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Reactions of *t*-Butyl Nitrones and Trimethylsilyl Nitronates. Synthesis and Reactions of Isoxazolidines and 2-Isoxazolines

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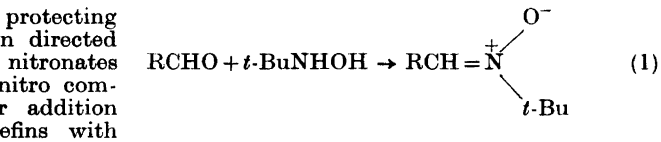
t-Butyl nitrones are unsuitable as a protecting group for the aldehyde function in directed aldol condensation. Trimethylsilyl nitronates are easily prepared from primary nitro compounds. They undergo 1,3-dipolar addition to negatively monosubstituted olefins with formation of isoxazolidines and 2-isoxaxolines. The structures of some rearrangement products have been elucidated.

Reactions of nitrones. Nitrones are easily formed from *N*-(*t*-butyl)hydroxylamine and simple aliphatic aldehydes and cinnamaldehyde but acrolein and crotonaldehyd, *2a* and *2b*, gave the isoxazolidines *3a* and *3b* by 1,4-addition. Rapid base catalyzed hydrogen exchange in *1a* was observed by NMR spectroscopy in D_2O. The condensation of benzaldehyde with *1a* was tested under a variety of conditions with the purpose of investigating the utility of *t*-butylnitrones in directed aldol condensation.[1] The *t*-butyl group prevents Behrend's rearrangement [2] and deactivates the nitron as electrophile. The best results were obtained with potassium *t*-butoxide in *t*-butylalcohol. In some cases considerable amounts of the *trans*-nitronization product *1d* were obtained [eqn. (2)]. *1a* could not be condensed with ketones. The hydrolysis of *1c* to cinnamaldehyde required several hours' refluxing in 4 M hydrochloric acid. Thus the nitrone function does not behave satisfactorily in aldol type condensation. Condensations between benzaldehyde and nitrones have been described earlier [3,4] as well as dimerization of nitrones.[5–7]



$$\mathrm{RCHO} + t\text{-BuNHOH} \rightarrow \mathrm{RCH{=}\overset{+}{N}(O^-)(t\text{-Bu})} \qquad (1)$$

1a, R = CH_3; *1b*, R = C_3H_7; *1c*, R = C_6H_5CH=CH; *1d*, R = C_6H_5

As shown in eqn. (4), *1b* could readily be converted to the relatively stable derivatives *4a* and *4b*. *4a* did not show any signs of rearrangement [3] to an α-hydroxy enamine below 150 °C.

Reactions of trimethylsilyl nitronates. Silylation of nitromethane gave the nitronate *6* that was supposed to be formed *via* the unstable intermediate *5*.[8] *5* was observed spectroscopically in solution.[9] The formation of *5* is proved by reacting nitromethane with chlorotrimethylsilane and triethylamine in the presence of a trapping olefin. In a regioselective 1,3-dipolar addition [eqn. (6)] isoxazolidines, *9*, are formed, Table 1, (*cf.* Ref. 10).

Trimethylsilanol elimination is acid catalyzed but occurs often spontaneously and 2-isoxazolines, *10*, are formed. *7* and *8*, can be purified by distillation but decompose on standing, sometimes within a few hours. Triethylamine was found to be an effective stabilizer. The ^1H NMR of *7* and *8* showed the presence of one isomer only. 2-Nitropropane could not be silylated by this method but it has been transformed to silyl nitronate under more drastic reaction conditions.[9] Nitroethane, trimethylsilanol, bis-trimethylsilyl ether and 3,4-dimethylisoxadiazol *N*-oxide, *11*, were identified by ^1H NMR from the decomposition of *7*, eqn. (7).

