Efficient Synthesis of Trifluoromethyl-Substituted 5,6-Dihydro-4*H*-1,2-oxazines by the Hetero-Diels–Alder Reaction of 1,1,1-Trifluoro-2-nitroso-2-propene and Electron-Rich Olefins†

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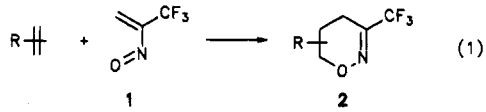
1,1,1-Trifluoro-2-nitroso-2-propene (1) was generated in situ by treatment of the α-bromo oxime **5** with base. Moderate to excellent yields of the 3-trifluoromethyl-substituted 1,2-oxazines **17–27** were obtained from the reaction of **1** and the silyl enol ethers **6–16**, respectively. Other dienophiles, i.e., allyltrimethylsilane, cyclopentadiene, furan, and dihydropyran, upon reaction with **1** provided the cycloadducts **31–34**, respectively, in good yield. The results demonstrated that **1** is probably the most reactive heterodiene that has so far been employed in this type of Diels–Alder reaction (i.e., Diels–Alder reaction with inverse electron demand). The mechanism of the reaction and diastereoselectivity of the cycloadditions are discussed. The reaction of **1** with indole and acetyl acetone afforded the oxime **38** and a mixture of the isomers **40–42**, respectively. Also, ring openings and other transformations of the trifluoromethyl-substituted 1,2-oxazines were effected. Acid-induced desilylation of the silylated 1,2-oxazines provided oximes like **46** and **48** or 6-hydroxy-1,2-oxazines like **47**. Treatment of the 1,2-oxazines with $Mo(CO)_6$ in the presence of trifluoroacetic acid produced 2-trifluoromethyl-substituted pyrroles (e.g., **18** → **50**). The reduction of the 1,2-oxazines afforded either γ-hydroxy oximes (e.g., **19** → **51**) or amino alcohols (e.g., **32** → **52**, **31** → **55**). The reduction of the indole derivative **38** by $LiAlH_4$ provided the trifluoromethyl-substituted tryptamine **56**. The results of these explorative studies demonstrated that readily available trifluoromethyl-substituted 1,2-oxazines could be efficiently converted into other compounds that bear a trifluoromethyl group.

There is much current interest in fluoro- and per(poly)fluoroalkyl-substituted organic compounds because they often display biological activity.[1] For example, certain enzyme inhibitors bear CF_3CO groups[2] and many heterocycles that incorporate per(poly)fluoroalkyl groups have been evaluated as pharmaceuticals or agricultural chemicals.[3]

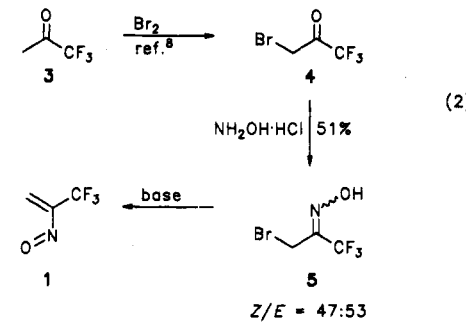
Using the results of the fundamental investigations of the chemistry of nitroso alkenes by Gilchrist[4a–e] as a basis, we recently extended the scope of the [4 + 2] cycloadditions of such heterodienes by trapping them with silyl enol ethers, other silylated olefins,[5,6] and methoxyallene.[7] Here, we disclose the results of the cycloaddition of 1,1,1-trifluoro-2-nitroso-2-propene (**1**), a highly reactive nitroso alkene, to silyl enol ethers. This reaction provides flexible and efficient access to a large variety of trifluoromethyl-substituted 1,2-oxazines **2**. We also give examples of the conversion of trifluoromethyl-substituted 1,2-oxazines into polyfunctional acyclic compounds. The results demonstrate that the [4 + 2] cycloaddition of **1** to silyl enol ethers is a valuable method for preparing compounds that incorporate a trifluoromethyl group.



(1)

1 **2**

Generation of 1,1,1-Trifluoro-2-nitroso-2-propene and Its Cycloaddition to Silyl Enol Ethers. Commercially available 1,1,1-trifluoroacetone (**3**) was brominated to yield the α-bromo ketone **4**.[8] Treatment of **4** with hydroxylamine hydrochloride in a two-phase system ($CHCl_3/H_2O$) and careful distillation gave the desired α-bromo oxime **5**, as a 47:53 mixture of *Z* and *E* isomers, in reasonable yield.



(2)

Z/*E* = 47:53

Nitroso alkene **1** was generated in the presence of the dienophile by treating the α-bromo oxime **5** with base. The

† Dedicated to Professor Jürgen Sauer, Regensburg, on the occasion of his 60th birthday.

‡ Ph.D. Dissertation, Reinhold Zimmer, Technische Hochschule Darmstadt, 1990.

(1) (a) Filler, R. In *Organofluorine Chemicals and Their Industrial Applications*; Banks, R. E., Ed.; Ellis Horwood LTD: Chichester, 1979; p 123 and references cited therein. (b) Filler, R.; Naqui, S. M. In *Biochemical Aspects of Fluorine Chemistry*; Filler, R.; Kobayashi, Y., Eds.; Kodansha LTD; Tokyo Elsevier Biomedical: Amsterdam, 1982; p 1 and references cited therein. (c) *Fluorine-Containing Molecules. Structure, Reactivity, Synthesis and Applications*; Liebman, J. F., Greenberg, A., Dolbier, W. R., Jr., Eds.; VCH: Weinheim, New York, 1988. (d) See also: Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 1320 and references 91–101 in this most comprehensive review.

(2) (a) Walsh, C. *Adv. Enzymol. Relat. Areas Mol. Biol.* **1983**, *55*, 197. (b) Imperiali, B.; Abeles, R. H. *Biochemistry* **1986**, *25*, 3760. (c) Welch, J. T. *Tetrahedron* **1987**, *43*, 3123. (d) Bégué, J.-P.; Bonnet-Delpon, D. *Tetrahedron* **1991**, *47*, 3207.

(3) For examples, see: (a) Burger, K.; Hoess, E.; Geith, K. *Synthesis* **1990**, 357, 360 and references cited therein. (b) Tanaka, K.; Masuda, H.; Mitsuhashi, K. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 3901 and earlier reports by this group.

(4) (a) Faragher, R.; Gilchrist, T. L. *J. Chem. Soc., Perkin Trans. 1* **1979**, 249. (b) Davies, D. E.; Gilchrist, T. L.; Roberts, T. G. *Ibid.* **1983**, 1275. (c) Gilchrist, T. L.; Roberts, T. G. *Ibid.* **1983**, 1283. (d) Gilchrist, T. L.; Iskander, G. M.; Yagoub, A. *Ibid.* **1985**, 2769. (e) Review: Gilchrist, T. L. *Chem. Soc. Rev.* **1983**, *12*, 53. (f) For examples of the intramolecular reaction, see: Denmark, S. E.; Dappen, M. S.; Sternberg, J. A. *J. Org. Chem.* **1984**, *49*, 4741. (g) For reactions with optically active enol ethers, see: Arnold, T.; Reissig, H.-U. *Synlett* **1990**, 514.

(5) Hippeli, C.; Reissig, H.-U. *Liebigs Ann. Chem.* **1990**, 217.

(6) Hippeli, C.; Reissig, H.-U. *Synthesis* **1987**, 77.

(7) (a) Zimmer, R.; Reissig, H.-U. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1518. (b) Zimmer, R.; Reissig, H.-U. *Liebigs Ann. Chem.* **1991**, 553. (c) Zimmer, R.; Reissig, H.-U. *Synthesis* **1989**, 908.

(8) Shapiro, B. L.; Johnston, M. D., Jr.; Lin, H. L. *J. Magn. Resonance* **1973**, *9*, 305.

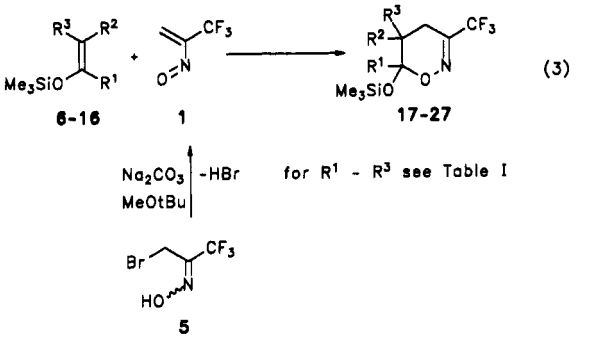
0022-3263/92/1957-0339$03.00/0

Table I. Synthesis of 5,6-Dihydro-3-(trifluoromethyl)-6-(trimethylsiloxy)-4*H*-1,2-oxazines 17–27 via the Cycloaddition of 1 to Silyl Enol Ethers

entry	silyl enol ether	R^1	R^2	R^3	1,2-oxazine	yield (%)
1	6	H	H	H	17	73
2	7[a]	H	H	Me	18[b]	94
3	8	H	Me	Me	19	70
4	9[c]	H	H	$OSiMe_3$	20[d]	29
5	10	*t*-Bu	H	H	21[e]	6
6	11	Ph	H	H	22[f]	33
7	12	$MeC{=}CH_2$	H	H	23	38
8	13	$-(CH_2)_3-$		H	24	86
9	14	$-(CH_2)_4-$		H	25	61
10	15	$-CH(CH_2)_3-$ (Me)		H	26	29
11	16	$-(CH_2)_4-$		Me	27	44

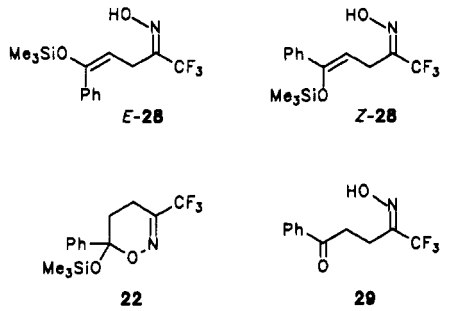
[a] 10:90 mixture of *E*/*Z* isomers. [b] 37:63 mixture of trans/cis isomers. [c] Pure *Z* silyl enol ether. [d] 33:67 mixture of trans/cis isomers. [e] Product contains small quantities of impurities. [f] **22**:(*E*/*Z*)-**28**:**29** = 31:17:52.

