92. Synthesis of 4-Alkoxy-1,3-oxazol-5(2*H*)-ones, Precursors of 1-Alkoxy-Substituted Nitrile Ylides

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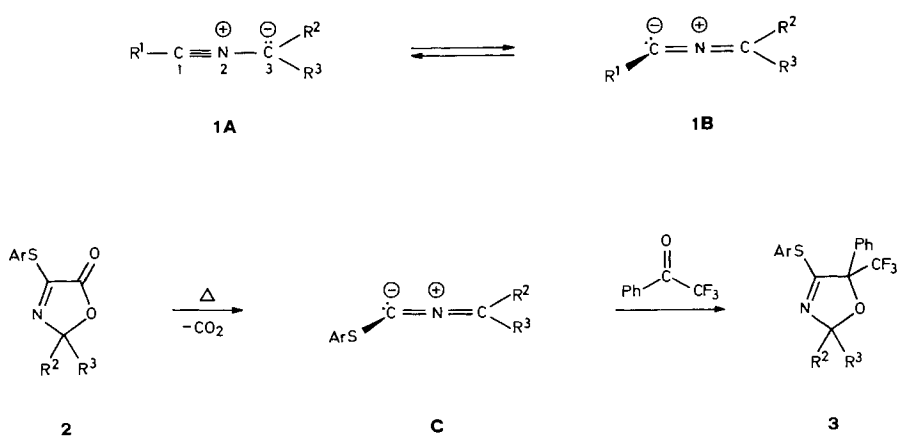
(28.III.89)

4-Alkoxy-1,3-oxazol-5(2*H*)-ones of type **4** and **7** were synthesized by two different methods: oxidation of the 4-(phenylthio)-1,3-oxazol-5(2*H*)-one **2a** with *m*-chloroperbenzoic acid in the presence of an alcohol gave the corresponding 4-alkoxy derivatives **4**, presumably *via* nucleophilic substitution of an intermediate sulfoxide (*Scheme 2*). The second approach is the BF_3-catalyzed condensation of imino-acetates of type **6** and ketones (*Scheme 3*). The yields of this more straightforward method were modest due to the competitive formation of 1,3,5-triazine tricarboxylate **8**. At 155°, 1,3-oxazol-5(2*H*)-one **7b** underwent decarboxylation leading to an alkoxy-substituted nitrile ylide which was trapped in a 1,3-dipolar cycloaddition by trifluoro-acetophenone to give the dihydro-oxazoles *cis*- and *trans*-**9** (*Scheme 4*). In the absence of a dipolarophile, 1,5-dipolar cyclization of the intermediate nitrile ylide yielded isoindole derivatives **10** (*Schemes 4* and *5*).

1. Introduction. – Recently, we have reported on 1,3-dipolar cycloadditions of nitrile ylides **1** bearing a benzylthio or arylthio substituent at the 'nitrile C-atom' C(1) [1]. Irrespective of the substitution of the 'ylide C-atom' C(3), all cycloadditions proceeded regioselectively. With trifluoroacetophenone, for example, cycloadducts of type **3** (*Scheme 1*) were formed in good yields.

Scheme 1



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According to MO calculations (STO-3G and MINDO/3 level) of *Houk* and coworkers [2], the regioselectivity of the $HOMO_{(Dipole)}$-controlled 1,3-dipolar cycloaddition of nitrile ylides depends on the geometry of these reactive intermediates. The linear 'propargyl structure' **1A** is energetically more favorable, when R^2 and/or R^3 are electron-withdrawing substituents, whereas the bent 'allenyl structure' **1B** is preferred for the parent compound and for R^2, R^3 having electron-donating character (*cf.* also [3]). In structure **1A**, the 'ylide C(3)-atom' shows the largest coefficient of the HOMO. In contrast, the HOMO of the 'allenyl structure' **1B** displays the largest coefficient on the 'nitrile C(1)-atom'. As a consequence, nitrile ylides of type **1B** undergo a cycloaddition with ketones to give 2,5-dihydro-1,3-oxazoles of type **3** [1][4][5], whereas nitrile ylides of type **1A** lead to the isomeric 4,5-dihydro-1,3-oxazoles [6][2]).