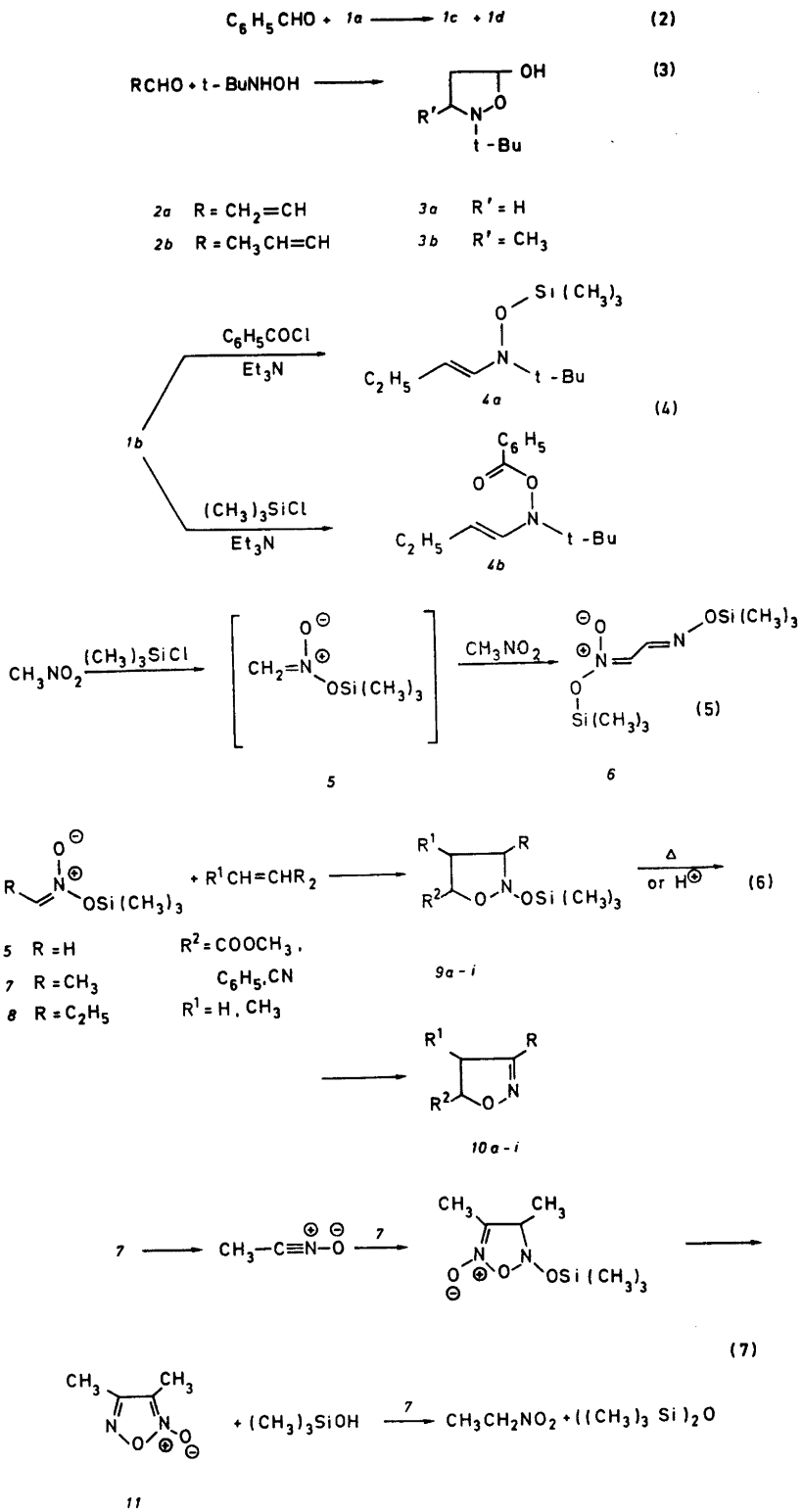


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Table 1. Isoxazolidines from 1,3-dipolar addition of trimethylsilyl nitronates to olefins, eqn. (6).

Trimethylsilyl nitronate	Olefin R^1	Olefin R^2	Isoxazolidine	Yield (%)	Reaction conditions h	Reaction conditions °C	Boiling point °C/mmHg
5	H	$COOCH_3$	9a	57	18	20	64–68/0.3
5	H	C_6H_5	*9b* [a]	small	18	20	–
5	CH_3	$COOCH_3$	*9c* [b]	~31	18	20	48–50/0.25
7	H	$COOCH_3$	*9d* [c]	64	0.5	80	54–60/0.27
7	H	C_6H_5	*9e* [c]	69	2	80	81–90/0.24 [d]
7	CH_3	$COOCH_3$	*9f* [e]	~30	48	50	78–88/0.63
8	H	$COOCH_3$	*9g*	86	72	20	74–75/1.4
8	H	C_6H_5	*9h*	62	2	80	118–120/0.8
8	H	CN	*9i*	72	48	20	56–58/0.2
7	H	CN	*9j*	0 [f]	1	80	
5	H	CN	*9k*	0 [g]	3.5	20	

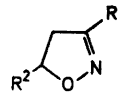
[a] The major product is 5-phenyl-2-isoxazoline. [b] Major component, mixture of isomeric isoxazolidines. [c] Mixture of stereo-isomers. [d] Upon distillation trimethylsilanol often eliminates, 2-isoxazolin is formed. [e] Complex mixture of isomers. [f] The products were *19* (49 %) and *21*. [g] The product was *18* (58 %).

