but an expected strong fragmentation peak at *m/e* 162.

Crude *2* (11.8 g) was refluxed in methanol (80 ml, 5 % dry HCl) for 2 h. Evaporation of the methanol, addition of ice-water (*ca.* 50 ml, neutralization with solid sodium bicarbonate (pH *ca.* 9) and extraction with methylene chloride gave 10.2 g of crude 5-phenylisoxazolidine, *3*. Distillation caused partial decomposition. 8.5 g of the crude *3* gave 4 g of pure *2*, $b.p._{0.1}$ 105−108 °C. ^{1}H NMR (CCl_4): δ 1.9−2.9 (2H, m), 3.11 (2H, t, *J* 7 Hz), 4.73 (1H, t, *J* 7 Hz), 5.0 (1H, br.s.), 7.10 (5H, s). (Found: C 72.55; H 7.24. Calc. for $C_9H_{11}NO$: C 72.46; H 7.43 %). MS: 149 (M^+).

1-Phenyl-3-aminopropanol, 4, was obtained practically quantitatively as an oil by refluxing *3* with lithium aluminium hydride in ether for 1 h. Distillation of the product in a "Kugelrohr" apparatus at 162 °C/0.1 mmHg gave pure *4*. ^{1}H NMR ($CDCl_3$): δ 1.72 (2H, q, *J* 6 Hz), 2.8 (3H, br.s.), 2.85 (2H, t, *J* 6 Hz), 4.78 (1H, t, *J* 6 Hz), 7.23 (5H, br.s).

5-Propenyl-isoxazolidine, 5. Acetone oxime (5.85 g, 0.080 mol) and formalin (12.0 g, 40 % aqueous solution, 0.16 mol) was equilibrated for 1 h at 50 °C in a 100 ml flask equipped with stirrer and condenser. Tetrahydrofuran (7 ml), 1,3-pentadiene (6.81 g, 0.1 mol), and 3 drops of acetic acid were added and the mixture was stirred at 50 °C for 82 h. The solution was neutralized with sodium hydroxide and extracted with methylene chloride (3×25 ml). Evaporation of the organic solvent gave a yellow oil (7.8 g) which was treated with 0.5 M methanolic perchloric acid (131 ml) at 40 °C for 48 h. Evaporation of the solvent, adjustment of the pH to 8 and extraction with methylene chloride gave 5.2 g of crude *5*. A "Kugelrohr" distillation at *ca.* 100 °C/0.2 mmHg gave *5* as a colourless liquid. The yield was 43 %. ^{1}H NMR ($CDCl_3$): δ 1.70 (3H, d, *J* 5.8 Hz), 1.5−2.7 (2H, m), 3.18 (2H, br.t, *J*~7 Hz), 4.1−4.9 (1H, m), 5.1−6.0 (3H, m). MS: 113 (M^+).

5-Vinyl-isoxazolidine, 6. Acetone oxime (1.46 g, 0.020 mol), formalin (3.0 g, 40 % aqueous solution, 0.040 mol), one drop of acetic acid, 1,3-butadiene (3.2 g, 0.06 mol), and tetrahydrofurane (3 ml) were stirred in a pressure flask at 50 °C for one week. The mixture was extracted with methylene chloride (3×10 ml) and evaporation of the solvent gave 1.8 g of a product which was treated with 0.5 M methanolic perchloric acid (34 ml) at 40 °C for 48 h. The workup procedure described for *5* was used. A "Kugelrohr" distillation gave *6* (0.64 g, 31 %). ^{1}H NMR ($CDCl_3$): δ 1.5−2.8 (2H, m), 2.8−3.5 (2H, m), 4.35 (1H, br.q., *J*~7 Hz), 4.7 (1H, br.s.), 5.0−6.1 (3H, m). MS: 99 (M^+). The ^{1}H NMR spectrum showed that addition of methanol had occurred to some extent across the double bond.

