1,3-DIPOLAR CYCLOADDITIONS WITH 1-ALKOXY-SUBSTITUTED NITRILE YLIDES

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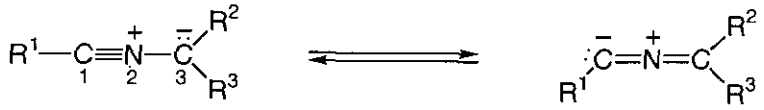
(Dedicated to Prof. Dr. K. Nakanishi on the occasion of his 75th birthday)

Abstract - Thermolysis of 4-alkoxy-1,3-oxazol-5(2*H*)-ones (**2**) (X = O) leads to reactive nitrile ylides (**1**) bearing an alkoxy substituent at the nitrile C-atom. These intermediates can be trapped by C,C-, C,O-, C,N-, and C,S-dipolarophiles, yielding 5-membered heterocycles *via* 1,3-dipolar cycloaddition. In the case of 1,3-thiazole-5(4*H*)-thiones (**11**) as dipolarophiles, two regioisomeric cycloadducts were obtained. The results of the cycloadditions are discussed with respect to the influence of the alkoxy substituent on the structure of the nitrile ylide.

INTRODUCTION

Nitrile ylides are known to be useful intermediates in the synthesis of 5-membered *N*-heterocycles, undergoing 1,3-dipolar cycloadditions with C,C-, C,N-, C,O-, N,N-, N,O-, and C,S-multiple bonds.[2,3] Most of the reported reactions have been performed with 1-aryl- and 1-alkyl-substituted nitrile ylides (**1**) (R^1 = aryl, alkyl). Depending on the substitutents R^2 and R^3, the dipoles (**1**) belong either to the 'propargyl-type' (**A**) (R^2,R^3 = electron withdrawing substituents) or to the 'allenyl-type' (**B**) (R^2,R^3 = electron donating substituents).[4]



A **1** **B**

According to MO-calculations (STO-3G and MINDO/3 level) of Houk and coworkers,[4] the regioselectivity of the $HOMO_{(Dipole)}$-controlled 1,3-dipolar cycloaddition of **1** [5] depends on its structure as the largest coefficient of the HOMO of the linear **1A** is located at the 'ylide-C(3)-

atom', whereas the HOMO of the bent **1B** displays the largest coefficient at the 'nitrilium-C(1)-atom'.

Only little is known about the influence of R^1 on the geometry of the nitrile ylide (**1**). MO-calculations showed [3] that σ-donors as well as π-acceptors at C(1) diminish the energy difference between **1A** and **1B** (cf. also ref. 6) and flatten the nitrile ylide. Optimizations of the geometry of nitrile ylides with heteroatom-substituents at C(1)[7] suggest that the influence of an S-atom (R^1 = SH) is not significantly different from that of a methyl group (*Table 1*). On the other hand, the dipole with an OH group at C(1) is significantly more bent and shows a definite 'allenyl structure'. It is especially worth mentioning that the nitrile ylide with two electron withdrawing CF_3-groups at C(3) seems to prefer the bent 'allenyl structure' if R^1 = OH, but the linear 'propargyl structure' in the case of R^1 = SH .

Table 1. Calculated bond angles and bond lengths for $R^1CNC(CH_3)_2$ and $R^1CNC(CF_3)_2$ [7]

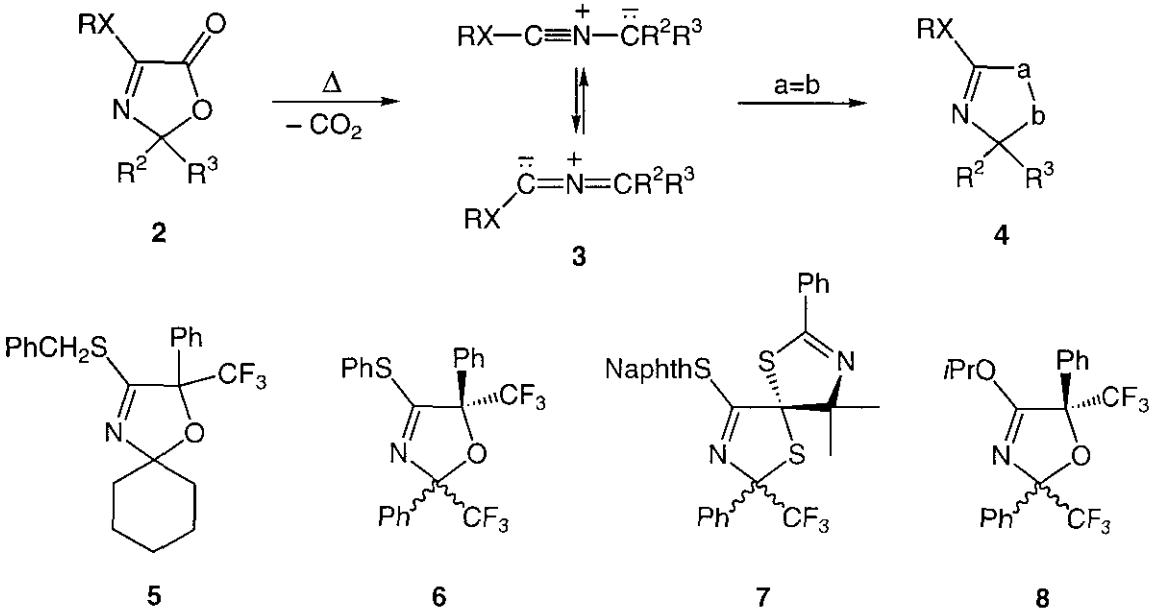
R^1	R^1-C-N [°]	C-N-C [°]	C(1)-N [Å]	N-C(3) [Å]	R^1-C-N [°]	C-N-C [°]	C(1)-N [Å]	N-C(3) [Å]
Me	145.8	166.4	1.209	1.296	178.3	179.0	1.170	1.316
OH	117.1	163.8	1.288	1.270	121.4	159.9	1.284	1.262
SH	141.5	168.0	1.218	1.289	175.1	178.4	1.182	1.301