Our attempts to react the presumed activated β-position of the nitronates with electrophiles (benzyl bromide, benzaldehyde, acetone) in a base catalyzed reaction were unsuccessful. 1-Phenyl-2-nitropropyl trimethylsilyl ether, *12*, was obtained from the reaction of *7* with benzaldehyde and triethylamine. The ^1H NMR spectrum of *12* showed the presence of diastereomers. The reaction does not seem to be general for carbonyl compounds.

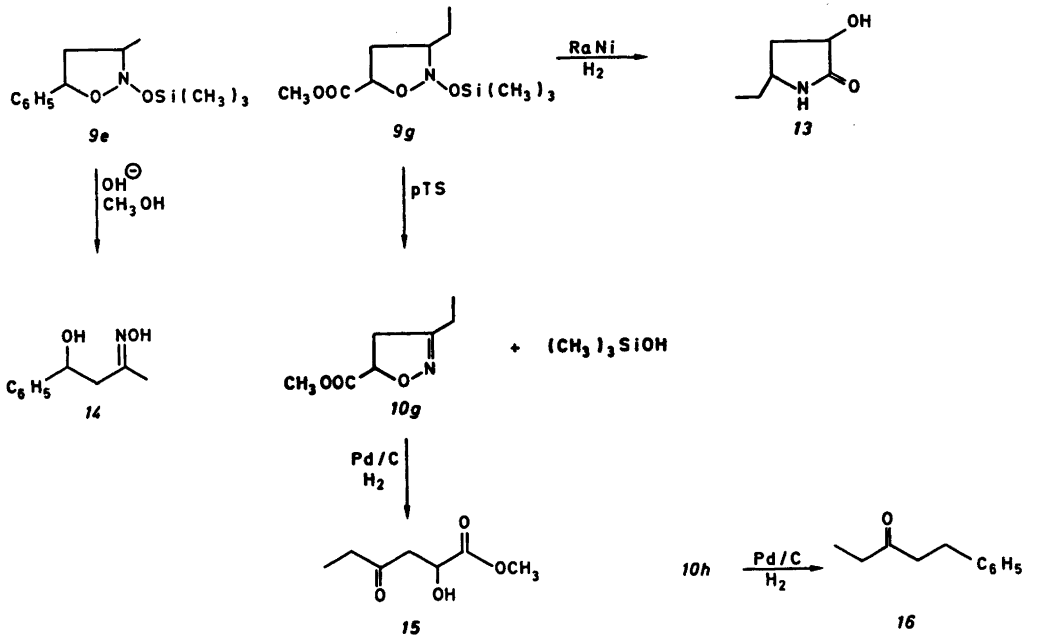
$$C_6H_5CHO + 7 \xrightarrow{(C_2H_5)_3N} CH_3CH(NO_2)CH(C_6H_5)OSi(CH_3)_3 \quad (8)$$

As noted earlier the nitronates undergo 1,3-dipolar additions. We investigated this reaction since it was thought that functionalized olefins could be produced by this route. The addition [eqn. (6)] proceeds satisfactorily for monosubstituted olefins carrying electron withdrawing groups. Ethyl vinyl ether, 1-hexene, cyclohexene, *cis*-1,2-dichloroethene and trisubstituted olefins do not react or give very low yields. Methyl crotonate demands prolonged reaction time at a higher temperature and gives a complex mixture. The ^1H and ^{13}C NMR spectra of *9b* showed peaks appearing in pairs indicating stereoisomers, which on acid catalyzed trimethylsilanol elimination gave a single 2-isoxazolin, *10b*, Table 2. Thus, the inversion barrier around nitrogen in *9* is too high to allow rapid isomerization. Treatment

Table 2. Preparation of 2-isoxazolines, eqn. 6.