The influence of substituents at C(1) of a nitrile ylide is still not quite clear [3]). Only a few reactions of nitrile ylides with a heteroatom at C(1) are known: amino-substituted nitrile ylides have been generated by photolysis of 2,2-dimethyl-3-amino-2*H*-azirines [10]. The 1,3-dipolar cycloadditions of these dipoles as well as their protonation show the same regioselectivity as the corresponding benzonitrilio-methanides. The previously mentioned nitrile ylides with a $PhCH_2S$ or arylthio substituent at C(1) have been formed on thermolysis of the corresponding 1,3-oxazol-5(2*H*)-ones **2** [1] (*Scheme 1*). With R^2, R^3 = alkyl, again only one cycloadduct is observed from the reaction with trifluoroacetophenone or with the C=S bond of 1,3-thiazole-5(4*H*)-thione; the regioselectivity has been established again to be the same as with benzonitrilio-dialkylmethanides. Most surprising was the observation that even the nitrile ylide **C** with R^2 = Ph, R^3 = CF_3, *i.e.* with two electron-withdrawing substituents, and trifluoroacetophenone or 1,3-thiazole-5(4*H*)-thione forms cycloadducts with the same regioselectivity. This result leads to the assumption that all nitrile ylides with a thio substituent at C(1) belong to the 'allenyl type'.

Is it possible that the π-donating character of a thio substituent at C(1) overcompensates the influence of the substituents R^2 and R^3 on the dipole structure? We attempted to answer this question by experimental and computational studies. Since alkoxy groups are more convenient for calculations than alkylthio groups, we tried to synthesize 4-alkoxy-1,3-oxazol-5(2*H*)-ones as possible precursors of alkoxy-substituted nitrile ylides.

2. Synthesis of 4-Alkoxy-1,3-oxazol-5(2*H*)-ones. – In our first approach to synthesize the title compounds in analogy to [11], we treated a mixture of ethyl cyanoformate and EtOH, i-PrOH, or phenol with Et_2NH, $TiCl_4$, a ketone, and $BF_3 \cdot Et_2O$. However, we failed to isolate an oxazolone under several reaction conditions and with variable ratios of reagents. A second approach was more promising (*Scheme 2*): treatment of a $CHCl_3$ solution of 4-(phenylthio)-1,3-oxazolone **2a** with 1–2 equiv. of *m*-chloroperbenzoic acid in the presence of EtOH leads to the formation of the 4-ethoxy-1,3-oxazolone **4a** in 20–40% yield. Without

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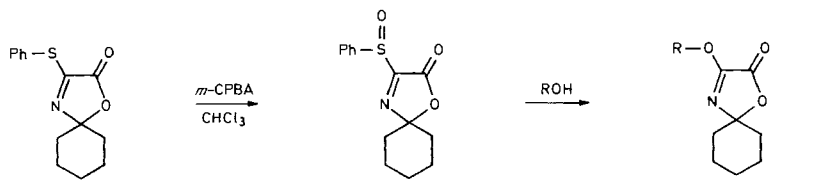
[2]) The protonation site of nitrile ylides (*cf.* [3]), for example with alcohols, clearly indicates where the highest electron density in the HOMO is located. Benzonitrilio-dialkylmethanides (**1**; R^1 = Ph, R^2, R^3 = alkyl), for example, are protonated at C(1) [4][7][8], but benzonitrilio-bis(trifluoromethyl)methanide (**1**; R^1 = Ph, R^2, R^3 = CF_3) is protonated at C(3) [9].