Some years ago, we succeeded in generating nitrile ylides (**3**) bearing benzylthio-, arylthio-, and alkoxy-substituents at C(1) (R^1 = $PhCH_2S$, ArS, and RO, respectively) by thermolysis of the corresponding 4-substituted 1,3-oxazol-5(2*H*)-ones (**2**) (*Scheme 1*).[10,11] Trapping of the reactive intermediates with dipolarophiles yielded cycloadducts of the type (**4**). Several 1,3-dipolar cycloadditions with **3** (RX = $PhCH_2S$, PhS, and β-NaphthS) and symmetrical dipolarophiles were carried out .[10]

The regioselectivity of the additions was studied using the unsymmetrical dipolarophiles trifluoroacetophenone and 4,4-dimethyl-2-phenyl-1,3-thiazole-5(4*H*)-thione. In almost all cases, the cycloaddition occurred regioselectively yielding the products of the type (**5**-**7**).[10,12] The same type of cycloadduct (**8**) was formed in the case of the isopropoxy-substituted dipole and trifluoroacetone.[11] It is remarkable that the regioselectivity is always the same as with 1-phenyl-substituted nitrile ylides of the 'allenyl-type' (**B**) [1] albeit in the cases of R^2 = Ph, R^3 = CF_3 these two substituents are expected to stabilize the 'propargyl-type' structure (**A**).

In the present paper, we report on further cycloadditions of 1-alkoxy-substituted nitrile ylides.

Scheme 1

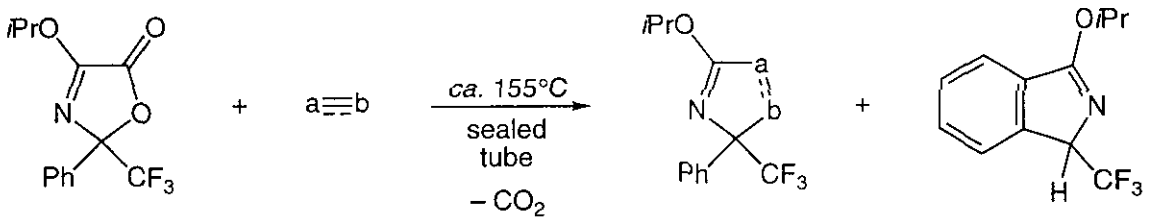


2 **3** **4** **5** **6** **7** **8**

RESULTS AND DISCUSSION

A *ca.* 1:2-mixture of 4-isopropoxy-2-phenyl-2-trifluoromethyl-1,3-oxazol-5(2*H*)-one (**2a**) and dimethyl acetylenedicarboxylate, diethyl azodicarboxylate, dimethyl fumarate, and ethyl cyanoformate, respectively, in a degassed and sealed tube was heated to *ca.* 155°C for 1-2.5 h. After chromatographical workup, a cycloadduct (**9**) and the 1*H*-isoindole (**10**) [11] were isolated (*Scheme 2*, *Table 2*). The structure of the adducts follows from the spectral data. In the case of **9c**, the two ester groups are in *trans*-relation, and the relative configuration of the phenyl and trifluoromethyl group at C(2) is proposed as shown in **9c** (NOE). Also with ethyl cyanoformate as the dipolarophile, only one cycloadduct was formed; according to the absorption of C(2) in the ^{13}C-NMR spectrum (δ = 100.1 ppm), it is the 2*H*-imidazole (**9d**).[13]

Scheme 2

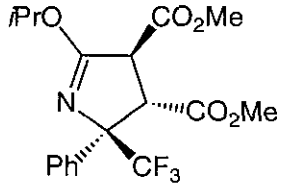


2a **9** **10**

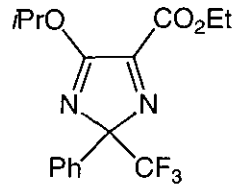
Table 2. Thermolysis of **2a** in the presence of dipolarophiles a = b

Dipolarophile a = b		**2a** [%]	Cycloadduct [%]	**10** [%]
MeO_2C-C≡C-CO_2Me	neat	1	**9a** 48.4	13.4
EtO_2C-N=N-CO_2Et	toluene	26	**9b** 18.5	22.4
MeO_2C-CH=CH-CO_2-Me	toluene	11	**9c** 23.0	58.6
N≡C-CO_2Et	neat	-	**9d** 36.5	52.0
O=C(Ph)CF_3 [11]	neat	50	**8** 21.3 + 19.3	6.0

It is worth mentioning that the cycloaddition occurred selectively with the C≡N group and no adduct with the ester-C=O group was observed.[14]