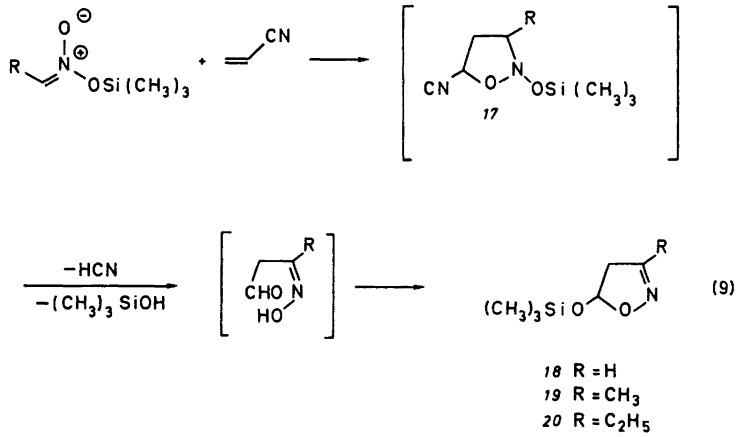


2-Isoxazoline	R	R^2	B.p./°C (mmHg)	Yield
10a	H	CO_2CH_3	66–67/0.45	34
10b	H	C_6H_5	92–96/0.6	41
10d	CH_3	CO_2CH_3	116–117/0.7	52
10e	CH_3	C_6H_5	78–98/0.12	56
10g	C_2H_5	CO_2CH_3	84–86/0.3	86
10h	C_2H_5	C_6H_5	92/0.2	79
10i	C_2H_5	CN	91/1.5	50
18	H	$(CH_3)_3SiO$	56–76/0.5	58
19	CH_3	$(CH_3)_3SiO$	84–100/9	49
20	C_2H_5	$(CH_3)_3SiO$	45/0.3	23

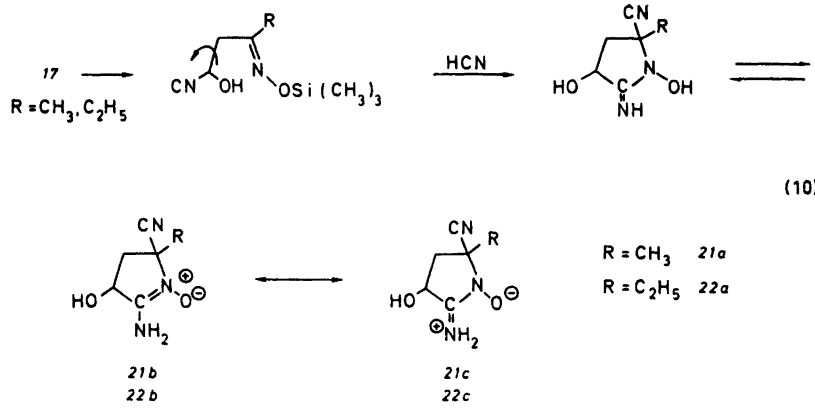


Scheme 1.

of *9* with base in methanol or catalytic reduction caused ring cleavage. Scheme 1 summarizes the reactions performed. The results are in general agreement with the work by Kashutina *et al.*[9] The addition of acrylonitrile to nitronates took a different course [eqn. (9)]. The addition product *17* rapidly eliminates hydrogen cyanide and trimethyl silanol and the intermediate aldehyde ring closes and becomes resilylated. For R = H and CH_3 *17* could not be isolated but rearranged to *18* and *19*. *17* is isolated from silyl ester ($R = C_2H_5$) but at temperatures higher than 70 °C *20* is also obtained. In the synthesis of *19* and *20* a high-melting solid byproduct was formed. The methyl derivative analyzed for $C_6H_7N_3O_2$, and according to the ^1H and ^{13}C NMR spectra it has three exchangeable protons, one *C*-methyl, one cyano group, a C=N and a $-CH-CH_2-$ function. The UV (H_2O, 238 nm, log ε 3.98) and IR spectra (KBr: 3300 s br, 2550 s br, 1700 s, cm^{-1}; no visible CN absorption) were at first

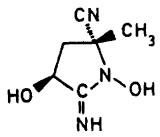


18 R = H
19 R = CH_3
20 R = C_2H_5



(10)

puzzling but *21a* was suggested as a tentative structure formed according to eqn. (10). This was later confirmed by an X-ray study [11] but from the bond lengths it was deduced that the tautomers *21b* and *21c* are a better representation of the structure. The UV and IR are better explained in terms of contributions from the latter nitrone and immonium structures. The stereochemistry is depicted in *21*.



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EXPERIMENTAL

Melting and boiling points are uncorrected.

N-(Ethylidene)-t-butylamine N-oxide, 1a. To *N*-(*t*-butyl)hydroxylamine (9.5 g, 0.107 mol) and sodium sulfate (15 g) in methylene chloride (30 ml) acetaldehyde (7.8 ml, 0.16 mol) was added slowly at room temperature. After 0.5 h the solution was filtered, evaporated and distilled. *1a* (7.1 g) distilling at 46 °C/1.4 mmHg was obtained. ^{1}H NMR ($CDCl_3$): δ 1.33 (9 H,s), 1.99 (3 H, d, J 6 Hz), 7.47 (1 H, q, J 6 Hz).

N-(Propylidene)-t-butylamine N-oxide, 1b, was obtained similarly from butanal in a yield of 82 %; b.p. 87–90 °C/10 mmHg. *p*-Toluenesulfonic acid (0.1 g) was added as a catalyst and the solution was filtered after 18 h. ^{1}H NMR ($CDCl_3$): δ 0.98 (3 H, t, $J\sim7$ Hz), 1.41 (2 H, hext, $J\sim7$ Hz), 1.50 (9 H, s), 2.49 (2 H, q, $J\sim7$ Hz), 6.85 (1 H, t, J 5.5 Hz).