[3]) *Houk*'s calculations [2] have shown that π-acceptor substituents at C(1) diminish the energy difference between structures **1A** and **1B** and, thus, lead to a more linear structure of the nitrile ylide. σ-Donors at C(1) seem to have a similar effect. So far, no results of calculations for π-donor substituents are available.

the oxidizing reagent, no product was formed neither in $CHCl_3$ nor in a mixture of AcOH and $CHCl_3$. After addition of 1 equiv. of *m*-chloroperbenzoic acid (*m*-CPBA) to the unchanged reaction mixture in AcOH/$CHCl_3$, again **4a** was formed; the product was isolated in 40% yield. We assume that the substitution of the PhS group by the EtO group proceeds *via* the intermediate sulfoxide **D** (or the corresponding sulfone). This oxidation results in an increased electrophilicity of C(4) of the oxazolone, enabling, under the acidic reaction conditions, the nucleophilic attack of EtOH.

Scheme 2

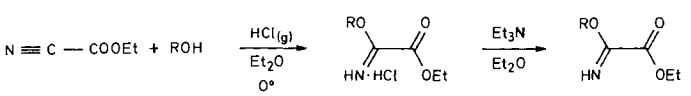


2a **D** **4 a** R = CH_3CH_2; **b** R = CH_3; **c** R = $(CH_3)_2CH$

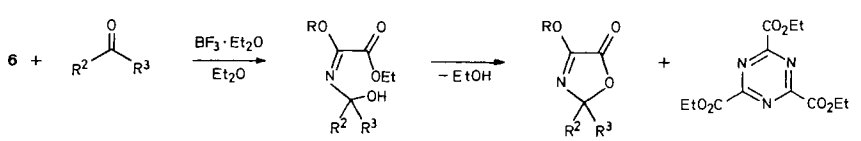
Unfortunately, the scope of this substitution reaction seems to be very limited. With i-PrOH instead of EtOH, we were not able to increase the yield of **4** above 4%; even after a very long reaction time, and with $PhCH_2OH$, we did not observe any formation of the desired oxazolone.

The synthesis depicted in *Scheme 3* turned out to be more convenient. The imino-esters of type **6** were synthesized according to *Pinner* (*cf.* [12]). A mixture of ethyl cyanoformate and EtOH, i-PrOH, or phenol[4]) in Et_2O was treated with HCl gas at 0°, leading to hydrochlorides **5** (*Table 1*). Deprotonation of **5** with Et_3N in Et_2O yielded the free bases **6**.

Scheme 3



5 **6**



E **7** **8**

[4]) It is important to use equimolar quantities of the cyanoformate and the alcohol. Excess of the alcohol leads to the formation of dialkyl oxalate *via* alcoholysis of imino-ester.

Table 1. *Formation of Imino-esters* **6**

ROH	**5** (Yield [%])	**6** (Yield [%])	B.p. [°]
EtOH	**5a** (90)	**6a** (55)	125/30 Torr
i-PrOH	**5b** (98)	**6b** (86)	125/15 Torr
PhOH	**5c** (72)	**6c**[a])	[b])

[a]) Yield not determined.
[b]) Decomposition on heating.

The condensation of imino-ester **6** and a ketone was achieved in the presence of catalytic amounts of $BF_3 \cdot Et_2O$. For example, a solution of **6b** in Et_2O was added at room temperature to an equimolar amount of trifluoroacetophenone in Et_2O. After addition of a few drops of $BF_3 \cdot Et_2O$, the solution was stirred for 24 h. The precipitated triazine-triester **8** was removed by filtration. Evaporation of the solvent and remaining trifluoroacetophenone, followed by chromatography, gave the 4-isopropoxy-1,3-oxazolone **7b** in 28% yield.