9c

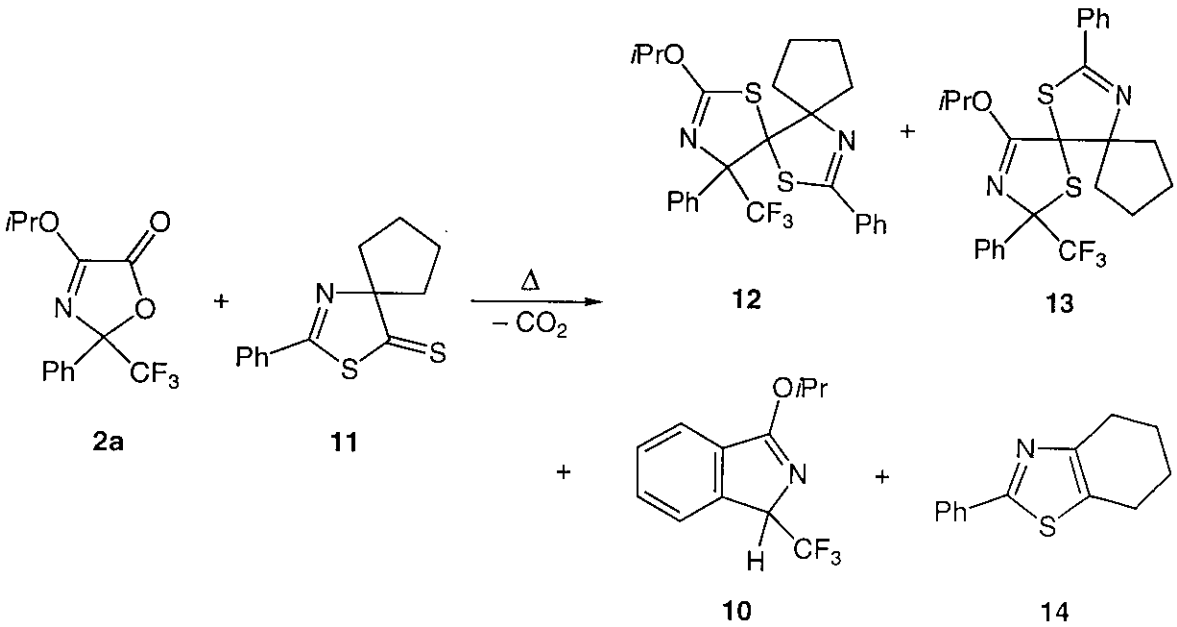


9d

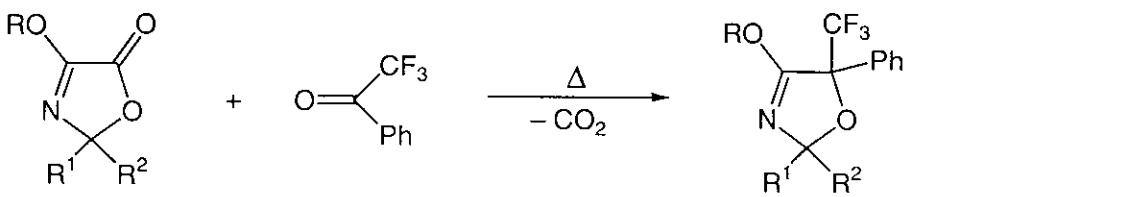
A non-regiospecific cycloaddition occurred when a mixture of **2a** and 1,3-thiazole-5(4*H*)-thione (**11**) was heated to 150-155°C (*Scheme 3*). After 4 h, when 50% of **11** were consumed, chromatographic workup yielded **12** and **13** (9 and 4%, respectively), in addition to **11** (51%), **10** (22%), and **14** (7.4%).[16]

The formation of compounds (**12**) and (**13**) can be rationalized by the 1,3-dipolar cycloaddition of the intermediate 1-isopropoxy-substituted nitrile ylide with the C=S group of **11**.[10, 11,17,18] The structures of **12** and **13** follow from the spectral data, especially ^{13}C-NMR: the chemical shifts of the spiro-C(5)-atoms (102.4 and 85.9, respectively) are characteristic for two regioisomeric adducts. 1,5-Dipolar electrocyclization of the nitrile ylide leads to **10**,[15] and **14** is a product of the thermal decomposition of **11**.[19]

Scheme 3

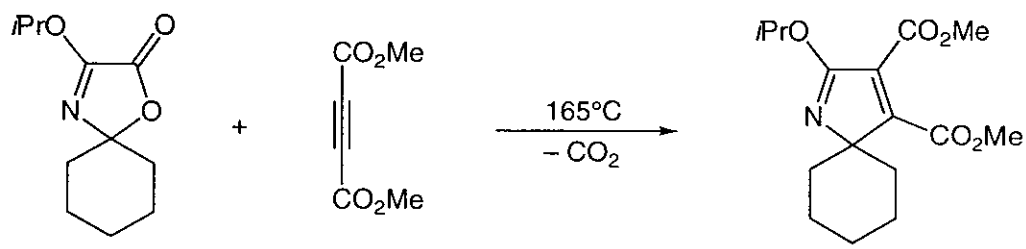


Scheme 4



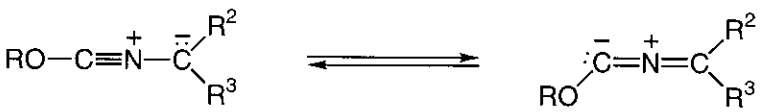
2b R = *i*Pr, R^1–R^2 = -$(CH_2)_5$-
c R = Et, R^1–R^2 = -$(CH_2)_5$-
d R = *i*Pr, R^1 = Ph, R^2 = H

15a R = *i*Pr, R^1–R^2 = -$(CH_2)_5$-
b R = Et, R^1–R^2 = -$(CH_2)_5$-
c R = *i*Pr, R^1 = Ph, R^2 = H



Trifluoroacetone was shown to be a very efficient dipolarophile in thermal reactions with the 4-alkoxy-1,3-oxazol-5(2*H*)-ones (**2b-d**) yielding **15a-c** (*Scheme 4*).[11] After 2.5 h at 155°C, still 47% of **2b** were recovered in addition to **15a** (47%). In the case of **2c**, 8.5% of the starting material and 45% of **15b** were isolated. With the unsymmetrically substituted **2d**, a mixture of two diastereoisomers of type (**15c**) was formed (38 and 48%, ^{1}H-NMR).
Heating of a mixture of **2b** and dimethyl acetylenedicarboxylate in a sealed tube to 165°C for 30 min yielded, after chromatography, 18% of the spirocyclic 2*H*-pyrroledicarboxylate (**16**) (*Scheme 4*).

In conclusion, the thermolysis of 4-alkoxy-1,3-oxazol-5(2*H*)-ones of type (**2**) proved to be a convenient access to 1-alkoxy-substituted nitrile ylides (**3a-d**), which can be trapped by various dipolarophiles. With the strongly polarized trifluoroacetophenone, the formation of only one regioisomer in the 1,3-dipolar cycloaddition was observed, suggesting an 'allenyl-type' nitrile ylide. These experimental results are in support of the calculations suggesting a bent 'allenyl structure' for 1-alkoxy-substituted nitrile ylides irrespective of the substituents at C(3). With the less polar (C=S) group of 1,3-thiazole-5(4*H*)-thione (**11**) both regioisomers were formed.