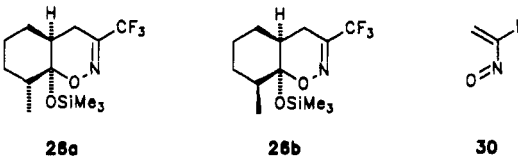
best results in terms of yield and product purity were obtained by using freshly pulverized sodium carbonate in methyl *tert*-butyl ether (MtB). Under these conditions low stationary concentrations of 1 were produced, and therefore side reactions (e.g., polymerization) of the highly reactive nitroso alkene were suppressed. In general, 5 equiv of olefin to 1 equiv of 1 were employed. However, less reactive dienophiles were used in greater excess in order to obtain reasonable yields of the cycloadducts.



Eleven silyl enol ethers (i.e., **6**–**16**) were selected to explore what effects the number and the nature of the substituents on the dienophile had on the [4 + 2] cycloaddition of 1. As Table I shows, the alkenes reacted with 1 to give the trifluoromethyl-substituted 5,6-dihydro-4*H*-1,2-oxazines **17**–**27**, respectively. The yields were generally good. However, the outcomes of several of the reactions deserve comment. Silyl enol ethers that bear substituents (R^1) larger than ethyl (e.g. phenyl or *tert*-butyl) did not yield cycloadducts upon reaction with the nitrosostyrene **30**.[5] However, the nitroso alkene 1 was able to add to such relatively unreactive dienophiles (see entries 5–7), although the yields of cycloadducts were only low to moderate. The reaction of α-(trimethylsiloxy)styrene (**11**) and 1 gave a mixture of 1,2-oxazine **22**, the silyl enol ether oximes (*E*)- and (*Z*)-**28**, and the ketone **29**. Desilylation of the mixture by treatment with 2 N aqueous HCl afforded ketone **29**, which is configurationally homogeneous with respect to the oxime unit; i.e., only one isomer, *Z* or *E*, was produced. This implies that **28** and **29** are very likely generated via the acid-catalyzed ring opening of cycloadduct **22**.

The cycloaddition of 1 to the chiral silyl enol ether **15** provided an 85:15 mixture of the diastereomeric 1,2-oxazines **26a** and **26b** (entry 10). The structures depicted are assigned tentatively because the NMR data available do not permit an unequivocal assignment of structure. If, however, the high propensity for nitroso alkenes to approach olefins from the sterically less hindered side[5] is taken into consideration, the assigned structures are very plausible.





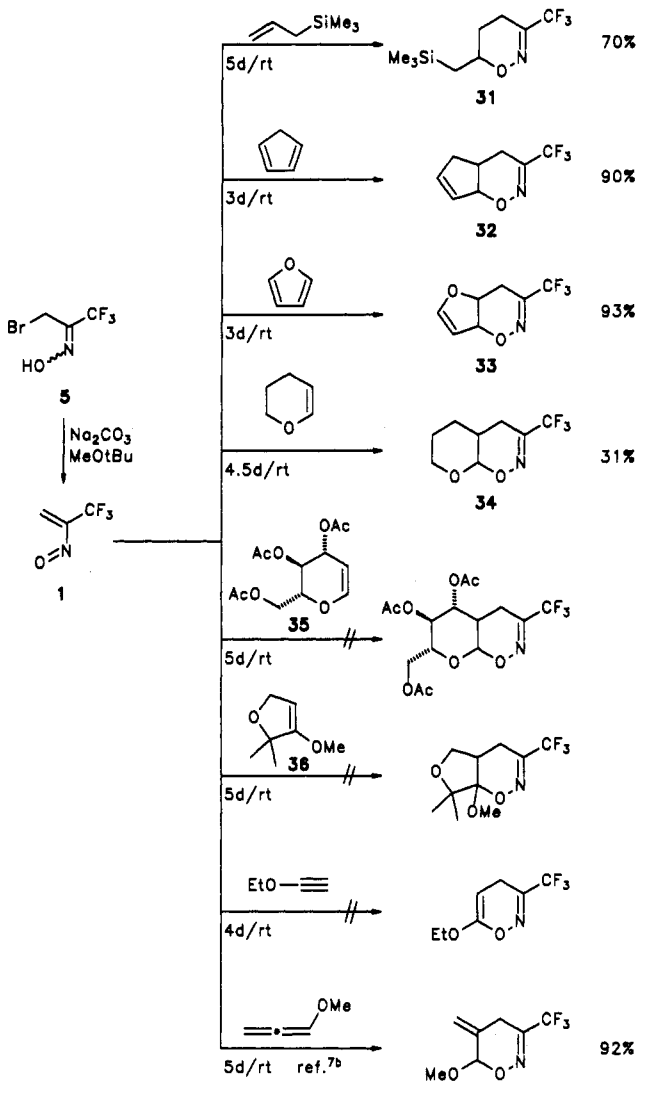
The reaction of the nitrosostyrene **30** and dienophile **15** afforded only one diastereomer (an analogue of **26a**), and that in only very poor yield.[5] This result demonstrates again that 1 is remarkably more reactive than **30**. However, the diastereofacial selectivity of the cycloaddition of 1 seems to be lower. The high reactivity of 1 is also illustrated by its cycloaddition to olefin **16**, which provided the 1,2-oxazine **27** (entry 11, Table I). Silyl enol ether **16** was unreactive towards the nitrosostyrene **30**.[5]

The reaction of the (*Z*)-1,2-bissiloxyethene (*Z*)-**9** and 1 gave a mixture of the cis and trans isomers of the cycloadduct **20** in moderate yield. Similar results had been obtained from the reaction of (*Z*)-**9** and the nitrosostyrene **30**.[5] Because the stereospecificity of the hetero-Diels–Alder reaction of nitroso alkenes and other *E*/*Z* isomeric silyl enol ethers has been established, it must be assumed that *Z*/*E* isomerization occurred during the cycloaddition of 1 to (*Z*)-**9**.[9] The reaction of the remarkably more reactive (*E*)-**9** and **30** provided only the trans cycloadduct.[9] This result suggested that the reaction of (*E*)-**9** and 1 would efficiently yield *trans*-**20**. That *E* alkenes generally react more rapidly with nitroso alkenes than do the corresponding *Z* alkenes[9] is also demonstrated by the result shown in entry 2. From a 10:90 mixture of (*E*)- and (*Z*)-**7** a 37:63 mixture of *trans*- and *cis*-**18** was obtained, in excellent yield.

Cycloadditions of 1 toward Other Dienophiles. 1,1,1-Trifluoro-2-nitroso-2-propene (1) also cycloadds to other electron-rich olefins, as the examples in Scheme I show. From allyltrimethylsilane, the 6-(trimethylsilyl)-methyl-substituted 1,2-oxazine **31** was obtained in good yield. Cyclopentadiene and furan acted as 2_π-components and afforded the bicyclic 1,2-oxazines **32** and **33**, respectively, in excellent yield and with the expected regioselectivity (see Discussion).[10] However, the yield of the cycloadduct **34**, obtained from the reaction 1 and dihydropyran, was only moderate, even when a large excess of the dienophile was employed. This result was not very surprising because nitroso alkenes generally display rather

(9) Reissig, H.-U.; Hippeli, C.; Arnold, T. *Chem. Ber.* **1990**, *123*, 2403.
(10) Nitrosostyrene and these dienophiles also react to give the corresponding cycloadducts. See refs 4a,c and Faragher, R.; Gilchrist, T. L. *J. Chem. Soc., Chem. Commun.* **1976**, 581.

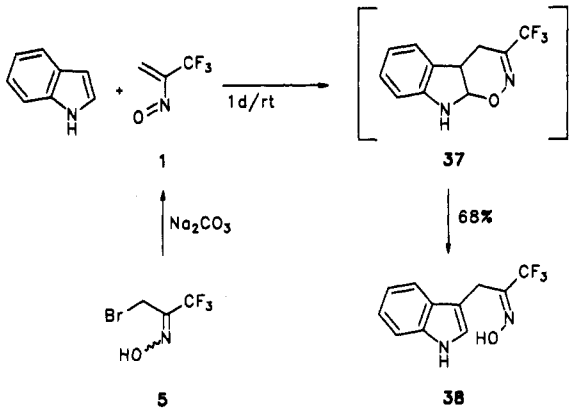
Scheme I



low reactivity toward *Z* enol ethers.[9]

The protected glucal **35** and the cyclic enol ether **36**[11] were totally unreactive toward **1**. This may reflect the inductive effect of the acetoxy groups of **35**, whereas in the case of **36**, steric hindrance may be the major reason for the low reactivity. As expected, ethoxyacetylene and **1** did not provide a 4*H*-1,2-oxazine. In general, acetylenes are considerably less reactive toward nitroso alkenes than are the corresponding olefins.[4,5]

Nitroso alkenes also cycloadd to methoxyallene and derivatives thereof. Such cycloadditions, including those of **1**, and the transformations of the resulting *exo*-methylene-substituted 1,2-oxazines are described elsewhere.[7] Indole also yields adducts upon reaction with nitroso alkenes, as was first reported by Ottenheijm and co-workers.[12] The initial cycloadducts are not stable, but rearrange to aromatic oximes. Such behavior was also observed in the reaction of **1** with indole, which provided the oxime **38** in good yield. In this case it is likely that the cycloadduct **37** is an intermediate, because only one isomer (*Z* or *E*) of **38** was formed. A nucleophilic attack by indole on the olefin **1** (or the bromo compound **5**) would be expected to produce a mixture of *E* and *Z* oximes.[13]



The Mechanism of Cycloaddition. The results demonstrate that **1** is a very powerful heterodiene, remarkably more so than either nitrosostyrene or ethyl α-nitrosoacrylate.[4,5] Even dienophiles which react very sluggishly with, or are completely unreactive toward, the latter compounds are able to trap **1**. The accelerative effect of the CF_3 group is probably mainly electronic in nature. This belief is supported by MNDO calculations, which indicate that the HOMO and LUMO energies of **1** are both considerably more negative than those of nitrosoethylene or nitrosostyrene.[14] For an inverse electron demand Diels–Alder reaction[15] a lower LUMO energy of the (hetero)diene would lead to higher reactivity toward electron-rich olefins. The regioselectivities that are observed, i.e., the donor substituents are located at C-6 of the cycloadducts, are also consistent with the frontier MO model.[16]

Although the results reported here do not prove that the [4 + 2] cycloaddition is a concerted process, they do strongly support such a belief, in accordance with earlier results.[9,17] Even in those cases where an acyclic oxime was isolated, it seemed to have arisen from a cycloadduct and not from an initial electrophilic attack of **1** on the olefin, because the configuration of the product oxime was always uniform (see **22**, **28**, **29**). Also, the formation of a nitrone,[18] which could occur either by rearrangement of the 1,2-oxazine or by ring closure of a zwitterion obtained from s-transoid **1** via attack by the oximate's nitrogen, was never observed in the reactions of **1**.