The structure of **7b** has been determined by spectral data. In the IR spectrum (CCl_4), two strong absorption bands appear at 1829 and 1660 cm^{-1} for C=O and C=N, respectively. ^{1}H-NMR ($CDCl_3$) clearly indicates the presence of an i-PrO group with two diastereotopic Me groups. The MS shows the molecular ion at *m/z* 287 with low intensity and peaks for the following fragment ions: *m/z* 218 ($M^+ - CF_3$), 200 ($M^+ - CO_2 - (CH_3)_2CH$), 176 ($218 - (CH_2{=}CHCH_3)$), 105 ($PhCO^+$), 77 ($C_6H_5^+$), and 43 ($(CH_3)_2CH^+$). Of special value for the identification of the structure is the ^{13}C-NMR spectrum ($CDCl_3$): the ring C-atoms absorb at 159.0, 157.9 (C(4), C(5)), and 97.4 ppm (C(2)) [13]. In the ^{1}H-decoupled spectrum, C(2) absorbs as a *quartet* with $^2J(C,F) = 32.4$ Hz.

To improve the yield of **7b**, we have repeated the reaction with some other *Lewis* acids ($AlCl_3$, $ZnCl_2$) and under different reaction conditions. However, only in the presence of BF_3 formation of **7b** was observed in reasonable yields. Under all conditions, **8** was formed as the main product[5]). After treatment of **6b** with BF_3 in the absence of a ketone, **8** was the only product isolated[6]). Another side product has been identified as the diester of oxalic acid.

Table 2. *Formation of 4-Alkoxy-1,3-oxazol-5(2*H*)-ones*

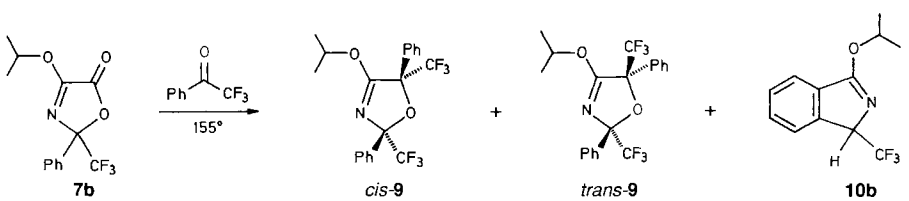
Starting material	Carbonyl compound		Reaction conditions	1,3-Oxazolone (Yield [%])
	R^2	R^3		
6a, R = Et	$-(CH_2)_5-$		r.t., 12 h	**4a** (11.3)
6b, R = i-Pr	$-(CH_2)_5-$		r.t., 3 d	**4c** (21.8)
5b, R = i-Pr	$-(CH_2)_5-$		−10°, 2 d; r.t., 20 d	**4c** (25.8)
5b, R = i-Pr	$-(CH_2)_4-$		r.t., 15 h	**4d** (3.2)
6a, R = Et	Ph	CF_3	r.t., 15 h	**7a** (14.0)
6b, R = i-Pr	Ph	CF_3	r.t., 24 h	**7b** (28.3)
5b, R = i-Pr	Ph	CF_3	r.t., 15 h	**7b** (20.0)
6b, R = i-Pr	CCl_3	CCl_3	r.t., 4 d	**7c** (4.7)
6c, R = Ph	CCl_3	CCl_3	−10°, 36 h	**7d** (4.2)
6b, R = i-Pr	CH_3	CH_3	r.t., 10 d	**7e** (2.0)
6b, R = i-Pr	Ph	H	r.t., 8 d	**7f** (7.3)

[5]) Using BF_3 in equimolar quantity, **8** was formed in high yield, and only traces of **7b** have been detected.
[6]) For comparison of the spectral data, **8** was synthesized from ethyl cyanoformate by treatment with HCl gas at 0° in 63% yield [14].