3a R = *i*Pr, R^2 = Ph, R^3 = CF_3
b R = *i*Pr, R^2–R^3 = -$(CH_2)_5$-
c R = Et, R^2–R^3 = -$(CH_2)_5$-
d R = *i*Pr, R^2 = Ph, R^3 = H

EXPERIMENTAL

Melting points were determined on a *Mettler FP-5* apparatus and are uncorrected. IR spectra were recorded on a *Perkin-Elmer 781* instrument (CCl_4, cm^{-1}), ^{1}H-NMR and ^{13}C-NMR spectra on a *Varian-XL-200* ($CDCl_3$, 200 and 50.4 MHz, respectively, δ in ppm, TMS as internal standard, *J* in Hz), and MS spectra on a *Varian-MAT-1225* or *Finnigan MAT-90* (70 eV; CI with isobutane). Column chromatography (CC) or PTLC on silica gel (SiO_2).

General procedure. A degassed mixture of the 4-alkoxy-1,3-oxazol-5(2*H*)-one (**2**) and an excess (2-10 fold) of the dipolarophile was sealed in a *Pyrex* tube under vacuum and heated in an oven to 150-160°C for 1-4 h. After evaporation of excess dipolarophile, the crude mixture was separated by CC or PTLC.

*Reactions with 4-isopropoxy-2-phenyl-2-trifluoromethyl-1,3-oxazol-5(2*H*)-one* (**2a**).[11]
With dimethyl acetylenedicarboxylate: **2a** (88 mg, 0.31 mmol), dimethyl acetylenedicarboxylate (280 mg, 1.97 mmol), sealed tube, 1 h, 155°C; CC (ether/hexane 1:20 to 1:10): 57 mg (48.4%) of *dimethyl 5-isopropoxy-2-phenyl-2-trifluoromethyl-2*H*-pyrrole-3,4-dicarboxylate* (**9a**), 10 mg (13.4%) of *3-isopropoxy-1-trifluoromethyl-1*H*-indole* (**10**),[11] and 1 mg (1.1%) of **2a**. **9a**: Colorless solid; mp 110-110.5°C. IR: 2960*s*, 2930*s*, 2870*m*, 2860*m*, 1746*m* (broad), 1650*w*, 1590*m*, 1583*m*, 1468*m*, 1405*m*, 1435*w*, 1400*w*, 1308*m*, 1270*m*, 1250*m*, 1185*m*, 1170*m*, 1110*w*, 1080*w*, 1070*w*, 1015*w*, 948*w*, 910*w*, 726*w*, 695*w*. ^{1}H-NMR: 7.6-7.5 (*m*, 2 arom. H); 7.4-7.3 (*m*, 3 arom. H); 5.32 (*sept.*, *J* = 6.2, Me_2CHO); 3.87, 3.81 (2*s*, 2 MeO); 1.44 (*d*, *J* = 6.2, Me_2CHO). ^{13}C-NMR: 168.4, 161.8 (2*s*, 2 CO_2Me); 161.1 (*s*, C(5)); 155.4 (*s*, C(3)); 134.8 (*s*, C(4)); 131.2 (*s*, 1 arom. C); 129.1, 128.4, 127.6 (3*d*, 5 arom. CH); 123.8 (*q*, ^1J(C,F) = 284, CF_3); 81.8 (*q*, ^2J(C,F) = 28, C(2)); 74.1 (*d*, Me_2CHO); 52.8, 52.7 (2*q*, 2 CO_2Me); 21.6, 21.4 (2*q*, Me_2CHO). EI-MS: 385 (2, $M^{+\cdot}$), 354 (3, [*M*-OCH_3]+), 344 (27), 343 (14), 312 (44), 311 (100, [*M*-($(CH_3)_2CH$ + CH_3O)]+), 274 (23), 268 (11), 253 (11), 91 (14), 77 (16).

With diethyl azodicarboxylate: **2a** (128 mg, 0.44 mmol), diethyl azodicarboxylate (153 mg, 0.88 mmol), toluene (1.5 ml), sealed tube, 1 h, 158°C; CC (ether/hexane 1:20 to 1:3): 34 mg (18.5%) of *diethyl 5-isopropoxy-3-phenyl-3-trifluoromethyl-3*H*-1,2,4-triazole-1,2-dicarboxylate* (**9b**), 24 mg (22.4%) of **10**, and 33 mg (26.2%) of **2a**. **9b**: Colorless oil. IR: 3060*w*, 3040*w*, 2980*m*, 2940*w*, 2910*w*, 2870*w*, 1765*s*, 1750*s*, 1650*s*, 1497*w*, 1480*w*, 1468*m*, 1452*w*, 1445*w*, 1385*m*, 1370*s*, 1310*s*, 1278*s*, 1188*s*, 1175*s*, 1142*w*, 1110*s*, 1070*m*, 1040*m*, 1015*m*, 980*w*, 955*m*, 925*m*, 865*w*, 835*w*, 730*w*, 695*m*. ^{1}H-NMR: 7.55-7.45 (*m*, 2 arom. H); 7.4-7.35 (*m*, 3 arom. H); 5.16 (*sept*, *J* = 6.2, Me_2CHO); 4.4-4.25 (*ABX*$_3$, CH_3CH_2O); 3.95-3.8, 3.7-3.55 (*ABX*$_3$, CH_3CH_2O); 1.45, 1.43 (2*d*, *J* = 6.2, Me_2CHO); 1.32, 0.79 (2*t*, *J* = 7.0, 2 CH_3CH_2O). ^{13}C-NMR: 157.0 (*s*, C(5)); 154.1, 150.6 (2*s*, 2 CO_2Et); 134.5 (*s*, 1 arom. C); 129.3, 128.2, 127.0 (3*d*, 5 arom. CH); 123.2 (*q*, ^1J(C,F) = 287, CF_3); 89.7 (*q*, ^2J(C,F) = 30, C(3)); 77.3 (*d*, Me_2CHO); 63.9, 62.7 (2*t*, 2 CH_3CH_2O); 21.5, 21.3 (2*q*, Me_2CHO); 14.0, 13.4 (2*q*, 2 CH_3CH_2O). EI-MS: 417 (8, $M^{+\cdot}$), 373 (17), 349 (11), 348 (23, [*M*-CF_3]+), 304 (20), 277 (16), 276 (84), 234 (47), 230 (18), 218 (22), 201 (11), 200 (100), 191 (12), 190 (84), 174 (12), 167 (16), 163 (11), 162 (99), 150 (10), 127 (10), 105 (15), 104 (13), 103 (11), 77 (23).