Synthesis of Other Trifluoromethyl-Substituted Compounds. Nitroso alkenes are known to react with the enolates or enols of carbon acids in a Michael-type fashion.[4e] Thus, oxime **5** and acetyl acetone **39** combined in

(11) Hoff, S.; Brandsma, L.; Arens, J. F. *Recl. Trav. Chim. Pays-Bas* **1969**, *88*, 609.

(12) (a) Plate, R.; Niveaud, R. J. F.; Ottenheijm, H. C. J. *J. Chem. Soc., Perkin Trans. 1* **1987**, 2473. See also: (b) Li, J. P.; Newlander, K. A.; Yellin, T. O. *Synthesis* **1988**, 73.

(13) The ^1H NMR and ^{13}C NMR data for the cycloadducts (Tables IV and V) are similar to those of other 1,2-oxazines.[5] That the heterocycles assume a half-chain conformation in which the 6-trimethylsiloxy group occupies a pseudoaxial position is unequivocally indicated by the values of the coupling constants. Thus, the anomeric effect (Deslongchamps, P. *Stereoelectronic Effects in Organic Chemistry*; Pergamon Press: London, 1983) is also operating in 1,2-oxazines. Alkyl substituents at C-6 prefer the pseudoequatorial position. It is noteworthy that the long-range fluorine pseudoaxial 4-H proton coupling constant is approximately 1 Hz for most compounds. The signal for that proton appears at 0.15–0.4 ppm, i.e., at lower field than the signal for the corresponding pseudoequatorial 4-H proton. The fluorine–carbon coupling constants observed in the ^{13}C NMR spectra are approximately 275 Hz for the CF_3 groups ($\delta \approx 120$ ppm) and 33 Hz for C-3 ($\delta \approx 148$ ppm).

(14) Reissig, H.-U. Unpublished calculations. For the syn form of **1** the HOMO energy was calculated to be −11.91 eV and the LUMO energy −1.50 eV. The corresponding values for *syn*-nitrosoethylene were −10.83 and −0.66 eV, respectively.

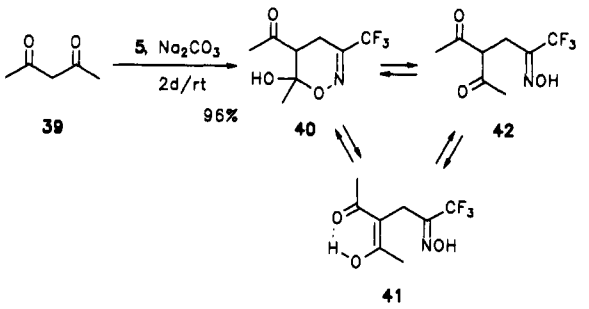
(15) For a review, see: Boger, D. L.; Weinreb, S. M. *Hetero Diels–Alder Methodology in Organic Synthesis*; Academic Press: New York, 1987.

(16) Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*; John Wiley & Sons: London, 1976, p 86 and references cited therein.

(17) The cycloaddition of nitrosostyrene **30** to a crowded allene derivative seems to occur step-by-step, via a zwitterion. See ref 7b.

(18) The formation of nitrones during the cycloaddition of nitrosoalkenes has been reported. See ref 4b.

the presence of sodium carbonate to give an almost quantitative yield of adducts. The products consisted of a ca. 70:30 mixture of the cis and trans isomers of the 1,2-oxazine **40**, diketone **42**, and its enol **41**. After purification the ratio **40:42:41** was close to 50:30:20.

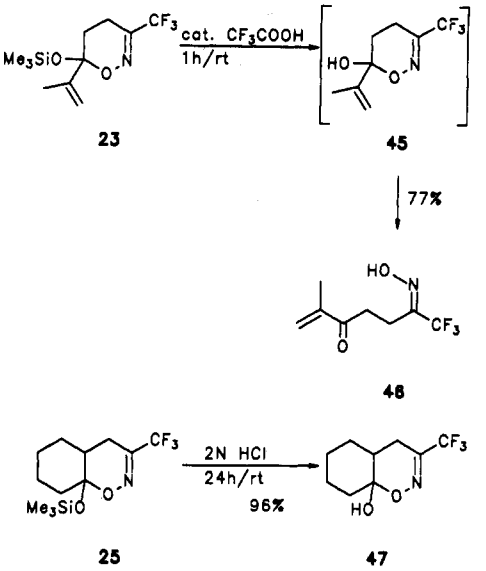


Interestingly, both the oximes **41** and **42** are configurationally homogeneous. That this was so might be used as evidence that all the products resulted from the cycloaddition of **1** to the enol of **39**. However, because it is not known whether the oximes **41** and **42** are in the *E* or the *Z* form, such a conclusion would be only speculative. From a preparative point of view, it should be noted that the adducts **40–42** possibly could be used to prepare heterocycles that bear a side chain which incorporates both a trifluoromethyl group and an oxime function.

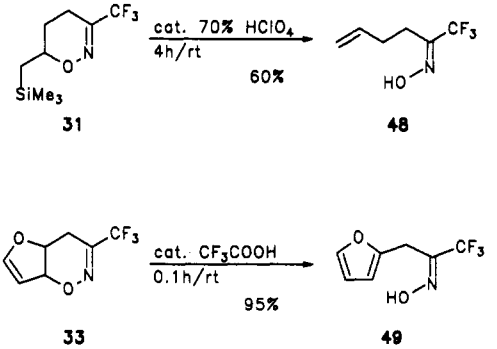
Simple nucleophiles also add to the nitroso alkene **1**. Thus, α-substituted oximes like the diethylamine adduct **43** (*E*:*Z* = 3:1) are accessible in good yield. From the attempted cycloadditions of **1** to insufficiently reactive olefins (e.g., methylenecyclopropane) small amounts of **44**, the product of the addition of water to **1**, were isolated. It should be possible to prepare **44** in higher yield by the deliberate reaction of **1** with water.

1,2-Oxazines can be smoothly desilylated and ring-opened by treatment with acid[19] to provide oximes (e.g., **22** → **29**). Likewise, the reaction of the 1,2-oxazine **23** with trifluoroacetic acid produced oxime **46**, which incorporates an enone moiety, via intermediate **45**. On the other hand, the heterocycle **25** was only desilylated and gave the hydroxy-substituted 1,2-oxazine **47**. Apparently, the position of the equilibrium established between the cyclic and acyclic tautomers of the monooximes of such 1,4-diketones is strongly influenced by the nature of the substituent R^1 located at C-6 of the 1,2-oxazine. If R^1 is unsaturated, conjugation with the carbonyl group would shift the equilibrium in favor of the acyclic tautomer. This behavior has also been observed in structurally similar compounds that do not bear a trifluoromethyl group.[20] Deoximation[19] of **29**, **46**, and **47** should afford the corresponding fluorinated 1,4-diketones, but so far it has not been attempted.

Treatment of the allyl silane adduct **31** with a catalytic amount of strong acid smoothly transformed it into the unsaturated oxime **48**. Interestingly, no deoximation was observed under these conditions whereas structurally similar compounds that bear a carboxylic ester function[20] or a phenyl group[6] rather than a trifluoromethyl group

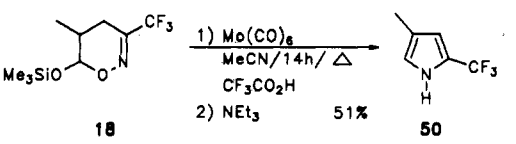


gave the corresponding γ,δ-unsaturated ketones directly. In all cases, including **48**, the carbon–carbon double bond was formed via a Peterson-type acid-induced ring cleavage.



As mentioned above, the reaction of **1** with indole provided the oxime **38**. This should be compared with the smooth formation of the cycloadduct **33** by the reaction of **1** and furan. However, compound **33** was very acid sensitive and upon brief treatment with trifluoroacetic acid, gave, in almost quantitative yield, the aromatic oxime **49**.

The conversion of 1,2-oxazines into pyrroles can be easily achieved with the aid of $Fe_3(CO)_{12}$,[21] or more conveniently, $Mo(CO)_6$.[19] Thus, the 1,2-oxazine **18** was readily transformed into the desired pyrrole derivative **50** by treatment with $Mo(CO)_6$ in the presence of trifluoroacetic acid. Although **50** was obtained in only moderate yield, this result shows that trifluoromethyl-substituted pyrroles are accessible via 1,2-oxazines.



Finally, a few reductive transformations of 1,2-oxazines were accomplished. As expected from the behavior of other 1,2-oxazines,[22,23] cycloadduct **19** was smoothly reduced by sodium borohydride in methanol to the oximated

(19) For examples of the acid-induced desilylation of 6-siloxy-substituted 1,2-oxazines and other transformations, see: Hippeli, C.; Zimmer, R.; Reissig, H.-U. *Liebigs Ann. Chem.* **1990**, 469.

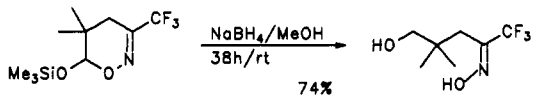
(20) Nakanishi, S.; Higuchi, M.; Flood, T. C. *J. Chem. Soc., Chem. Commun.* **1986**, 30.

(21) Nakanishi, S.; Shirai, Y.; Takahashi, K.; Otsuji, Y. Chemistry Lett. **1981**, 869; Nakanishi, S.; Otsuji, Y.; Itoh, K.; Hayashi, N. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 3395.

(22) Bravo, P.; Gaudiano, G.; Ponti, P. P.; Umani-Ronchi, A. *Tetrahedron* **1970**, *26*, 1315.

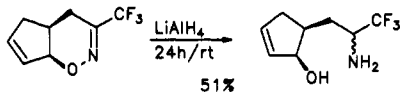
(23) Hippeli, C.; Reissig, H.-U. *Liebigs Ann. Chem.* **1990**, 475.

γ-hydroxy ketone **51** in good yield. A plausible explanation for this transformation is that the desilylation of **19**, induced by sodium methoxide generated in situ, was followed by the reduction of the acyclic tautomer of the intermediate 6-hydroxy-1,2-oxazine.