N-(Styrylidene)-t-butylamine N-oxide, 1c, was obtained from cinnamaldehyde according to the same method in a yield of 75 %, m.p. 67–68 °C. ^{1}H NMR ($CDCl_3$): δ 1.54 (9 H, s), 7.7–6.8 (8 H, m).

1c was also obtained by reacting benzaldehyde (8.48 g, 0.08 mol), *1a* (9.20 g, 0.08 mol) and potassium *t*-butoxide (10.08 g, 0.09 mol) in *t*-butyl alcohol (100 ml) at room temperature with stirring for 24 h. The mixture was poured onto ice (300 g) and sulfuric acid (4 N, 24 ml), extracted with methylene chloride and the solvent dried (Na_2SO_4) and evaporated. The crude product, *1c*, was recrystallized from light petroleum; yield: 10.2 g, 62 %, m.p. 66–68 °C, identical with the compound above.

Cinnamaldehyde was obtained in a yield of 37 % by refluxing the crude product, *1c*, in 4 N hydrochloric acid (25 % methanol) for 4 h.

2-(t-Butyl)-5-hydroxyisooxazolidine, 3a. To acrolein (4.4 g, 0.079 mol) in methylene chloride (20 ml) *N-t*-butylhydroxylamine (5.22 g, 0.059 mol) was added in small portions at 0 °C with stirring. After 18 h at 25 °C the solvent was evaporated and the product crystallized from acetonitrile cooled to −70 °C, yield: 5.85 g, 67 %, m.p. 102–104 °C. Found: C 57.88; H 10.29; N 9.86. Calc. for $C_7H_{15}NO_2$: C 57.93; H 10.42; N 9.66. ^{1}H NMR ($CDCl_3$): δ 1.12 (9 H, s), 3.2–2.1 (4 H, m) 5.6–5.3 (1 H, m).

2-(t-Butyl)-5-hydroxy-3-methylisoxazolidine, 3b, was obtained similarly from crotonaldehyde, m.p. 66–68 °C from light petroleum yield: 48 %. Found: C 60.08; H 10.78; N 8.83. Calc. for $C_8H_{17}NO_2$: C 60.34; H 10.75; N 8.80. The ^{1}H NMR spectrum indicated the presence of two anomers.

N-(t-Butyl)-N-(1-butenyl)-O-trimethylsilyl hydroxylamine, 4b. Chlorotrimethylsilane (5.0 g, 0.046 mol), triethylamine (4.7 g, 0.047 mol) and *1b* (6.3 g, 0.044 mol) were refluxed for 18 h in benzene (50 ml). The mixture was filtered, evaporated and distilled giving *4a* (6.9 g, 73 %), b.p. 71–72 °C/11 mmHg. ^{1}H NMR ($CDCl_3$): δ 0.13 (9 H, s), 0.98 (3 H, t, J 7.5 Hz), 1.08 (9 H, s), 2.02 (2 H, ddt, J 7.5, 6.6, 1.3 Hz), 5.11 (1 H, d, q, J 13.4, 6.6 Hz), 5.97 (H, dt, J 13.4, 1.3 Hz).

N-(t-Butyl)-N-vinyl-O-trimethylsilyl hydroxylamine was prepared as above from *1a*, reaction time 4 h, yield: 36 %, b.p. 62 °C/26 mmHg. Found: C 57.87; H 11.34; N 8.02. Calc. for $C_9H_{21}NOSi$: C 57.68; H 11.30; N 7.48. ^{1}H NMR ($CDCl_3$): δ 0.15 (9 H, s), 1.12 (9 H, s), 4.30 (1 H, dd, *J* 9.0, 1.2 Hz), 4.42 (1 H, dd, *J* 15.0, 1.2), 6.32 (1 H, dd, *J* 15.0, 9.0 Hz).

N-(t-Butyl)-N-(1-butenyl)-O-benzoyl hydroxylamine, 4a. Benzoyl chloride (1.96 g, 0.014 mol), triethylamine (1.42 g, 0.014 mol) and *1b* (2.00 g, 0.014 mol) was stirred in benzene (10 ml) at room temperature for 18 h, filtered, solvent evaporated and fractionated. *4a* (0.90 g, 27 %) distilled at 96 – 106 °C/0.8 mmHg. ^{1}H NMR ($CDCl_3$): δ 1.03 (3 H, t, *J* 7.5 Hz), 1.18 (9 H, s), 2.10 (2 H, pent., $J \sim 7$ Hz), 5.43 (1 H, dt, *J* 14.5, 6.5 Hz). 7.71 – 7.30 (4 H, m), 8.08 – 8.25 (2 H, m).