With dimethyl fumarate: **2a** (116 mg, 0.4 mmol), dimethyl fumarate (115 mg, 0.8 mmol), toluene (0.5 ml), sealed tube, 2.5 h, 155°C; CC (ether/hexane 1:30 to 1:5): 35 mg (23%) of *dimethyl* trans-*3,4-dihydro-5-isopropoxy-2-phenyl-2-trifluoromethyl-2*H*-pyrrole-3,4-dicarboxylate* (**9c**), 57 mg (58.6%) of **10**, and 13 mg (11.3%) of **2a**. **9c**: Colorless oil. IR: 2980*m*, 2960*m*, 2938*m*, 2880*w*, 1745*s* (broad), 1655*s*, 1495*w*, 1465*w*, 1450*w*, 1436*m*, 1375*m*, 1328*m*, 1265*m*, 1250*m*, 1225*w*, 1190*s*, 1165*s*, 1110*m*, 1070*w*, 1035*w*, 1000*w*, 970*w*, 957*w*, 915*w*, 727*w*, 698*w*. 1H-NMR: 7.45-7.3 (*m*, 5 arom. H); 5.25 (*sept*, *J* = 6.1, Me_2CHO); 4.29, 4.19 (2*d*, *J* = 7.0, H-C(4), H-C(3)); 3.78, 3.32 (2*s*, 2 MeO); 1.45, 1.37 (2*d*, *J* = 6.1, Me_2CHO).

No NOE between H-C(3), H-C(4), and PhC(2). ^{13}C-NMR: 169.8, 168.8, 168.1 (3*s*, 2 *C*O_2Me, C(5)); 134.6 (*s*, 1 arom. C); 128.7, 128.0, 126.84, 126.80 (4*d*, 5 arom. CH); 125.7 (*q*, ^1J(C,F) = 284, CF_3); 79.6 (*q*, ^2J(C,F) = 27, C(2)); 74.1 (*d*, Me_2*C*HO); 53.7, 52.8, 52.5, 52.1 (2*q*, 2*d*, 2 CO_2*Me*, C(4), C(3)); 21.8, 21.3 (2*q*, *Me*$_2$CHO). EI-MS: 387 (3, *M*$^{+\cdot}$), 346 (20), 318 (15, [*M*-CF_3]+), 276 (11), 254 (10), 244 (37), 216 (16), 200 (15), 174 (12), 167 (25), 150 (12), 149 (61), 145 (90), 114 (12), 113 (100), 103 (10), 87 (10), 85 (14), 83 (10), 82 (17), 77 (17).

With ethyl cyanoformate: **2a** (115 mg, 0.4 mmol), ethyl cyanoformiate (500 mg, 5.0 mmol), sealed tube, 1.5 h, 155°C; CC (ether/hexane 1:20): 50 mg (36.5%) of *ethyl 5-isopropoxy-2-phenyl-2-trifluoromethyl-2*H*-imidazole-4-carboxylate* (**9d**) and 51 mg (52%) of **10**. **9d**: Colorless oil. IR: 3070*w*, 2980*w*, 2940*w*, 1745*s*, 1632*m*, 1588*m*, 1468*w*, 1450*w*, 1403*w*, 1385*m*, 1375*w*, 1330*m*, 1320*w*, 1305*m*, 1263*s*, 1185*s*, 1123*m*, 1115*m*, 1100*s*, 1075*w*, 1040*w*, 1030*w*, 1015*w*, 958*m*, 920*m*, 730*m*, 697*m*. ^{1}H-NMR: 7.9-7.85 (*m*, 2 arom. H); 7.45-7.25 (*m*, 3 arom. H); 5.26 (*sept*, *J* = 6.2, Me_2C*H*O); 4.44 (*q*, *J* = 7.1, CH_3CH_2O); 1.47, 1.43 (2*d*, *J* = 6.2, *Me*$_2$CHO); 1.41 (*t*, *J* = 7.1, CH_3CH_2O). ^{13}C-NMR: 165.7 (*s*, C(5)); 159.9, 157.9 (2*s*, C(5), C(4)); 132.4 (*s*, 1 arom. C); 129.64, 129.57, 128.2 (3*d*, 5 arom. CH); 122.6 (*q*, ^1J(C,F) = 285, CF_3); 100.1 (*q*, ^2J(C,F) = 29, C(2)); 75.8 (*d*, Me_2*C*HO); 62.8 (*t*, CH_3CH_2O); 21.3 (*q*, *Me*$_2$CHO); 13.9 (*q*, CH_2CH_2O). EI-MS: 342 (6, *M*$^{+\cdot}$), 301 (14), 284 (10), 273 (16, [*M*-CF_3]+), 231 (15), 227 (15), 202 (26), 201 (13), 200 (50), 185 (10), 132 (20), 105 (11), 104 (41), 103 (11), 87 (13), 77 (23), 44 (100).