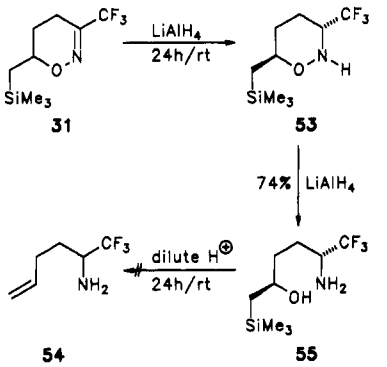
19 **51**

Attempts to reduce 6-trialkylsiloxy-substituted 1,2-oxazines with $LiAlH_4$ were entirely unsuccessful and provided only intractable mixtures.[24] Unfortunately, this also proved true for trifluoromethyl-substituted 1,2-oxazines. However, cycloadducts lacking a trimethylsiloxy group at C-6 were smoothly converted into the expected amino alcohols by treatment with $LiAlH_4$.[25] The reduction of the cyclopentadiene adduct **32** by $LiAlH_4$ afforded the fluorinated amino alcohol **52**, but the reduction proceeded with low diastereoselectivity. Nevertheless the ratio of the diastereomers in the crude material (57:43) could be dramatically improved by one recrystallization. However, with the data at hand the relative configurations of the two diastereomers could not be established unambiguously.

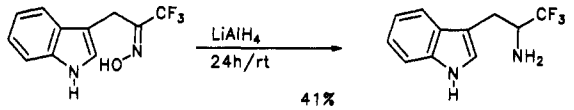


32 **52**

The reduction of the 1,2-oxazine **31**, obtained from the reaction of **1** and allyltrimethylsilane, proceeded with higher stereoselectivity. The amino alcohol **55** was isolated in good yield as a 92:8 mixture of isomers. The β-hydroxy silane **55** did not undergo acid-induced Peterson fragmentation.[6] In a second experiment, "aged" $LiAlH_4$, which had been exposed to air for several weeks, was accidentally employed. The products were the saturated 1,2-oxazine **53** (30%, isomeric ratio: 89:11), which possessed an intact N–O bond, and the γ,δ-unsaturated amine **54** (25%). The ^1H NMR spectrum of **53** indicated that the major diastereomer has trans stereochemistry. Therefore, the configuration of the major isomer of **55** is probably that depicted.



As expected, the indole oxime **38** was converted into the trifluoromethyl-substituted tryptamine derivative **56** by treatment with $LiAlH_4$, albeit in moderate yield. Attempted reduction with Zn/HOAc[12b] or Al/Hg[26] failed completely. In both cases only the starting material (**38**) was recovered. Nevertheless, the indole derivative **56** is now accessible in two simple steps and may prove to be a versatile starting material for the synthesis of fluorinated heterocycles (e.g. β-carbolines[27] via Pictet–Spengler cyclization).

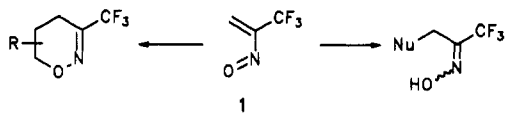


38 **56**

The results demonstrate that most of the transformations possible for "simple" 1,2-oxazines are also possible for their trifluoromethyl-substituted analogues.

Conclusion

A large variety of trifluoromethyl-substituted 1,2-oxazines are accessible via the [4 + 2] cycloaddition of **1** to silyl enol ethers. The method is highly flexible in that it permits the introduction of a variety of substituents at C-5 and C-6 of the products. The use of the very reactive heterodiene **1** also opens a novel route to other fluorinated compounds due to the marked ability of compound **1** to add nucleophiles.



1

The results of this exploratory study also demonstrate that trifluoromethyl-substituted 1,2-oxazines can be efficiently converted into other polyfunctional trifluoromethylated heterocyclic or acyclic compounds. Thus, an important addition has been made to the methods that can be used to prepare such fluorinated species.

Experimental Section

For general information, see ref 5. 1,1,1-Trifluoroacetone was commercially available (Janssen, 97%) and was used as received. Na_2CO_3 was freshly pulverized (electric coffee mill, Braun KSM 1G) before use. Methyl *tert*-butyl ether (MtB) was dried over basic Al_2O_3 and Na wire. Silyl enol ethers **6–16** were synthesized by standard methods.[28]

1-Bromo-3,3,3-trifluoropropan-2-one 2-Oxime (5). A solution of 1-bromo-3,3,3-trifluoropropan-2-one[8] (19.1 g, 100 mmol) and $CHCl_3$ (100 mL, filtered through basic Al_2O_3 before use) was treated with a water solution (20 mL) of $H_2NOH{\cdot}HCl$ (10.4 g, 150 mmol). The mixture was then refluxed for 24 h. The two liquid phases were separated, and the aqueous layer was extracted with $CHCl_3$ (3 × 30 mL). The combined organic phases were dried (Na_2SO_4) and concentrated. The residue was distilled at 80–90 °C (85 Torr) to provide 10.4 g (51%) of **5**, a colorless liquid (*Z*:*E* = 47:53; in the crude product, *Z*:*E* = 63:37): ^1H NMR δ 9.97 (br s, 1 H, NOH), 4.35, 4.19 (2 s, 0.94 H, and 1.06 H, CH_2); ^{13}C NMR δ 146.5, 146.2 (2 q, J_{CF} = 32 and 33 Hz, C-2), 120.3, 120.2 (2 q, J_{CF} = 273 Hz, C-1), 28.8 (t, *E*-CH_2), 12.4 (t, *Z*-CH_2); IR (film) 3580–3150 (OH), 3000–2900 (CH), 1650 (C=N), 1205, 1155 (CF_3) cm^{-1}. Anal. Calcd for $C_3H_3BrF_3NO$: C, 17.50; H, 1.47; N, 6.80.

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(25) See also: ref 4a and Reissig, H.-U.; Hippeli, C. *Chem. Ber.* **1991**, *124*, 115. For the reduction of other heterocycles possessing N–O bonds, see: Jäger, V.; Müller, I.; Schohe, R.; Frey, M.; Ehrler, R.; Häfele, B.; Schröder, D. *Lect. Heterocycl. Chem.* **1985**, *8*, 79. Kozikowski, A. P. *Acc. Chem. Res.* **1984**, *17*, 410. Baraldi, P. G.; Barco, A.; Benetti, S.; Pollini, G. P.; Simoni, D. *Synthesis* **1987**, 857. Curran, D. P. *Adv. Cycloaddition* **1988**, *1*, 129 and references cited therein. Torssell, K. B. G. *Nitrile Oxide, Nitrones, and Nitronates in Organic Synthesis, Novel Strategies in Synthesis*; VCH Verlagsgesellschaft: Weinheim, 1988.

(26) Chrystal, E. J. T.; Gilchrist, T. L.; Stretch, W. *J. Chem. Res., Synop.* **1987**, 180; *J. Chem. Res., Miniprint* **1987**, 1563.

(27) For a review, see: Torreilles, J.; Guérin, M.-C.; Previero, A. *Biochimie* **1985**, *67*, 929. For the results of recent interesting work that employed *N*-hydroxytryptamine derivatives, see: Hermkens, P. H. H.; Maarseveen, J. H.; Berens, H. W.; Smits, J. M. M.; Kruse, C. G.; Scheeren, H. W. *J. Org. Chem.* **1990**, *55*, 2200.

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Table II. Synthesis of 5,6-Dihydro-3-(trifluoromethyl)-6-(trimethylsiloxy)-4*H*-1,2-oxazines 17–27 According to the General Procedure

oxime 5, g (mmol)	silyl enol ether	g (mmol)	time (d)	1,2-oxazine (cis:trans ratio)	yield in grams (% yield)
1.03 (5.00)	6	2.90 (25.0)	6	17	0.880 (73)
1.03 (5.00)	7	3.90 (30.0)	6	18 (63:37)	1.20 (94)
1.03 (5.00)	8	3.60 (25.0)	6	19	0.943 (70)
0.618 (3.00)	9	3.06 (15.0)	6	20 (67:33)	0.288 (29)
0.824 (4.00)	10	3.44 (20.0)	5	21	0.070[a] (6)
0.412 (2.00)	11	1.62 (8.44)	8	22[b]	0.208 (33)
0.618 (3.00)	12	2.34 (15.0)	5	23	0.320 (38)
0.618 (3.00)	13	2.34 (15.0)	3	24	0.723 (86)
3.29 (16.0)	14	13.6 (80.0)	4	25	2.86 (61)
0.824 (4.00)	15	3.68 (20.0)	3	26[c]	0.360 (29)
0.824 (4.00)	16	3.68 (20.0)	8.5	27	0.540 (44)

[a] Product contains small quantities of impurities. [b] 22:28:29 = 31:17:52. [c] 85:15 mixture of diastereomers.

Found: C, 17.29; H, 1.53; N, 6.64.

General Procedure for the Synthesis of 5,6-Dihydro-4*H*-1,2-oxazines. The cycloadditions were performed in dry reaction vessels under a slight pressure of dry N_2. Thus, oxime **5** was dissolved in methyl *tert*-butyl ether (40 mL/mmol of **5**). Then the dienophile (4–20 equiv, as indicated in Table II or VI) and Na_2CO_3 (5–6 equiv) were added. The suspension that resulted was stirred mechanically at rt for the time indicated. The progress of the reaction was monitored by TLC (polygram Sil G/UV_{254} or polygram Alox N/UV_{254}, Macherey-Nagel). After the oxime had been consumed, the mixture was filtered through a sintered glass plug that held a pad of Celite. The filtrate was concentrated in vacuo (30–35 °C (150 Torr)). The excess olefin was recovered by Kugelrohr distillation. The crude cycloadduct was then purified by column chromatography on activity III neutral alumina (pentane/EtOAc (4:1)) and subsequent Kugelrohr distillation or crystallization. The analytical and spectroscopic data are compiled in Tables III–V.

Further Analytical or Spectroscopic Data. 1,2-Oxazine **21**: ^{1}H NMR (60 MHz) δ 2.55–0.80 (m, 4 H, 4-H, 5-H), 1.10 (s, 9 H, *t*-Bu), 0.20 (s, 9 H, $SiMe_3$); MS *m/z* (rel intensity) 297 (4, M^+), 240 (27, $M^+ - t$-Bu), 73 (100, $SiMe_3^+$).

1,2-Oxazine **25**: ^{1}H NMR δ 2.55 (qdd, J_{HF} = 1 Hz, J = 7, 18 Hz, 1 H, 4-H_a), 2.15–2.01, 1.83–1.71, 1.62–1.29, 1.12 (3 m, m_c, 1 H, 2 H, 4 H, 2 H, 4-H_e, CH_2), 0.95 (qd, J = 3, 13 Hz, 1 H, 5-H_e), 0.10 (s, 9 H, $OSiMe_3$).

1,2-Oxazines **26a** and **26b**: ^{1}H NMR δ 2.68 (br dd, J = 7, 18 Hz, 0.15 H, 4-H_a, **b**), 2.61 (qdd, J_{HF} = 1 Hz, J = 7, 18.5 Hz, 0.85 H, 4-H_a, **a**), 2.25, 2.10–1.30 (m_c, m, 1 H, 8 H, CH, CH_2), 1.13, 1.04 (2 d, J = 7 Hz, 0.45 and 2.55 H, 8a-CH_3, **b** and **a**), 0.15, 0.13 (2 s, 1.35 and 7.65 H, $OSiMe_3$, **b** and **a**).