Trimethylsilylester of aci-*nitroethane*, 7. To nitroethane (30 g, 0.40 mol), triethylamine (40.4 g, 0.40 mol) in benzene (200 ml) chlorotrimethylsilane (43.2 g, 0.40 mol) was added. The mixture was stirred for 18 h at room temperature, filtered, evaporated and distilled *in vacuo*. The yield of *7* was 64 % (37.8 g), b.p. 64 °C/25 mmHg.

Trimethylsilylester of aci-*nitropropane*, 8, was obtained from nitropropane in a yield of 79 % according to the same method, b.p. 58 °C/12 mmHg. The ^{1}H NMR spectra of *7* and *8* agree with earlier data.[9]

1-Phenyl-2-nitropropyl trimethylsilyl ether, 12. *7* (10.0 g, 0.068 mol), triethylamine (6.6 g, 0.067 mol) and benzaldehyde (6.8 g, 0.064 mol) were refluxed in benzene (40 ml) for 18 h. The solvent was evaporated and the remainder distilled *in vacuo*. 6.8 g of *12* (42 %) was obtained, b.p. 80 – 84 °C/0.4 mmHg. Found: C 56.93; H 7.64; N 5.71. Calc. for $C_{13}H_{19}NO_3Si$: C 56.91; H 7.51; N 5.53. The ^{1}H NMR spectrum showed the presence of two diastereomers.

2-Trimethylsilyloxy-5-(carbomethoxy)isoxazolidine, 9a. To methyl acrylate (4.30 g, 0.05 mol), triethylamine (5.05 g, 0.05 mol) and chlorotrimethylsilane (5.40 g, 0.05 mol) in benzene (50 ml) nitromethane (3.05 g, 0.05 mol) was added dropwise at room temperature with stirring and cooling with tap water. After 18 h the solution was filtered, evaporated and distilled giving *9a* (6.19 g, 57 %), b.p. 64 – 68 °C/0.3 mmHg. ^{1}H NMR ($CDCl_3$): δ 0.32 (9 H, s) 3.47 – 2.22 (4 H, m), 3.80 and 3.77 (3 H, s), 5.00 – 4.73 (1 H, m). According to the ^{1}H NMR spectrum the crude product of *9a* (8.6 g) was fairly pure. On distillation some 2-isoxazoline *10a* was formed.

2-Trimethylsilyloxy-5-phenylisoxazolidine, 9b, prepared as above from styrene as dipolarophile was obtained only in minor amounts as evidenced by the ^{1}H NMR of the crude product. The major product is *10b*, which was obtained as sole product on distillation, see below.

5-Trimethylsilyloxy-2-isoxazoline, 18, was obtained in a yield of 58 %, b.p. 56 – 76 °C/0.5 mmHg when *5* was generated as above in the presence of acrylonitrile. The compound decomposes on standing. ^{1}H NMR ($CDCl_3$): δ 0.17 (9 H, s), 2.77 (1 H, ddd, *J* 18.0, 2.3, 1.5 Hz), 3.13 (1 H, ddd, 18.0, 5.1, 1.5 Hz), 5.87 (1 H, dd, *J* 5.1, 2.3 Hz), 7.29 (1 H, t, *J* 1.5 Hz).

2-Trimethylsilyloxy-4-methyl-5-(carbomethoxy)isoxazolidine, *9c* was obtained as a major product along with isomers from methyl crotonate and *5* generated according to the previous method in a yield of 31 % (impure), b.p. 48 – 50 °C/0.25 mmHg. ^{1}H NMR ($CDCl_3$): δ 0.16 (9 H, s), 1.46 (3 H, d, *J* 7.6 Hz), $\sim$2.5 – 3.5 (3 H, m), 3.79 (3 H, s), 4.61 (1 H, d, *J* 6.5 Hz). The compound decomposes on standing with elimination of trimethylsilanol.

General procedure for the preparation of 9d – 9h. Trimethylsilyl nitronate, *7* or *8* (0.05 mol), olefin (0.05 mol) and triethylamine (0.02 – 0.05 mol) as stabilizer were reacted in benzene (30 ml) at the appropriate temperature and time. The solvent was evaporated and the remainder distilled *in vacuo*. In some instances trimethylsilanol eliminates during the fractionation and isoxazolines are formed, *e.g.* from *9b* and *9e*.