With 2-phenyl-3-thia-1-azaspiro[4.4]non-1-ene-4-thione (**11**): **2a** (292 mg, 1.02 mmol), **11** (140 mg, 0.57 mmol), round-bottom flask, N_2-atmosphere, 4 h, 150-155°C; CC (ether/hexane 1:50): 44 mg (9%) of *2-isopropoxy-4,12-diphenyl-4-trifluoromethyl-1,13-dithia-3,11-diazaspiro[4.0.4.3]tridec-2,11-diene* (**12**), 21 mg (4%) of *4-isopropoxy-2,12-diphenyl-2-trifluoromethyl-1,13-dithia-3,11-diazaspiro[4.0.4.3]tridec-3,11-diene* (**13**), 54 mg (22%) of **10**, 24 mg (7.4%) of *4,5,6,7-tetrahydro-2-phenyl-1,3-benzothiazole* (**14**), 53 mg (18%) of **2a**, and 72 mg (51%) of **11**. **12**: Colorless crystals; mp 155-161°C. IR: 3060*w*, 3025*w*, 2975*m*, 2950*s*, 2930*m*, 2900*s*, 2870*s*, 1615*s*, 1490*w*, 1465*w*, 1450*m*, 1380*w*, 1370*w*, 1320*w*, 1270*s*, 1255*m*, 1245*s*, 1200*m*, 1175*s*, 1160*s*, 1100*s*, 1065*w*, 955*m*, 940*s*, 915*s*, 710*m*, 685*m*, 660*s*. ^{1}H-NMR: 7.85-7.75 (*m*, 2 arom. H); 7.65-7.6 (*m*, 3 arom. H); 7.45-7.25 (*m*, 5 arom. H); 5.33 (*sept.*, *J* = 6.2, Me_2C*H*O); 2.6-2.45 (*m*, 1 H); 2.4-2.3 (*m*, 2 H); 2.2-2.1 (*m*, 1 H); 2.1-1.8 (*m*, 3 H); 1.65-1.5 (*m*, 1 H); 1.47, 1.38 (2*d*, *J* = 6.2, *Me*$_2$CHO). ^{13}C-NMR: 170.9, 164.2 (2*s*, C(4), C(12)); 137.0, 133.3 (2*s*, 2 arom. C); 131.3, 129.2, 128.3, 128.0, 127.9 (5*d*, 10 arom. CH); 125.6 (*q*, ^1J(C,F) = 289, CF_3); 102.4 (*s*, C(5)); 90.3 (*s*, C(6)); 84.6 (*q*, ^2J(C,F) = 29, C(2)); 75.6 (*d*, Me_2*C*HO); 36.7, 35.0, 24.9, 24.5 (4*t*, 4 CH_2); 22.0, 21.5 (2*q*, *Me*$_2$CHO). CI-MS: 493 (13), 492 (27), 491 (100, [*M*+1]$^+$), 337 (13).

13: Colorless crystals; mp 98-101°C. IR: 3065*w*, 3030*w*, 2980*m*, 2960*m*, 2935*w*, 2865*w*, 1645*s*, 1635*m*, 1620*w*, 1600*w*, 1570*w*, 1490*w*, 1465*w*, 1450*m*, 1380*w*, 1370*w*, 1355*w*,

1310*m*, 1250*m*, 1175*s*, 1120*m*, 1105*m*, 950*m*, 940*m*, 920*w*, 900*w*, 890*m*, 715*m*, 690*m*. ^{1}H-NMR: 7.85-7.7 (*m*, 2 arom. H); 7.65-7.55 (*m*, 3 arom. H); 7.5-7.35 (*m*, 5 arom. H); 5.14 (*sept*, *J* = 6.2, Me_2CHO); 2.25-1.38 (*m*, 8 H); 1.33, 1.25 (2*d*, *J* = 6.2, Me_2CHO). ^{13}C-NMR: 170.6, 163.2 (2*s*, C(2), C(12)); 138.3, 133.5 (2*s*, 2 arom. C); 131.1, 128.9, 128.5, 128.2, 127.9, 127.2 (6*d*, 10 arom. CH); 124.9 (*q*, ^1J(C,F) = 283, CF_3); 90.8, 85.9 (2*s*, C(5), C(6)); 83.7 (*q*, ^2J(C,F) = 31, C(4)); 75.3 (*d*, Me_2CHO); 40.5, 32.8, 25.4, 25.0 (4*t*, 4 CH_2); 21.5, 21.0 (2*q*, Me_2CHO). CI-MS: 493 (10), 492 (21), 491 (78, $[M+1]^+$), 388 (35), 279 (20), 278 (100).

14: Colorless oil. UV (hexane): λ_{max} 216 (8200), 254 (2140), 310 (15350). IR: 3080*w*, 3030*w*, 2955*s*, 2920*m*, 2870*m*, 1600*m*, 1590*m*, 1560*m*, 1510*w*, 1470*m*, 1450*m*, 1385*m*, 1290*w*, 1265*s*, 1230*m*, 1190*w*, 1080*w*, 1020*m*, 990*s*, 960*w*, 920*w*, 840*s*, 730*s*, 695*s*. ^{1}H-NMR: 7.95-7.8 (*m*, 2 arom. H); 7.45-7.3 (*m*, 3 arom. H); 2.85-1.75 (*m*, 3 H); 2.05-1.85 (*m*, 5 H). ^{13}C-NMR: 164.5 (*s*, C(2)); 151.5 (*s*, C(3a)); 134.1 (*s*, 1 arom. C); 129.2 (*s*, C(7a)); 129.4, 128.7, 126.2 (3*d*, 5 arom. CH); 26.9, 23.7, 23.4, 23.0 (4*t*, 4 CH_2). EI-MS: 216 (18), 215 (100, $M^{+\cdot}$), 187 (42), 182 (24), 121 (11), 112 (19), 104 (15), 84 (47), 79 (78), 77 (27).