5-Methoxycarbonylisoxazolidine, 8, 5-methoxycarbonyl-2-β-methoxycarbonylethylisoxazolidine, 7, and *bis 2-(5-methoxycarbonylisoxazolidinyl)methane, 12.* Acetone oxime (10.0 g) was heated for 30 min at 60 °C with formalin (40 %, 50.0 g). Methyl acrylate (12.0 g) was added and the mixture was stirred for 5 h at 70 °C. Extraction with methylene chloride gave 14.5 g of crude

7+8+12. A small sample was purified by TLC (SiO_2, ether). ^1H NMR ($CDCl_3$) *7*: δ 2.3–3.3 (8H, m), 3.62 (3H, s), 3.68 (3H, s), 4.34 (1H, t, *J* 7 Hz). *12*: δ 2.2–2.7 (4H, m), 2.8–3.3 (4H, m), 3.64 (3H, s), 3.8 (2H, br.s.), 4.45 (2H, dd, *J* 6 and 8 Hz). MS: 144 (M^+ missing). The crude product was refluxed for 5 h in methanolic hydrogen chloride (200 ml, 2 %). The solvent was evaporated and water was added. The solution was extracted once with ether. Adjustment of the pH to *ca.* 9, and extraction with methylene chloride gave a product which by distillation *in vacuo* gave *8*, 4.1 g, 23 %, $b.p._{0.1}$ 70–71 °C and *7*, 2.5 g, $b.p._{0.1}$ 117–120 °C. The higher boiling fraction contained *ca.* 20 % of *8*. ^1H NMR (CCl_4) *8*: δ 2.0–3.3 (4H, m), 3.66 (3H, m), 4.39 (1H, dd, *J* 5 and 8 Hz), 5.6 (1H, br.s).

2-β-Methoxycarbonylethyl-3,3-dimethyl-5-methoxycarbonylisoxazolidine, 10a, and 2-β-methoxycarbonylethyl-3,3-dimethyl-4-methoxycarbonylisoxazolidine, 11a. Acetone oxime (3.0 g) and methyl acrylate (7.42 g) were heated at 90 °C for 4 h. Distillation of the product gave a light yellow liquid, 7,7 g, 77 %, $b.p._{0.13}$ 123–128 °C which according to ^1H NMR and GLC consisted of *10a* (77 %) and *11a* 23 %. The components were separated by HPLC. ^1H NMR ($CDCl_3$) *10a*: δ 1.20 (6H, br.s), 2.33 (2H, d, *J* 8 Hz), 2.5–3.1 (4H, m), 3.63 (3H, s), 3.69 (3H, s), 4.43 (1H, t, *J* 8 Hz). *11a*: δ 1.06 (3H, s), 1.34 (3H, s), 2.45–3.05 (4H, m), 3.17 (1H, dd, *J* 7.6 and 8.4 Hz), 3.65 (3H, s), 3.70 (3H, s), 4.00 (1H, dd, *J* 8.4 and 8 Hz), 4.20 (1H, dd, *J* 7.6 and 8 Hz). MS: 245 (M^+). (*10a*, Found: C 53.11; H 7.70. Calc. for $C_{11}H_{19}NO_5$: C 53.87; H 7.81 %).

2-β-Methoxycarbonylethyl-3-methyl-5-methoxycarbonylisoxazolidine, 10b, was obtained as a mixture of stereoisomers together with *11b* (*ca.* 10–15 %) by heating methyl acrylate (9.2 g) and acetaldoxime (3.0 g) at 80 °C for 4 h, $b.p._{0.1}$ 112–120 °C, 8.6 g, 72 %. ^1H NMR ($CDCl_3$) *10b*: δ 1.11 (3H, d, *J* 6 Hz), 2.0–3.1 (7H, m), 3.55 (3H, s), 3.62 (3H, s), 4.30 (1H, dd, *J* 4 and 9 Hz). C^5H_2 of *11b* is centred at δ 3.9 (m). MS: 231 (M^+), 158.

2-β-Methoxycarbonylethyl-3-phenyl-5-methoxycarbonylisoxazolidine, 10c, and 2-β-methoxycarbonyl-3-phenyl-4-methoxycarbonylisoxazolidine, 11c, were obtained as a mixture of stereoisomers by heating methyl acrylate (2.5 mol) with benzaldoxime (1.0 mol) at 75 °C for 72 h. The yield of the crude product after evaporation of excess of methyl acrylate was 84 %. Traces of benzaldoxime were present in the product. The ratio *10c: 11c* was 2:1 (^1H NMR, CCl_4). H-5 of *10c* is located at δ 4.5 (dd) and H_2-5 of *11c* at δ 3.9 (m). The OCH_3 groups are located at δ 3.55 and 3.70. MS: 293 (M^+), 220.