Preparation of 2-trimethylsilyloxy-3-ethyl-5-cyanoisoxazolidine, 9i, *3-ethyl-5-trimethylsilyloxy-2-isoxazoline*, 20, *and 1,3-dihydroxy-2-imino-5-ethyl-5-cyanopyrrolidine*, 22. The general procedure for the preparation of *9* was followed but care was taken that the temperature during distillation was kept below 70 °C. *9i* distilled at 56 – 58 °C/0.2 mmHg in a yield of 72 %. ^{1}H NMR ($CDCl_3$): δ 0.15 and 0.20 (9 H, s), 0.9 (3 H, t br, $J \sim 7$ Hz), 3.65 – 1.0 (5 H, m), 5.1 – 4.7 (1 H, m). At a higher temperature the first formed product *9i* transforms into *20*. This reaction can also be brought about by refluxing *9i* in toluene for 3 h. *20* was obtained as a liquid in a yield of 23 %, b.p. 45 °C/0.3 mmHg. ^{1}H NMR ($CDCl_3$): δ 0.15 (9 H, s), 1.18 (3 H, t, *J* 7.5), 2.43 (2 H, tq, *J* 7.5, $\sim$1 Hz), 2.80 (1 H, dt, *J* 2.0, $\sim$1 Hz), 2.93 (1 H, dt, *J* 5.5, $\sim$1 Hz), 5.83 (1 H, dd, *J* 5.5, 2.0 Hz). In the flask from distillation of *9i* a solid remained that was recrystallized from ethanol (yield 1.8 g of *22* from 23.8 g *8* and 8.1 g acrylonitrile), dec. 190 °C. Found: C 49.72; H 6.56; N 24.85. Calc. for $C_7H_{11}N_3O_2$: C 49.95; H 6.60; N 24.74. ^{1}H NMR (D_2O) of *22*: δ 1.10 (3 H, t, *J* 7.2 Hz), 2.08 (2 H, q, *J* 7.2 Hz), 2.14 (1 H, dd, *J* 14.1, 6.0 Hz), 3.09 (1 H, dd, *J* 14.1, 8.2 Hz), 4.7 (3 H, sbr), 5.13 (1 H, dd, *J* 8.2, 6.0 Hz). UV (H_2O): λ_{max} 238 nm, log ε 4.03. This absorption vanishes on acidification. IR (KBr): 3240 (sbr), 2540 (sbr), 1700 (s) cm^{-1}.

3-Methyl-5-trimethylsilyloxy-2-isoxazoline, 19, *and 1,3-dihydroxy-2-imino-5-methyl-5-cyanopyrrolidine*, 21. *7* (10 g, 0.068 mol), acrylonitrile (3.6 g, 0.068 mol) and triethylamine (3.43 g) in benzene (30 ml) were refluxed for 1 h, solvent removed and the product distilled. The fractions boiling at 84 – 100 °C/9 mmHg were

combined and consisted of rather pure *19*, (5.8 g, 49 %). A middle fraction was used for analysis. Found: C 48.70; H 8.82; N 8.29. Calc. for $C_7H_{15}NO_2Si$: C 48.53; H 8.73; N 8.10. ^1H NMR ($CDCl_3$): δ 0.16 (9 H, s), 2.05 (3 H, t, $J \sim 1$ Hz), 2.80 (1 H, dq, J 2, ~ 1 Hz), 2.95 (1 H, dq, J 5.5, ~ 1 Hz), 5.82 (1 H, dd, J 5.5, 2 Hz).

In the flask remained a solid, *21*, that was recrystallized from methanol:water, 1.8 g dec. ~ 200 °C. Found: C 46.61; H 5.92; N 27.42. Calc. for $C_6H_9N_3O_2$: C 46.45; H 5.85; N 27.08. ^1H NMR (D_2O): δ 1.82 (3 H, s), 2.13 (H, dd, J 6.0, 14.3 Hz), 3.20 (1 H, dd, J 8.2, 14.3 Hz), 4.70 (3 H, sbr), 5.10 (1 H, dd, J 6.0, 8.2 Hz).

1-Hydroxy-1-phenyl-3-iminoxybutane, 14. *9e* (5 g) was treated with methanolic sodium hydroxide (15 ml, 0.3 g) for 1 h. Water was added and the mixture extracted with methylene chloride. Evaporation of the organic solvent afforded crude *14* in good yield. ^1H NMR (CD_3OD): δ 1.71 (3 H, s), 2.78 (1 H, d, $J \sim 8$ Hz), 2.86 (1 H, d, $J \sim 8$), 4.7 (2 H, sbr), 5.10 (1 H, dd, J 8.5, 7.5 Hz), 7.38 (5 H, sbr).

3-Hydroxy-5-ethyl-2-pyrrolidone, 13. *9g* (0.99 g, 0.004 mol) was hydrogenated with RaNi in ethanol (25 ml) at 760 mmHg for 96 h. Usual work-up and recrystallization of the product from benzene:acetonitrile (2:1) gave *13* (0.33 g, 64 %), m.p. 143–145 °C. ^1H NMR ($CDCl_3$+ DMSO, d_6): δ 0.94 (3 H, t, J 7 Hz), 2.80–1.20 (4 H, m), 3.65–3.10 (1 H, m), 4.25 (1 H, t, J 8.5 Hz), 5.15 (1 H, sbr), 7.65 (1 H, sbr). IR (KBr): 3250 (s), 2920 (m), 1685 (s), 1450 (w). MS: 129, M+.