*Reactions of 4-alkoxy-1,3-oxazol-5(2*H*)-ones and trifluoroacetophenone.*

With 2-isopropoxy-1-aza-4-oxaspiro[4.5]dec-1-en-3-one (**2b**): **2b** (76 mg, 0.36 mmol), trifluoroacetophenone (206 mg, 1.18 mmol), round-bottom flask, N_2-atmosphere, 2.5 h, 155°C; CC (ether/petrolether 1:5): 58 mg (47%) of *2-isopropoxy-3-phenyl-3-trifluoromethyl-4-oxa-1-azaspiro[4.5]dec-1-ene* (**15a**) and 36 mg (47%) of **2b**. **15a**: Colorless oil. IR: 3060*w*, 2983*w*, 2939*m*, 1672*s*, 1497*w*, 1448*w*, 1379*w*, 1358*w*, 1273*m*, 1223*w*, 1176*s*, 1144*w*, 1072*m*, 987*w*, 976*w*, 831*w*, 725*w*, 696*w*. ^{1}H-NMR: 7.8-7.75 (*m*, 2 arom. H); 7.4-7.3 (*m*, 3 arom. H); 5.03 (*sept*, *J* = 6.2, Me_2CHO); 1.8-1.45 (*m*, 5 CH_2); 1.41, 1.34 (2*d*, *J* = 6.2, Me_2CHO). ^{13}C-NMR: 159.8 (*s*, C(2)); 134.8 (*s*, 1 arom. C); 128.8, 128.0, 126.5 (3*d*, 5 arom. CH); 122.8 (*q*, ^1J(C,F) = 286, CF_3); 107.1 (*s*, C(5)); 76.6 (*q*, ^2J(C,F) = 32, C(3)); 74.0 (*d*, Me_2CHO); 38.3, 37.7, 25.1, 23.3, 23.2 (5*t*, 5 CH_2); 21.4, 21.2 (2*q*, Me_2CHO). EI-MS: 342 (15), 341 (40, $M^{+\cdot}$), 299 (35), 298 (10), 270 (12), 257 (12), 256 (100), 186 (30), 140 (10), 105 (40), 81 (15), 77 (15).

With 2-ethoxy-1-aza-4-oxaspiro[4.5]dec-1-en-3-one (**2c**): **2c** (24 mg, 0.12 mmol), trifluoroacetophenone (130 mg, 0.74 mmol), 2.75 h, 155°C; CC (ether/hexane 1:20): 18 mg (45%) of *2-ethoxy-3-phenyl-3-trifluoromethyl-4-oxa-1-azaspiro[4.5]dec-1-ene* (**15b**) and 2 mg (8.5%) of **2c**. **15b**: Colorless oil. IR: 3060*w*, 2980*w*, 2940*m*, 2860*w*, 1675*s*, 1500*w*, 1480*w*, 1450*m*, 1380*m*, 1335*m*, 1330*m*, 1315*m*, 1275*s*, 1220*w*, 1185*s*, 1175*s*, 1150*w*, 1120*w*, 1100*m*, 1070*m*, 1055*m*, 1035*m*, 1020*w*, 1000*w*, 975*w*, 950*m*, 935*w*, 920*w*, 910*w*, 880*w*, 725*m*, 700*w*. ^{1}H-NMR: 7.8-7.75 (*m*, 2 arom. H); 7.4-7.35 (*m*, 3 arom. H); 4.45-4.25 (*m*, CH_3CH_2O); 1.8-1.45 (*m*, 5 CH_2); 1.41 (*t*, *J* = 7.1, CH_3CH_2O). ^{13}C-NMR: 160.6 (*s*, C(2)); 134.6 (*s*, 1 arom. C); 128.9, 128.1, 126.4 (3*d*, 5 arom. CH); 122.4 (*q*, ^1J(C,F) = 286, CF_3); 107.0 (*s*, C(5)); 76.7 (*q*, ^2J(C,F) = 32, C(3)); 66.3 (*t*, CH_3CH_2O); 38.3, 37.7, 25.0, 23.2, 23.1 (5*t*, 5 CH_2); 14.0 (*q*, CH_3CH_2O). EI-

MS: 327 (40, $M^{+}\cdot$), 298 (19), 285 (17), 284 (100), 257 (10), 256 (69), 202 (13), 105 (45), 87 (14), 81 (12), 77 (20).

*With 4-isopropoxy-2-phenyl-1,3-oxazol-5(2*H*)-one* (**2d**): **2d** (42 mg, 0.19 mmol), trifluoroacetophenone (750 mg, 4.3 mmol), 1 h, 155°C; CC (ether/hexane 1:40): 25 mg (38%) and 32 mg (48%) of two stereoisomeric (*cis/trans*) *2,5-dihydro-4-isopropoxy-2,5-diphenyl-5-trifluoromethyl-1,3-oxazoles* (**15c** and **15c'**): **15c**: Colorless oil. IR: 3070*w*, 3035*w*, 2980*w*, 2960*w*, 2930*w*, 2875*w*, 2860*w*, 1670*s*, 1495*w*, 1468*w*, 1450*w*, 1375*m*, 1360*w*, 1315*m*, 1305*m*, 1285*m*, 1270*m*, 1210*w*, 1190*s*, 1172*s*, 1145*w*, 1115*m*, 1095*w*, 1070*m*, 1048*s*, 1030*m*, 950*m*, 910*m*, 825*w*, 725*m*, 698*m* . ^{1}H-NMR: 7.75-7.65 (*m*, 2 arom. H); 7.4-7.3 (*m*, 8 arom. H); 6.69 (*s*, H-C(2)); 5.14 (*sept*, *J* = 6.2, Me_2CHO); 1.46, 1.36 (2*d*, *J* = 6.2, Me_2CHO). ^{13}C-NMR: 162.6 (*s*, C(4)); 139.0, 133.0 (2*s*, 2 arom. C); 129.0, 128.9, 128.4, 128.1, 126.7, 126.6 (6*d*, 10 arom. CH); 126.4 (*q*, ^{1}J(C,F) = 287, CF_3); 102.1 (*d*, C(2)); 85.5 (*q*, ^{2}J(C,F) = 31, C(5)); 75.0 (*d*, Me_2CHO); 21.5, 21.3 (2*q*, Me_2CHO). EI-MS: 349 (26, $M^{+}\cdot$), 307 (38), 306 (17), 264 (10), 209 (12), 195 (11), 186 (29), 167 (10), 132 (65), 106 (10), 105 (100), 104 (17), 77 (57).