2-β-Methoxycarbonylethyl-3,3-spiro-pentamethylene-5-methoxycarbonylisoxazolidine, 10d, and 2-β-methoxycarbonylethyl-3,3-spiro-pentamethylene-4-methoxycarbonylisoxazolidine, 11d, were formed quantitatively in the ratio 3:1 by refluxing cyclohexanone oxime with methyl acrylate (1:2.2) at 90 °C for 4 h. Attempted distillation of the oily product at 150 °C, 0.1 mmHg caused fragmentation of *10d* and *11d* into the starting materials. ^1H NMR (CCl_4) *10d:* δ 1.5 (10H, br.s.), 2.0–3.0 (6H, m), 3.57 (3H, s), 3.63 (3H, s), 4.32 (1H, t, *J* 8 Hz). *11d*: C^5H_2 gives an ABX spectrum the centre lines of which appear at δ 3.97, *J* 3.5 Hz, and 4.10, *J* 3.0 Hz.

2-β-Cyanoethyl-3,3-dimethyl-5-cyanoisoxazolidine, 10e, and 2-β-cyanoethyl-3,3-dimethyl-4-cyanoisoxazolidine, 11e, were obtained as an oil in the ratio 2:1 by heating acetone oxime and acrylonitrile (1:2.2) at 80 °C for 5 h. The yield was practically quantitative. Attempted distillation at 140 °C/0.2 mmHg proceeded under substantial decomposition. *11e* survived the heating better than *10e* and was enriched in the distillate. A small sample was purified by prep. TLC (SiO_2, ether:petrolether, 4:1). ^1H NMR ($CDCl_3$) *10e*: δ 1.11 (3H, s), 1.27 (3H, s), 2.2–3.0 (6H, m), 4.62 (1H, t, *J* 7 Hz). *11e*: 1.26 (3H, s), 1.34 (3H, s), 2.3–3.1 (4H, m), 3.18 (1H, dd, *J* 9 and 6 Hz), 3.93 (1H, dd, *J* 9 and 6 Hz), 4.15 (1H, t, *J* 9 Hz).

2-β-Cyanoethyl-3,3-spiro-pentamethylene-5-cyanoisoxazolidine, 10f, and 2-β-cyanoethyl-3,3-spiro-pentamethylene-4-cyanoisoxazolidine, 11f, were obtained according to the same procedure in the ratio 7:3. The total yield was 61 %, purified by TLC (SiO_2, CH_2Cl_2, 10 % CH_3OH). ^1H NMR ($CDCl_3$) *10f*: δ 1.0–2.0 (10H, m), 2.3–3.2 (2H, m), 4.7 (1H, dd, *J* 6 and 8 Hz); *11f*: δ 1.0–2.0 (10H, m), *ca.* 2–3 (1H, m), 4.0–4.3 (2H, m).

Synthesis of 8 via 13. Acetone oxime (10 g) was equilibrated with formalin (33 g, 40 %) at 60 °C for 30 min. Three drops of acetic acid and acetonitrile (8 g) were added and the solution was stirred at 60 °C for 5–6 h. Extraction with methylene chloride gave 15 g of crude *13* containing *14*. The product was refluxed in methanolic hydrogen chloride (400 ml, 2.5 % HCl) for 48 h at 70 °C. The methanol was evaporated and water (10 ml) added. Neutralization with solid sodium bicarbonate and extraction with methylene chloride gave 15 g of crude *8* which was distilled *in vacuo*. 4.0 g of pure *8* was obtained, $b.p._{0.2}$ 72–76 °C. A large quantity of tarry material remained in the distillation flask.

3,3-Spiro-pentamethylene-5-methoxycarbonylisoxazolidine, 22a, and 3,3-spiro-pentamethylene-4-methoxycarbonylisoxazolidine, 22b. Dimethyl succinimidylsulfonium chloride *16* was