1,2-Oxazine **27**: ^{1}H NMR δ 2.33 (qd, J_{HF} = 1 Hz, J = 18.5 Hz, 1 H, 4-H_a), 2.0–1.7, 1.68–1.2 (2 m, 4 H, 5 H, CH, CH_2), 1.11 (s, 3 H, 4a-CH_3), 0.16 (s, 9 H, $OSiMe_3$).

1,1,1-Trifluoro-2-(hydroxyimino)-5-phenyl-5-(trimethylsiloxy)-4-pentene (28) (*Z*:*E* = 2:1): ^{1}H NMR δ 9.16, 9.06 (2 br s, 1 H, NOH), 7.65–7.30 (m, 5 H, Ph), 5.17 (t, J = 7 Hz, 0.67 H, 4-H), 5.04 (t, J = 7 Hz, 0.33 H, 4-H), 3.45, 3.43 (2 d, J = 7 Hz, 1.34 H, 0.66 H, 3-H), 0.14, 0.13 (2 s, 6 H, 3 H, $OSiMe_3$); ^{13}C NMR δ 149.5 (q, J_{CF} = 34 Hz, C-2), 142.4 (s, C-5), 130.3, 128.1, 128.0, 125.7 (s, 3 d, Ph)*, 120.9 (q, J_{CF} = 274 Hz, CF_3), 101.3, 101.2 (2 d, C-4), 34.0, 30.9 (2 t, C-3)*, 0.6, 0.3 (2 q, $OSiMe_3$)*; the signals marked with an * are exchangeable with those assigned to compound **22** (marked values Table V); IR (film) 3620–3150 (OH),

Table III. Analytical Data for the -5,6-dihydro-3-(trifluoromethyl)-6-(trimethylsiloxy)-4*H*-1,2-oxazines 17–27

name	1,2-oxazine	IR (cm^{-1})	mp/bp (°C) (Torr)	elem. anal.	C	H	N
	17	(film) 3020–2860 (CH), 1625 (C=N), 1195, 1130 (CF_3)	75–80 (2)	$C_8H_{14}F_3NO_2Si$			
				calcd	39.82	5.85	5.81
				found	39.34	5.67	5.82
5-methyl-	18	(film) 3000–2850 (CH), 1620 (C=N), 1190, 1135 (CF_3)	80 (1)	$C_9H_{16}F_3NO_2Si$			
				calcd	42.34	6.32	5.49
				found	42.58	6.50	5.46
5,5-dimethyl-	19	(film) 3000–2840 (CH), 1625 (C=N), 1190, 1125 (CF_3)	90 (5)	$C_{10}H_{18}F_3NO_2Si$			
				calcd	44.60	6.74	5.20
				found	45.02	6.69	4.95
5-trimethylsiloxy-	20	(film) 3000–2850 (CH), 1630 (C=N), 1195, 1170, 1135 (CF_3)	100 (2)	$C_{11}H_{22}F_3NO_3Si_2$			
				calcd	40.10	6.73	4.25
				found	40.38	6.77	4.16
6-*tert*-butyl	21	(film) 3040–2880 (CH), 1625 (C=N), 1190, 1140 (CF_3)	60 (0.5)	$C_{12}H_{22}F_3NO_2Si$			
				a			
6-phenyl-	22	(film) 3130–3020 (=CH), 3020–2840 (CH), 1595 (C=N), 1190, 1125 (CF_3)	80–90 (0.05)	$C_{14}H_{18}F_3NO_2Si$			
				b			
6-isopropenyl-	23	(film) 3110 (=CH), 3040–2780 (CH), 1645 (C=C), 1630 (C=N), 1190, 1160, 1130 (CF_3)	80 (3)	$C_{11}H_{18}F_3NO_2Si$			
				calcd	46.96	6.45	4.98
				found	46.84	6.48	4.75
c	24	($CHCl_3$) 3000–2830 (CH), 1645 (C=N), 1190, 1170, 1145 (CF_3)	35–36	$C_{11}H_{18}F_3NO_2Si$			
				calcd	46.96	6.45	4.98
				found	46.39	6.39	4.79
d	25	(CCl_4) 3000–2840 (CH), 1635 (C=N), 1195, 1145 (CF_3)	41	$C_{12}H_{20}F_3NO_2Si$			
				calcd	48.80	6.83	4.74
				found	48.57	6.68	4.71
e	26	(KBr) 3000–2850 (CH), 1630 (C=N), 1185, 1135 (CF_3)	46	$C_{13}H_{22}F_3NO_2Si$			
				calcd	50.47	7.17	4.53
				found	50.03	7.13	4.37
f	27	(film) 3000–2800 (CH), 1635 (C=N), 1195, 1140 (CF_3)	40 (0.2)	$C_{13}H_{22}F_3NO_2Si$			
				calcd	50.47	7.17	4.53
				found	50.33	7.28	4.14

[a] Product not obtained in analytically pure form. [b] Characterization completed after ring cleavage to **29**. [c] 4,4a,5,6,7,7a-Hexahydro-3-(trifluoromethyl)-7a-(trimethylsiloxy)-cyclopent[*e*]-1,2-oxazine. [d] 4a,5,6,7,8,8a-Hexahydro-3-(trifluoromethyl)-8a-(trimethylsiloxy)-4*H*-1,2-benzoxazine. [e] 4a,5,6,7,8,8a-Hexahydro-8-methyl-3-(trifluoromethyl)-8a-(trimethylsiloxy)-4*H*-1,2-benzoxazine. [f] 4a,5,6,7,8,8a-Hexahydro-4a-methyl-3-(trifluoromethyl)-8a-(trimethylsiloxy)-4*H*-1,2-benzoxazine.

Table IV. ^{1}H NMR Data for 1,2-Oxazines 17–24[a]

compd	δ 6-H (1H)	δ 4-H_a (1 H)	δ 4-H_e (1 H)	δ 5-H (1 H)	other signals (δ)	δ $OSiMe_3$ (9 H)
17	5.51, t (*J* = 2.5 Hz)	2.47[b], ddd (*J* = 7, 12, 18.5 Hz)	2.24, ddd (*J* = 2, 6.5, 18.5 Hz)	2.13–1.67,[c] m		0.18
cis-**18**[d]	5.28, d (*J* = 2 Hz)	2.8–1.7, m	2.8–1.7, m	2.8–1.7, m	1.10 (d, *J* = 7 Hz, 3 H, 5-CH_3)	0.05
trans-**18**[d]	5.10, d (*J* = 3 Hz)	2.8–1.7, m	2.8–1.7, m	2.8–1.7, m	1.05 (d, *J* = 7 Hz, 3 H, 5-CH_3)	0.05
19	4.72, s	2.11, 1.75, AB system J_{AB} = 18 Hz)			0.85, 0.73 (2 s, 6 H, 5-CH_3)	0.00
cis-**20**	5.15, d (*J* = 2 Hz)	2.42, dd[e] (*J* = 10, 18 Hz)	2.27, dd (*J* = 6.5, 18 Hz)	3.91–3.78, m		0.09 0.06
trans-**20**	5.01, d (*J* = 3 Hz)	2.46, dd[e] (*J* = 4.5, 18 Hz)	2.04, dd (*J* = 2, 18 Hz)	3.91–3.78, m		0.08 0.05
22		2.63, qddd ($^4J_{HF}$ ≈ 1 Hz, *J* = 7, 13, 18 Hz)	2.38, ddd (*J* = 1.5, 6, 18 Hz)	2.22, ddd (*J* = 1.5, 7, 13 Hz, 5-H_e), 1.74, dt (*J* = 6, 13 Hz, 5-H_a)	7.65–7.3 (m, 5 H, Ph)	0.25
23		2.47, qddd ($^4J_{HF}$ = 1 Hz, *J* = 7, 13, 18 Hz)	2.30, ddd (*J* = 2, 6, 18 Hz)	2.03, ddd (*J* = 2, 7, 13 Hz, 5-H_e), 1.67, dt (*J* = 6, 13 Hz, 5-H_a)	5.29 (br s, 1 H, =CH), 5.04 (quint, *J* = 1.5 Hz, 1 H, =CH), 1.82 (d, *J* = 1.5 Hz, 3 H, CH_3)	0.11
24		2.44, dd[e] (*J* = 7.5, 19 Hz)	2.22, dd (*J* = 7.5, 19 Hz)	*f*	2.37–2.13, 1.77, 1.21 (m, 2 m_c, 7 H)	0.15

[a] Spectra are of $CDCl_3$ solutions recorded at 300 MHz. [b] Broad signal. [c] 2 H. [d] 60-MHz spectrum. [e] Signal with fine coupling. [f] Signal hidden, see column "other signals".

Table V. ^{13}C NMR Data for 1,2-Oxazines 17, 19, 20, and 22–27

compd	δ CF_3 (q)[a]	δ C-3 (q)[a]	δ C-4 (t)	δ COSi (s)	other signals δ	δ $OSiMe_3$ (q)
17	120.3 (274)	147.8 (34)	23.1	91.1, d	13.3 (t, C-5)	–0.4
19	120.4 (274)	147.6 (34)	28.0	98.1, d	29.6 (s, C-5), 24.5, 23.3 (2 q, 5-CH_3)	–0.4
cis-**20**	120.0 (275)	147.5 (35)	24.2	92.8, d	62.9 (d, C-5)	0.0 –0.2
trans-**20**	120.4 (275)	146.2 (34)	22.8	93.0, d	61.6 (d, C-5)	–0.1 –0.3
22	120.9 (274)	149.5 (34)	22.8	98.1	136.0, 128.4, 128.2, 125.2 (s, 3 d, Ph),[b] 18.7 (t, C-5)[b]	1.0[b]
23	120.7 (275)	147.8 (34)	27.3	98.7	142.0 (s, 6-C), 114.1 (t, =CH_2), 16.0 (t, C-5), 18.5 (q, CH_3)	0.9
24	120.9 (274)	146.5 (34)	26.6	105.2	36.9 (d, C-4a), 36.1, 19.4, 18.4 (3 t, C-5, -6, -7)	1.0
25	120.5 (276)	146.6 (34)	29.8	98.0	36.9, 24.4, 23.0, 22.2 (4 t, C-5, -6, -7, -8), 34.2 (d, C-4a)	1.2
26a	120.6 (274)	146.8 (34)	29.4[c]	101.1	36.4, 29.7 (2 d, C-4a, -8), 28.9,[c] 22.3, 18.7, (3 t, C-5, -6, -7), 13.6 (q, 8a-CH_3)	1.0
26b	120.6 (274)	146.8 (34)	29.3[d]	99.3	41.9, 35.1 (2 d, C-4a, -8), 31.7,[d] 24.6, 23.1 (3 t, C-5, -6, -7), 14.3 (q, 8a-CH_3)	1.4
27	120.1 (275)	147.3 (34)	29.9[e]	101.7	34.0, 32.4,[e] 23.1, 20.3 (4 t, C-5, -6, -7, -8), 32.7 (s, C-4a), 21.5 (q, 4a-CH_3)	1.3

[a] In parentheses: J_{CF} (Hz). [b] Signals exchangeable with those of **28**. [c–e] Marked signals exchangeable.