15c': Colorless oil. IR: 3060*w*, 3030*w*, 2980*w*, 2940*w*, 1668*s*, 1495*w*, 1465*w*, 1450*w*, 1380*w*, 1320*w*, 1303*m*, 1285*m*, 1185*s*, 1178*s*, 1115*m*, 1098*w*, 1070*w*, 1048*m*, 1032*w*, 950*w*, 910*w*, 825*w*, 720*m*, 695*m*. ^{1}H-NMR: 7.85-7.75 (*m*, 2 arom. H); 7.55-7.35 (*m*, 8 arom. H); 6.45 (*s*, H-C(2)); 5.15 (*sept*, *J* = 6.2, Me_2CHO); 1.45, 1.40 (2*d*, *J* = 6.2, Me_2CHO). ^{13}C-NMR: 163.1 (*s*, C(4)); 138.6, 132.5 (2*s*, 2 arom. C); 129.4, 129.0, 128.5, 128.4, 126.8, 126.7 (6*d*, 10 arom. CH); 122.6 (*q*, ^{1}J(C,F) = 285, CF_3); 100.4 (*d*, C(2)); 85.4 (*q*, ^{2}J(C,F) = 32, C(5)); 74.9 (*d*, Me_2CHO); 21.5, 21.4 (2*q*, Me_2CHO). EI-MS: 349 (30, $M^{+}\cdot$), 307 (37), 306 (20), 264 (8), 209 (13), 195 (11), 186 (34), 167 (10), 132 (64), 106 (9), 105 (100), 104 (20), 77 (61).

Reaction of 2-isopropoxy-1-aza-4-oxaspiro[4.5]dec-1-en-3-one (**2b**) *and dimethyl acetylenedicarboxylate*: **2b** (170 mg, 0.8 mmol), dimethyl acetylenedicarboxylate (270 mg, 1.9 mmol), 0.5 h, 165°C; CC (ether/hexane 1:10): 45 mg (18%) *dimethyl 2-isopropoxy-1-azaspiro-[4.5]dec-1,3-diene-4,5-dicarboxylate* (**16**). Colorless oil. IR: 2980*w*, 2955*m*, 2930*m*, 2858*w*, 1750*s*, 1728*s*, 1645*m*, 1575*m*, 1465*w*, 1450*w*, 1435*m*, 1378*m*, 1305*s*, 1282*m*, 1264*s*, 1195*w*, 1167*w*, 1150*w*, 1114*m*, 1095*m*, 1053*w*, 1028*w*, 1005*w*, 975*w*, 935*w*, 910*w*, 860*w*, 833*w*. ^{1}H-NMR: 5.11 (*sept*, *J* = 6.2, Me_2CHO); 3.85, 3.81 (2*s*, 2 MeO); 2.15-1.65 (*m*, 7 H); 1.45-1.15 (*m*, 3 H). ^{13}C-NMR: 163.2, 162.6, 161.4 (3*s*, 2 CO_2Me, C(2), C(4)); 131.0 (*s*, C(3)); 76.1 (*s*, C(5)); 71.6 (*d*, Me_2CHO); 52.4, 52.1 (2*q*, 2 CO_2Me); 33.2, 25.4, 23.2 (3*t*, 5 CH_2); 21.4 (*q*, Me_2CHO). CI-MS: 311 (20), 310 (100, $[M+1]^{+}$), 280 (13), 278 (11), 269 (17), 268 (14), 266 (15), 252 (14), 238 (13), 236 (13), 224 (16), 212 (14), 210 (45), 208 (14), 152 (17), 99 (12), 97 (11), 85 (14), 83 (14), 81 (18), 79 (11).

Thermolysis of 2-phenyl-3-thia-1-azaspiro[4.4]non-1-ene-4-thione (**11**): In a round-bottom flask (N_2-atmosphere), **11** (52 mg, 0.21 mmol) was heated to 155-158°C for 4.5 h. The crude product was separated by CC (ether/hexane 1:40): 45 mg (87%) **11** and 5 mg (11%) **14**.

ACKNOWLEDGMENTS

We thank the analytical services of our institute for IR, NMR and mass spectra and the *Swiss National Science Foundation*, *F. Hoffmann-La Roche AG*, Basel, and the *Professor Hans E. Schmid-Stiftung* for financial support.

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12. Only in the case of **2** (RX = β-naphthylthio, R^2 = Ph, R^3 = CF_3) and trifluoroacetophenone, a third 1:1-adduct was isolated in addition to the two stereoisomers of the type (**6**). Because of the very low yield, its structure could not be determined with certainty.[10]
13. In the isomeric ethyl 2-isopropoxy-4-phenyl-4-trifluoromethyl-4*H*-imidazole-5-carboxylate, the sp^3-C(4)-atom should absorb at *ca.* 80-85 ppm (cf. **9a**).
14. The corresponding cycloaddition of benzonitrilium-phenylmethanide, generated photochemically from the corresponding 2*H*-azirine, and ethyl cyanoformate yielded a 1:2-mixture of the adducts with the C≡N and the C=O bonds.[15]
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16. Similar results were obtained with 2-isopropoxy-1-aza-3-oxaspiro[4.5]dec-1-en-3-one (**2b**) and **11**. In this case, the two 1:1-adducts (ratio 1:8) must be regioisomers because no diastereoisomers can be formed using achiral starting materials.
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19. Thermolysis of **11** in a sealed tube (4 h, 150°C) gave **14** in *ca.* 11% yield.

Received, 16th May, 1997