prepared from dimethylsulfide (1.36 g, 22 mmol) and NCS (2.93 g, 22 mmol) in acetonitrile (20 ml) at 0 °C. The temperature was lowered to −20 °C and a mixture of cyclohexanone oxime (2.3 g, 20 mmol, in 5 ml of methylene chloride) and methyl acrylate (2.5 g, 30 mmol) was added slowly. Triethyl amine (2.2 g, 22 mmol) was then added drop by drop over a period of *ca.* 6 min. The temperature was slowly raised and kept at 50 °C for 24 h. *Ca.* 3/4 of the solvent was evaporated *in vacuo*. The remainder was shaken with carbontetra chloride (25 ml) and water (15 ml), filtered and the organic phase was separated. It was once more washed with water (15 ml), dried over sodium sulfate, and evaporated. The product (3.8 g) consisted mainly of *21a* and *21b* (*ca.* 4:1). A small sample (600 mg), purified by preparative TLC (SiO_2, ether:petrolether 1:2) gave *21a* (430 mg, 53 %). ^1H NMR ($CDCl_3$) *21a*: δ 1.0−1.9 (10H, m), 2.21 (3H, s), 2.32 (1H, dd, *J* 16 and 6.8 Hz), 2.51 (1H, dd, *J* 16 and 8.5 Hz), 3.71 (3H, s), 3.90 (2H, s), 4.58 (1H, dd, *J* 6.8 and 8.5 Hz). *21b* showed a doublet at δ 4.24 (C^5H_2, *J* 8.3 Hz). The rest of the crude product (3.2 g) was hydrolyzed in refluxing methanolic hydrogen chloride (5 % 60 ml) for 4 h. The methanol was evaporated *in vacuo*, water was added (10 ml) and the solution was extracted with ether (10 ml). The aqueous phase was neutralized to pH 9 with sodium bicarbonate and extracted with methylene chloride. Evaporation of the organic solvent gave a mixture of rather pure *22a* and *22b* (*ca.* 4:1), 2.2 g. It was distilled in a Kugelrohr apparatus at *ca.* 135 °C/0.15 mmHg (partial decomposition). The distilled yield was 1.1 g, 28 %. ^1H NMR ($CDCl_3$) *22a*: δ 1.5 (10 H, br.s), 1.9 (1H, dd, *J* 12 and 6 Hz), 2.4 (1H, dd, *J* 12 and 9 Hz), 3.70 (3H, s), 4.54 (1H, dd, *J* 6 and 9 Hz). C^5H_2 of *22b* was located at δ 4.1, d, *J 6 Hz*.

The pyrrolidone 23 was obtained by hydrogenation of *22a* with RaNi/H_2 in ethanol, m.p. 209−212 °C (recrystallized from water). MS: M^+ 169. ^1H NMR ($CDCl_3$+D_2O): δ 1.5 (10H, br.s), 1.66 (1H, dd, *J* 13 and 8 Hz), 2.31 (1H, dd, *J* 13 and 8 Hz), 4.27 (1H, t, *J* 8 Hz).

3,3-Dimethyl-5-methoxycarbonylisoxazolidine, 24a, and 3,3-dimethyl-4-methoxycarbonylisoxazolidine, 24b. The procedures described for *21ab* and *22ab* were essentially followed. The crude yields of *20ab* (from 0.73 g, 10 mmol, of acetone oxime) was 2.3 g. The ratio of *20a:20b* was *ca.* 5:2. *20a,b* were purified by preparative TLC (SiO_2, CH_2Cl_2, CH_3CN, 10 %). ^1H NMR (CCl_4) *20a*: δ 1.15 (3H, s), 1.18 (3H, s), 2.16 (3H, s), 2.31 (2H, d, *J* 8 Hz), 3.7 (3H, s), 4.41 (1H, t, *J* 8 Hz). The acid hydrolysis of *20ab* was carried out in refluxing methanol (10 ml, 1.0 M H_2SO_4) for 1 h. The product was partioned between methylene chloride (20 ml) and water (20 ml) basified with sodium hydroxide (20 mmole). Evaporation of the organic phase gave *24ab* which was purified by TLC (SiO_2, CH_2Cl_2:CH_3CN, 9:1). The yield of *24ab* was 71 % and the isomeric ratio was *ca.* 5:2. ^1H NMR (CCl_4) *24a*: δ 1.15 (3H, s), 1.23 (3H, s), 1.91 (1H, dd, *J* 13 and 6 Hz), 2.28 (1H, dd, *J* 12 and 9 Hz), 3.66 (3H, s), 4.42 (1H, dd, *J* 9 and 6 Hz). *24b* gives a doublet from C^5H_2 at δ 4.0, *J* 7 Hz. C^4H_1 is centered at 2.92.

Conversion of aldoximes to nitriles. General procedure. Dimethyl succinimidylsulfonium chloride *16* was prepared from NCS (1.47 g, 11 mmol) and dimethylsulfide (0.68 g, 11 mmol) in acetonitrile (5 ml) at 0 °C. The aldoxime (10 mmol) in methylene chloride (4 ml) was added with stirring and after 15 min triethylamine was added slowly (11 mmol) at the same temperature. The reaction mixture was stirred for 24 h at room temperature, then shaken with a mixture of water (10 ml) and carbontetrachloride (10 ml) and filtered if necessary. The organic phase was separated, washed with water (10 ml) and evaporated. The nitrile formed was purified by distillation or chromatography. The yield ranged between 80−90 %. In the conversion of benzaldoxime into benzonitrile 100 % excess of *16* and triethylamine was used.

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