3130–3020, 3020–2840 (CH), 1645 (C=C), 1595 (C=N), 1190, 1135 (CF_3) cm^{-1}.

1,1,1-Trifluoro-2-(hydroxyimino)-5-phenylpentan-5-one (29). The mixture of **22**, **28**, and **29** (0.138 g, 0.494 mmol) was dissolved in THF (2.5 mL), and the solution was stirred with 2 N aq HCl (1.0 mL) for 30 min at rt. Extractive workup (CH_2Cl_2) and Kugelrohr distillation (90 °C (0.01 Torr)) provided 77 mg (64%) of **29**, a colorless liquid which slowly crystallized (mp 76–79 °C): ^{1}H NMR δ 8.86 (s, 1 H, NOH), 7.99–7.95, 7.62–7.45 (2 m, 2 H, 3 H, Ph), 3.37–3.27, 2.97–2.86 (2 m, 4 H, 3-H, 4-H); ^{13}C NMR δ 198.0 (s, C-5), 149.8 (q, J_{CF} = 32 Hz, C-2), 136.1, 133.6, 128.7, 128.1 (s, 3 d, Ph), 120.9 (q, J_{CF} = 274 Hz, C-1), 33.8 (t, C-4), 18.9 (t, C-3); IR (KBr) 3320 (OH), 3090–2750 (CH), 1680 (C=O), 1595 (C=N), 1195, 1170, 1120 (CF_3) cm^{-1}. Anal. Calcd for $C_{11}H_{10}F_3NO_2$: C, 53.88; H, 4.11; N, 5.71. Found: C, 53.93; H, 4.19; N, 5.69.

5,6-Dihydro-5-[(trimethylsilyl)methyl]-3-(trifluoromethyl)-4*H*-1,2-oxazine (31): bp 85 °C (0.8 Torr), a colorless liquid; ^{1}H NMR δ 3.80 (dtd, *J* = 2, 7, 11 Hz, 1 H, 6-H), 2.40-2.15 (m, 2 H, 4-H), 1.96 (dddd, *J* = 2, 3.5, 6, 14 Hz, 1 H, 5-H_e), 1.58 (dddd, *J* = 8, 9, 11, 14 Hz, 1 H, 5-H_a), 1.02, 0.82, 0.01 (2 dd, s, *J* = 7, 14 Hz, 1 H, 1 H, 9 H, 6-CH_2SiMe_3); ^{13}C NMR δ 146.8 (q, J_{CF} = 34 Hz, C-3), 120.7 (q, J_{CF} = 273 Hz, CF_3), 75.5 (d, C-6), 25.3, 22.4 (2 t, C-5, 6-CH_2), 19.1 (t, C-4), –1.0 (q, $SiMe_3$); IR (CCl_4) 3000–2820 (CH), 1620 (C=N), 1195, 1130 (CF_3) cm^{-1}. Anal. Calcd for $C_9H_{16}F_3NOSi$: C, 45.17; H, 6.74; N, 5.85. Found: C, 45.16; H, 6.72; N, 5.74.

Table VI. Synthesis of the Trifluoromethyl-Substituted 1,2-Oxazines 31–34, 38, and 40 (41/42)

oxime **5**, g (mmol)	dienophile, g (mmol)	time (d)	1,2-oxazine	yield in grams (% yield)
1.63 (7.92)	allyltrimethylsilane, 3.99 (35.0)	5	**31**	1.33 (70)
1.04 (5.00)	cyclopentadiene, 1.65 (25.0)	3	**32**	0.870 (90)
0.824 (4.00)	furan, 5.44 (80.0)	3[a]	**33**	0.719 (93)
0.824 (4.00)	dihydropyran, 6.72 (80.0)	4.5	**34**	0.260 (31)
0.824 (4.00)	indole, 1.87 (16.0)	1	**38**	0.660[b] (68)
0.412 (2.00)	acetylacetone, 2.00 (20.0)	2	**40** (41/42)	0.432[c] (96)

[a] CH_2Cl_2 solvent. [b] Excess indole was removed by digestion with $CHCl_3$. [c] **40**:**41**:**42** = 50:20:30.

4,4a,5,7a-Tetrahydro-3-(trifluoromethyl)cyclopent[*e*]-1,2-oxazine (32): bp 75 °C (4 Torr), a colorless liquid; ^{1}H NMR δ 6.11 (m_c, 1 H, 7-H), 5.84 (m_c, 1 H, 6-H), 4.98 (m_c, 1 H, 7a-H), 2.95–2.11 (m, 5 H, 4-H, 4a-H, 5-H); ^{13}C NMR δ 146.5 (q, J_{CF} = 34 Hz, C-3), 137.3 (d, C-7), 129.4 (d, C-6), 120.6 (q, J_{CF} = 273 Hz, CF_3), 84.5 (d, C-7a), 39.2, 22.3 (2 t, C-4, C-5), 34.4 (d, C-4a); IR (film) 3010–2800 (CH), 1630 (C=C, C=N), 1190, 1130 (CF_3) cm^{-1}. Anal. Calcd for $C_8H_8F_3NO$: C, 50.27; H, 4.22; N, 7.33. Found: C, 50.25; H, 4.14; N, 7.13.

4a,7a-Dihydro-3-(trifluoromethyl)-4*H*-furano[2,3-*e*]-1,2-oxazine (33): bp 80 °C (4 Torr), a colorless liquid (the compound decomposed during chromatography on neutral Al_2O_3); ^1H NMR δ 6.58 (d, J = 1 Hz, 1 H, 6-H), 5.39 (ddd, J = 1, 2.5, 8 Hz, 1 H, 7-H), 5.25–5.13 (m, 2 H, 4a-H, 7a-H), 2.60 (dd, J = 3.5, 16 Hz, 1 H, 4-H_e), 2.56 (dd, J = 5, 16 Hz, 1 H, 4-H_a); ^{13}C NMR δ 158.0 (q, J_{CF} = 36 Hz, C-3), 152.5 (d, C-6), 119.8 (q, J_{CF} = 274 Hz, CF_3), 100.5, 82.4, 78.9 (3 d, C-7, -4a, -7a), 22.1 (t, C-4); IR (CCl_4) 3090–2900 (CH), 1610 (C=N), 1160, 1140 (CF_3) cm^{-1}. Anal. Calcd for $C_7H_6F_3NO_2$: C, 43.52; H, 3.11; N, 7.25. Found: C, 42.97; H, 3.03; N, 7.16.

4,4a,5,6,7,8a-Hexahydro-3-(trifluoromethyl)pyrano[4,5-*e*]-1,2-oxazine (34): bp 75 °C (5 Torr), a colorless liquid; ^1H NMR δ 5.21 (d, J = 2.5 Hz, 1 H, 8a-H), 3.99 (ddd, J = 4.5, 7, 12 Hz, 1 H, 7-H), 3.77–3.68 (m, 1 H, 7-H), 2.51 (dd, J = 7, 19 Hz, 1 H, 4-H_a), 2.29 (dd, J = 4.5, 19 Hz, 1 H, 4-H_e), 2.18 (m_c, 1 H, 4a-H), 1.83–1.44 (m, 4 H, 5-H, 6-H); ^{13}C NMR δ 145.6 (q, J_{CF} = 34 Hz, C-3), 120.6 (q, J_{CF} = 275 Hz, CF_3), 96.6 (d, C-8a), 63.3 (t, C-7), 27.0 (d, C-4a), 24.3, 23.6, 22.8 (3 t, C-4, -5, -6); IR (CCl_4) 3000–2860 (CH), 1630 (C=N), 1205, 1140 (CF_3) cm^{-1}. Anal. Calcd for $C_8H_{10}F_3NO_2$: C, 45.94; H, 4.82; N, 6.70. Found: C, 46.29; H, 4.85; N, 6.41.

1,1,1-Trifluoro-3-(indol-3-yl)propan-2-one 2-oxime (38): mp 164–165 °C ($CHCl_3/CH_3OH$ (10:1)), colorless crystals; ^1H NMR ($CDCl_3$/DMSO-d_6) δ 10.25 (br s, 1 H, NOH), 7.65–6.60 (m, 6 H, NH, CH, C_6H_4), 3.70 (s, 2 H, CH_2); IR (KBr) 3400, 3650–3120 (NH, OH), 3100–3000, 2980–2780 (CH), 1680 (C=C), 1615 (C=N), 1205, 1135 (CF_3) cm^{-1}. Anal. Calcd for $C_{11}H_9F_3N_2O$: C, 54.55; H, 3.75; N, 11.57. Found: C, 54.58; H, 3.73; N, 11.41.

5-Acetyl-4,5-dihydro-6-hydroxy-6-methyl-3-(trifluoromethyl)-4*H*-1,2-oxazine (40) and 4-acetyl-1,1,1-trifluorohexane-2,5-dione 2-oxime (42) and its enol 41: bp 85 °C (0.06 Torr), a colorless liquid which slowly crystallized at rt (mp 53–55 °C). In the crude product, **40**:**41**:**42** = 60:10:30; in the product after distillation, **40**:**41**:**42** = 50:20:30; ratio of the diastereomers of **40**: 70:30.

40: ^1H NMR δ 4.7, 4.4 (2 br s, 0.3 and 0.7 H, OH), 3.22, 2.96–2.41 (t, J = 6 Hz, m, 0.3 H and 2.7 H, 4-H, 5-H), 2.39, 2.32 (2 s, 2.1 H, 0.9 H, 6-CH_3), 2.35 (s, 3 H, CH_3); ^{13}C NMR* δ 206.9 [206.3] (s, C=O), 147.5 (q, J_{CF} = 34 Hz, C-3), 120.2 (q, J_{CF} = 275 Hz, CF_3), 95.6 [96.8] (s, C-6), 48.8 [48.0] (d, C-5), 30.2 [31.0] (q, CH_3CO), 25.1 [22.4] (q, 6-CH_3), 19.2 [20.1] (t, C-4); * signals in brackets are due to the minor diastereomer of **40**; IR (film) 3700–3040 (OH), 3030–2890 (CH), 1705 (C=O), 1640, 1600 [C=C, C=N (weak)], 1185, 1145, 1110 (CF_3) cm^{-1}. Anal. Calcd for $C_8H_{10}F_3NO_3$: C, 42.67; H, 4.48; N, 6.22. Found: C, 42.75; H, 4.45; N, 5.99.