Methyl 2-Hydroxy-4-ketovalerate, 15. *10g* (7.85 g, 0.05 mol) was hydrogenated over Pd/C (10 %, 100 mg) in ethanol (50 ml) and acetic acid (25 ml) at room temperature and 3 atm. After 4 h the hydrogen absorption stopped and one equivalent was consumed. The catalyst was filtered and the solvent evaporated. The remainder was dissolved in methylene chloride, washed with saturated aqueous sodium bicarbonate until neutral. The water phase was made slightly alkaline, saturated with sodium chloride, and washed with methylene chloride. The combined organic phase was dried (Na_2SO_4), evaporated, and distilled. *15* (3.3 g, 41 %) b.p. 80–82 °C/0.4 mmHg was obtained. ^1H NMR ($CDCl_3$): δ 1.50 (3 H, t, J 7.5 Hz), 2.51 (2 H, q, J 7.5 Hz), 2.93 (2 H, d, J 5.5 Hz), 3.70 (1 H, s.br), 3.78 (3 H, s), 4.55 (1 H, t, J 5.5 Hz). IR ($CHCl_3$): 1750 (s), 1725 (s) cm^{-1}.

1-Phenyl-3-pentanone, 16, was obtained in a yield of 21 % from *10h* by catalytic reduction over Pd/C, 5 % in ethanol–acetic acid, 1:1, for 5 days at 760 mmHg (1.7 equiv. H_2 was absorbed).

Preparation of 2-isoxazolines, 10a *and* 10b. The procedures for the preparation of *9a* and *9b* were followed. After the addition of nitromethane the mixture was refluxed for 1 h and worked up. Vacuum distillation of the crude products gave *10a* and *10b* in a yield of 34 % and 41 %, respectively. ^1H NMR ($CDCl_3$) for *10a*: δ 3.33 (2 H, dd, J 9.3, 2 Hz), 3.75 (3 H, s), 4.99 (1 H, t, J 9.3 Hz), 7.25 (1 H, t, J 2 Hz), and for *10b*: δ 2.82 (1 H, ddd, J 18, 8.7, 2 Hz), 3.36 (1 H, ddd, J 18, 11, 2 Hz), 5.50 (1 H, dd, J 11, 8.7 Hz), 7.17 (1 H, t, $J \sim 2$ Hz), 7.32 (5 H, sbr).

Preparation of 2-isoxazolines, 10d,e,g,h,i. To the corresponding isoxazolidines, *9d,e,g,h,i*, in benzene, a small amount of *p*-toluenesulfonic acid was added. The temperature rose in the mixture which was stirred for 1 h, washed with aqueous sodium bicarbonate, dried over sodium sulfate, evaporated, and distilled *in vacuo*. The crude products are pure and the yields are high. ^1H NMR ($CDCl_3$) for *10d*: δ 2.01 (3 H, t, $J \sim 1$ Hz), 3.24 (2 H, dq, J 9.0, 1 Hz), 3.78 (3 H, s), 5.01 (1 H, t, J 9.0 Hz); *10e*: δ 1.98 (3 H, t, $J \sim 1$ Hz), 2.87 (1 H, ddq, J 17.0, 8.5 $\sim$ 1 Hz), 3.37 (1 H, ddq, J 17.0, 10.5, ~ 1 Hz), 5.51 (1 H, dd, J 10.5, 8.5 Hz), 7.30 (5 H, s); *10g*: δ 1.19 (3 H, t, J 7.2 Hz), 2.40 (2 H, tq, J 7.2, 1 Hz), 3.20 (2 H, dt, J 9.0, 1 Hz), 3.78 (3 H, s), 5.00 (1 H, t, J 9.0 Hz); *10h*: δ 1.17 (3 H, t, J 7.5 Hz), 2.40 (2 H, tq, J 7.5, ~ 1 Hz), 2.84 (2 H, ddq, J 17.5, 8.5, ~ 1 Hz), 3.37 (1 H, ddq, J 17.5, 10.3, ~ 1 Hz), 5.54 (1 H, dd, J 10.3, 8.5 Hz) 7.30 (5 H, sbr); *10i*: δ 1.20 (3 H, t, J 7.5 Hz), 2.38 (2 H, q, J 7.5 Hz), 3.35–3.25 (1 H, m), 3.48–3.39 (1 H, m), 5.25 (1 H, dd, J 9.0, 7.5 Hz).

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