41: ^1H NMR δ 16.85 (s, 1 H, enol OH), 10.0 (br s, 1 H, NOH), 3.62 (s, 2 H, CH_2), 2.14 (s, 6 H, 2 CH_3); ^{13}C NMR δ 192.5 (s, =CO), 96.6 (s, =C), 22.5 (q, CH_3).

42: ^1H NMR δ 10.0 (br s, 1 H, NOH), 4.11 (t, J = 7 Hz, 1 H, CH), 2.98 (d, J = 7 Hz, 2 H, CH_2), 2.25 (s, 6 H, 2 CH_3); ^{13}C NMR δ 202.9 (s, C=O), 147.4 (q, J_{CF} = 32 Hz, C=N), 120.6 (q, J_{CF} = 273 Hz, CF_3), 63.7 (d, CH), 29.2 (q, 2 CH_3), 22.3 (t, CH_2).

3-(Diethylamino)-1,1,1-trifluoropropan-2-one 2-Oxime (43). To a solution of $HNEt_2$ (0.876 g, 12.0 mmol) in dry methyl *tert*-butyl ether (15 mL) was added, over 1.5 h, a solution of **5** (1.24 g, 6.00 mmol) and methyl *tert*-butyl ether (5.0 mL). After 24 h of stirring at rt, the solid that precipitated was removed by filtration. The filtrate was concentrated, and the residue was purified by Kugelrohr distillation (85 °C (0.1 Torr)) to afford 0.759 g (64%) of **43** (*E*:*Z* = 3:1), a pale yellow liquid.

^1H NMR δ 10.8 (br s, 1 H, NOH), 3.60, 3.35 (2 s, 1.5 and 0.5 H, CH_2), 2.45, 2.40 (2 q, J = 7 Hz, 3 and 1 H, NCH_2), 1.15 (t, J = 7 Hz, 6 H, CH_3); IR (film) 3700–2200 (OH, CH), 1650, 1610 (C=N), 1185, 1165, 1130 (CF_3) cm^{-1}. Anal. Calcd for $C_7H_{13}F_3N_2O$: C, 42.42; H, 6.61; N, 14.14. Found: C, 42.46; H, 6.60; N, 13.86.

1,1,1-Trifluoro-3-hydroxypropan-2-one 2-oxime (44): mp 92–93 °C, colorless crystals; ^1H NMR (DMSO-d_6) δ 11.5 (s, 1 H, NOH), 4.52 (t, J = 6 Hz, 1 H, OH), 3.53 (d, J = 6 Hz, 2 H, CH_2); the signals at δ = 11.5 and 4.52 disappeared after treatment of the sample with D_2O, and the doublet at δ = 3.53 became a singlet; IR (CCl_4) 3700–3100 (OH), 1655, 1630 (C=N), 1200, 1135 (CF_3) cm^{-1}; MS m/z (rel intensity) 126 (10, 1 + H^+), 125 (100, 1). Anal. Calcd for $C_3H_4F_3NO_2$: C, 25.19; H, 2.82; N, 9.79. Found: C, 24.63; H, 2.71; N, 9.56.

Table VII. Acid-Induced Ring Cleavage of the 1,2-Oxazines 23, 25, 31, and 33 at Room Temperature

1,2-oxazine, g (mmol)	acid (quantity)	solvent[a]	time[b] (h)	product yield in grams (% yield)
23, 0.200 (0.712)	CF_3COOH (0.1 mL)	CH_2Cl_2	1	**46**, 0.115 (77)
25, 0.070 (0.237)	2 N aq HCl (0.5 mL)	THF	24[c]	**47**, 0.051 (96)
31, 0.450 (1.88)	$HClO_4$ (70%) (8 drops)	CH_2Cl_2	4[d]	**48**, 0.189 (60)
33, 0.097 (0.500)	CF_3COOH (1 drop)	$CHCl_3$	0.1	**49**, 0.092 (95)

[a] 5 mL/1 mmol of adduct. [b] Extractive workup (CH_2Cl_2). [c] THF evaporated before further workup. [d] H_2O (1 mL) was added before further workup.

Ring Cleavage Reactions with 1,2-Oxazines. The results of all the acid-induced ring cleavages of the 1,2-oxazines are collected in Table VII. Extractive workup (CH_2Cl_2) provided the crude products, which were then purified by Kugelrohr distillation or recrystallization.

1,1,1-Trifluoro-2-(hydroxyimino)-6-methyl-6-hepten-5-one (46): mp 75–77 °C, colorless crystals (pentane/methyl *tert*-butyl ether (9:1)); ^1H NMR δ 9.44 (s, 1 H, NOH), 6.00 (br s, 1 H, 7-H), 5.84 (q, J = 1 Hz, 1 H, 7-H), 3.09–2.98, 2.84–2.74 (2 m, 2 H each, 3-H, 4-H), 1.90 (t, J = 1 Hz, 3 H, 6-CH_3); ^{13}C NMR δ 199.8 (s, C=O), 149.9 (q, J_{CF} = 32 Hz, C-2), 143.9 (s, C-6), 125.6 (t, C-7), 120.9 (q, J_{CF} = 274 Hz, C-1), 32.7 (t, C-4), 19.1 (q, 6-CH_3), 17.6 (t, C-3); IR (KBr) 3600–3140 (OH), 3110, 3040–2700 (CH), 1660 (br, C=O, C=C), 1625 (shoulder, C=N), 1185, 1125 (CF_3) cm^{-1}. Anal. Calcd for $C_8H_{10}F_3NO_2$: C, 45.94; H, 4.82; N, 6.70. Found: C, 45.88; H, 4.76; N, 6.73.

4a,5,6,7,8,8a-Hexahydro-8a-hydroxy-3-(trifluoromethyl)-4*H*-1,2-benzoxazine (47): bp 90 °C (0.2 Torr), a colorless liquid which slowly crystallized (mp 64–67 °C); ^1H NMR δ 3.40 (br s, 1 H, OH), 2.75 (dd, J = 7, 18 Hz, 1 H, 4-H_a), 2.35–0.85 (m, 10 H, CH, CH_2); IR (KBr) 3420 (OH), 3040–2780 (CH), 1625 (C=N), 1190, 1135, 1115 (CF_3) cm^{-1}. Anal. Calcd for $C_9H_{12}F_3NO_2$: C, 48.43; H, 5.42; N, 6.28. Found: C, 48.53; H, 5.37; N, 6.16.

1,1,1-Trifluoro-2-(hydroxyimino)-5-hexene (48): bp 70 °C (5 Torr), a colorless liquid; ^1H NMR δ 9.45 (s, 1 H, NOH), 5.89–5.75 (m, 1 H, 5-H), 5.17–5.02 (m, 2 H, 6-H), 2.68–2.31 (m, 4 H, 3-H, 4-H); ^{13}C NMR δ 150.6 (q, J_{CF} = 32 Hz, C-2), 136.4 (d, C-5), 120.9 (q, J_{CF} = 275 Hz, C-1), 116.1 (t, C-6), 29.3, 23.7 (2 t, C-3, -4); IR (film) 3700–3120 (OH), 3040, 3010–2740 (CH), 1640 (C=C, C=N), 1185, 1135 (CF_3) cm^{-1}. Anal. Calcd for $C_6H_8F_3NO$: C, 43.12; H, 4.83; N, 8.38. Found: C, 43.30; H, 4.82; N, 7.91.

1,1,1-Trifluoro-3-(2′-furyl)propan-2-one 2-Oxime (49): bp 50 °C (2 Torr), a colorless liquid; ^1H NMR δ 9.50 (br s, 1 H, NOH), 7.40 (d, J = 4 Hz, 1 H, 5′-H), 6.50–6.10 (m, 2 H, 3′-H, 4′-H), 4.00 (s, 2 H, 3-H); IR (CCl_4) 3580, 3540–3160 (OH), 3130–3030, 3020–2880 (CH), 1610 (C=C, C=N), 1195, 1170, 1140 (CF_3) cm^{-1}. Anal. Calcd for $C_7H_6F_3NO_2$: C, 43.52; H, 3.11; N, 7.25. Found: C, 43.97; H, 2.69; N, 7.14.

4-Methyl-2-(trifluoromethyl)pyrrole (50). A mixture of 1,2-oxazine **18** (0.510 g, 2.00 mmol), $Mo(CO)_6$ (1.27 g, 4.80 mmol), CF_3CO_2H (0.680 g, 6.00 mmol), and dry CH_3CN (50 mL) was refluxed for 14 h. After the mixture was cooled to rt, Et_3N (0.610 g, 6.00 mmol) and silica gel (10.0 g) were added. The suspension that resulted was stirred for 14 h and then was filtered through a "dry" silica gel column (subsequently eluted with CH_2Cl_2). Evaporation of the solvent and Kugelrohr distillation (65 °C (15 Torr)) provided 0.153 g (51%) of **50**: ^1H NMR δ 8.40 (very br s, 1 H, NH), 6.65, 6.40 (2 m_c, 2 H, 3-H, 5-H), 2.15 (s, 3 H, 4-CH_3); IR (film) 3440 (NH), 3055, 3000–2820 (CH), 1190, 1140 (CF_3) cm^{-1}. Anal. Calcd for $C_6H_6F_3N$: C, 48.33; H, 4.06; N, 9.39. Found: C, 47.79; H, 3.95; N, 9.01.

1,1,1-Trifluoro-5-hydroxy-4,4-dimethylpentan-2-one 2-Oxime (51). A mixture of the 1,2-oxazine **19** (0.570 g, 2.10 mmol), $NaBH_4$ (0.760 g, 20.0 mmol), and dry CH_3OH (25 mL) was stirred for 38 h at rt. The mixture was then treated with H_2O (20 mL) and CH_2Cl_2 (20 mL). The liquid phases were separated. The pH of the aqueous phase was adjusted to 4 with 2 N aq HCl. The solution then was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic phases were dried (Na_2SO_4) and concentrated.

Table VIII. Reductions of 1,2-Oxazines 32 and 31 and of Oxime 38 Employing $LiAlH_4$

starting material	g (mmol)	$LiAlH_4$, g (mmol)	product	yield in grams (% yield)
32	0.403 (2.10)	0.229 (6.05)	**52**	0.208[a] (51)
31	0.360 (1.50)	0.285 (7.50)	**55**	0.270[b] (74)
31	0.600 (2.50)	0.285 (7.50)	**53**[c]	0.180 (30)
38	1.23 (5.05)	0.576 (15.2)	**56**	0.470 (41)

[a] 83:17 mixture of two diastereomers (in the crude material: 57:43). [b] 92:8 mixture of two diastereomers. [c] Compound **54** (95 mg) was also isolated.

The residue was distilled (100 °C (0.15 Torr)) to provide 0.310 g (74%) of **51**, a colorless liquid: ^1H NMR δ 9.60 (br s, 1 H, NOH), 3.60 (s, 1 H, OH), 3.45 (s, 2 H, 5-H), 2.60 (s, 2 H, 3-H), 1.00 (s, 6 H, 2 CH_3); IR (CCl_4) 3700–3000 (OH), 3000–2750 (CH), 1190, 1140 (CF_3) cm^{-1}. Anal. Calcd for $C_7H_{12}F_3NO_2$: C, 42.21; H, 6.07; N, 7.03. Found: C, 42.14; H, 5.81; N, 6.72.

Reduction with $LiAlH_4$: General Procedure. A mixture of the 1,2-oxazine (or oxime), Et_2O (20 mL/mmol oxazine or oxime), and $LiAlH_4$ (3 equiv) was stirred at rt. After 24 h the suspension was filtered through a sintered glass plug that held a pad of Celite (subsequently eluted carefully with Et_2O). The filtrate was treated with saturated aqueous NaCl (20 mL/mmol) and the whole was extracted with Et_2O (3 × 20 mL). The extract was dried (Na_2SO_4) and concentrated to provide the crude product. This was purified by recrystallization or Kugelrohr distillation. The results are collected in Table VIII.

(2-Amino-3,3,3-trifluoropropyl)cyclopent-2-en-1-ol (52): mp 52–55 °C, colorless crystals (Et_2O); ^1H NMR δ 6.04–5.89 (m, 2 H, =CH), 4.74–4.65 (m, 1 H, C*H*OH), 3.33, 3.18 (2 m_c, 0.83 H, 0.17 H, C*H*NH_2), 2.60–1.65 (m, 7.2 H, CH, CH_2, OH, NH_2), 1.58 (ddd, J = 4, 10, 14 Hz, 0.8 H, CH_2); ^{13}C NMR* δ 134.7, 134.0 [135.0, 132.8] (2 d, =CH), 127.0 (q, J_{CF} = 282 Hz, CF_3), 76.2 [75.3] (d, C-1), 51.8 (dq, J_{CF} = 29 Hz, *C*HNH_2), 38.3 [42.2] (d, C-2), 37.1, 29.6 [37.2, 29.7] (2 t, 2 CH_2); * signals in brackets are due to the minor diastereomer of **52**; IR (CCl_4) 3640–3100 (NH_2, OH), 2980–2820 (CH), 1630 (C=C), 1170, 1125 (CF_3) cm^{-1}. Anal. Calcd for $C_8H_{12}F_3NO$: C, 49.23; H, 6.20; N, 7.18. Found: C, 48.78; H, 6.37; N, 6.85.

2-Amino-1,1,1-trifluoro-6-(trimethylsilyl)hexan-5-ol (55): bp 100 °C (1 Torr), a colorless liquid; ^1H NMR δ 3.81 (dtd, J = 3, 7, 11 Hz, 0.08 H, 5-H), 3.73 (m_c, 0.92 H, 5-H), 3.07 (m_c, 1 H, 2-H), 2.00–1.20 (m, 7 H, 3-H, 4-H, NH_2, OH), AB-part of ABX-system (δ_A = 0.87, δ_B = 0.76, J_{AX} = 7.5 Hz, J_{BX} = 6 Hz, J_{AB} = 14.5 Hz, 2 H, 6-H), 0.01, 0.00 (2 s, 0.7 H, 8.3 H, $SiMe_3$); ^{13}C NMR* δ 128.5 (q, J_{CF} = 281 Hz, CF_3), 69.7 [69.1] (d, C-5), 54.3 (dq, J_{CF} = 29 Hz, C-2), 38.1, 27.3, 26.8 [36.6, 26.5, 25.8] (3 t, C-3, -4, -6), -0.8 (q, $SiMe_3$); * signals in brackets are due to the minor diastereomer of **55**; IR (film) 3700–3000 (NH_2, OH), 3000–2800 (CH), 1160, 1120 (CF_3) cm^{-1}. Anal. Calcd for $C_9H_{20}F_3NOSi$: C, 44.42; H, 8.28; N, 5.76. Found: C, 44.42; H, 8.20; N, 5.48.

3,4,5,6-Tetrahydro-6-[(trimethylsilyl)methyl]-3-(trifluoromethyl)-2*H*-1,2-oxazine (53). The reduction was performed with $LiAlH_4$ that had been exposed to air for several weeks. The workup procedure was modified somewhat. After filtration of the reaction mixture through Celite, the filtrate was stirred with concd aqueous HCl (10 mL) for 24 h at rt. Water (30 mL) was added, and the two liquid layers were separated. The aqueous layer was neutralized with aq $NaHCO_3$ and was then extracted with Et_2O. Concentration of the extract and Kugelrohr distillation (90 °C (3 Torr)) provided 0.180 g (30%) of **53** (trans:cis = 89:11), a colorless liquid. The aqueous phase was brought to pH 11 by addition of solid NaOH and then was extracted with Et_2O. Evaporation of the Et_2O afforded 95 mg (25%) of impure 1,1,1-trifluoro-2-hex-5-enylamine (**54**): ^1H NMR δ 6.15–5.60, 5.20–4.70 (2 m, 1 H and 2 H, CH=CH_2), 2.80–1.40 (m, 7 H, CH_2, CH, NH_2).

trans-**53**: ^1H NMR δ 5.29 (br s, 1 H, NH), 3.66 (dtd, J = 2, 7, 11 Hz, 1 H, 6-H), 3.51 (m_c, 1 H, 3-H), 2.02–1.54, 1.37 (m*, tdd, J = 4.5, 11, 13 Hz, 3 H, 1 H, 4-H, 5-H), 0.85, 0.71 (2 dd, J = 7, 14.5 Hz, 2 H, $SiCH_2$), 0.00 (s, 9 H, $SiMe_3$); * signals due to both isomers; for *cis*-**53** δ 5.60 (br s, 1 H, NH), 3.75 (m_c, 1 H, 6-H), 3.37–3.21 (m, 1 H, 3-H), 2.02–1.54 (m, 4 H, 4-H, 5-H), 0.86, 0.69 (2 dd, J = 7, 14 Hz, 2 H, $SiCH_2$); ^{13}C NMR* δ 124.1 [125.7] (q, J_{CF} = 280 Hz, CF_3), 78.0 [77.2] (d, C-6), 58.5 [55.5] (dq, J_{CF} = 28 Hz, C-3), 31.9, 23.1** [28.7, 20.8**] (2 t, 6-CH_2, C-4, C-5), -1.1 [-0.8] (q, $SiMe_3$); * signals in brackets are due to the minor diastereomer, ** two carbon atoms; IR (film) 3280 (NH), 3000–2820 (CH), 1190, 1165, 1120 (CF_3) cm^{-1}. Anal. Calcd for $C_9H_{18}F_3NOSi$: C, 44.79; H, 7.52; N, 5.80. Found: C, 45.02; H, 7.53; N, 5.70.

2-Amino-1,1,1-trifluoro-3-(3′-indolyl)propane (56): mp 79.5–81 °C, colorless crystals ($CHCl_3$); ^1H NMR δ 8.10 (very br s, 1 H, NH), 7.70–6.90 (m, 5 H, aromatic CH), 3.95–2.25 (m, 3 H, CH, CH_2), 1.35 (br s, 2 H, NH_2); IR (KBr) 3360, 3300 (NH), 3120–2800 (CH), 1160, 1145, 1130 (CF_3) cm^{-1}. Anal. Calcd for $C_{11}H_{11}F_3N_2$: C, 57.89; H, 4.86; N, 12.28. Found: C, 57.80; H, 4.91; N, 12.25.

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Registry No. **4**, 431-35-6; (*E*)-**5**, 137495-98-8; (*Z*)-**5**, 137495-99-9; **6**, 6213-94-1; (*E*)-**7**, 39162-68-0; (*Z*)-**7**, 50300-18-0; **8**, 6651-34-9; (*Z*)-**9**, 26327-98-0; **10**, 17510-46-2; **11**, 13735-81-4; **12**, 54781-31-6; **13**, 19980-43-9; **14**, 6651-36-1; **15**, 19980-33-7; **16**, 19980-35-9; **17**, 137496-00-5; *cis*-**18**, 137496-01-6; *trans*-**18**, 137496-02-7; **19**, 137496-03-8; *cis*-**20**, 137496-04-9; *trans*-**20**, 137496-05-0; **21**, 137496-06-1; **22**, 137496-07-2; **23**, 137496-08-3; **24**, 137496-09-4; **25**, 137496-10-7; **26a**, 137496-11-8; **26b**, 137567-67-0; **27**, 137496-12-9; (*E*)-**28**, 137515-60-7; (*Z*)-**28**, 137496-13-0; **29**, 137496-14-1; **31**, 137496-15-2; **32**, 137496-16-3; **33**, 137496-17-4; **34**, 137496-18-5; **35**, 2873-29-2; **36**, 22929-49-3; **38**, 137496-19-6; **39**, 123-54-6; **40** (isomer 1), 137496-20-9; **40** (isomer 2), 137496-21-0; **41**, 137496-22-1; **42**, 137496-23-2; (*E*)-**43**, 137496-24-3; (*Z*)-**43**, 137496-25-4; **44**, 137496-26-5; **46**, 137496-27-6; **47**, 137496-28-7; **48**, 137496-29-8; **49**, 137496-30-1; **50**, 137496-31-2; **51**, 137496-32-3; **52** (isomer 1), 137496-33-4; **52** (isomer 2), 137567-68-1; *cis*-**53**, 137496-34-5; *trans*-**53**, 137496-35-6; **54**, 137515-61-8; **55** (isomer 1), 137496-36-7; **55** (isomer 2), 137496-37-8; **56**, 137496-38-9; trimethyl-2-propenylsilane, 762-72-1; cyclopentadiene, 542-92-7; furan, 110-00-9; 3,4-dihydro-2*H*-pyran, 110-87-2.