Instead of imino-ester **6**, the hydrochloride **5** can be used directly. In this case, an equimolar amount of Et_3N was added to the reaction mixture before adding $BF_3 \cdot Et_2O$. The yield of oxazolone **7** depends on the nature of the ketone: ketones with electron-withdrawing substituents seem to react easier. Low yields in the reactions with hexachloroacetone can be explained by steric interactions of the bulky CCl_3 groups. The hemiaminal **E** (*Scheme 3*) which can be formed by nucleophilic attack of imino-ester onto the complexed C=O group of the ketone is a reasonable intermediate in the formation of **7**. Ring closure by loss of EtOH under acidic conditions leads to the oxazolone.

3. Thermal Reactions of 4-Alkoxy-2-phenyl-1,3-oxazol-5(2*H*)-ones. – Heating of a *ca.* 1:2 mixture of oxazolone **7b** and trifluoroacetophenone in a degassed and sealed tube for 30 min to 155° yielded a slightly yellow reaction mixture which, according to TLC analysis, consisted of three products (*Scheme 4*). After chromatography on silica gel, 50% of starting material **7b** was recovered in addition to 21.3% and 19.3% of two very similar 1:1 adducts and 6% of a product, showing a $M^{+\cdot}$ with *m/z* 243 in the MS and no C=O absorption in the IR spectrum. The structures of the 1:1 adducts *trans*-**9** and *cis*-**9** have been established on the basis of their spectral data.

Scheme 4



Of special importance were again the ^{13}C-NMR spectra ($CDCl_3$) with absorptions for the ring-C atoms at 165.1/165.0 (C(4)), 104.4/104.5 (C(2)), and 87.1/86.9 ppm (C(5)). The chemical shift of C(2), which absorbs as a *quartet* with $^2J(C,F) = 31–32$ Hz, is characteristic for a 2,5-dihydro-1,3-oxazole [4].

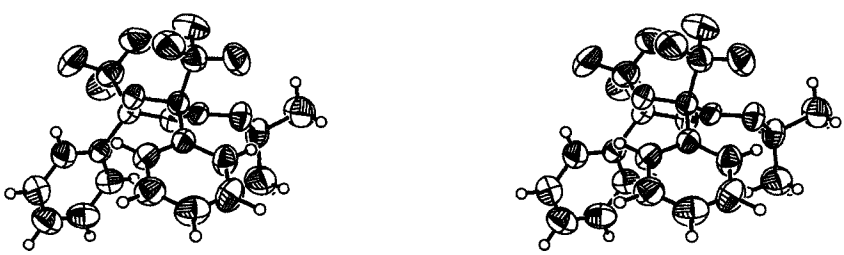


Fig. 1. *Stereoscopic view of the structure of* cis-**9**

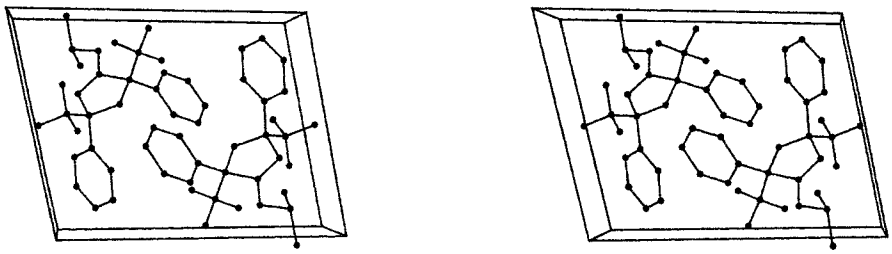


Fig. 2. *Packing of* cis-**9**

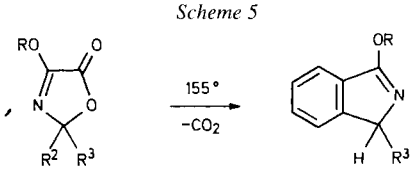
Since no decision could be made for the relative configuration of the two isomers, we have recrystallized the minor isomer from hexane. The structure was determined to be *cis*-**9** (*Figs. 1* and *2*) by X-ray structure analysis[7]).

For the third product, obtained in 6% yield, the structure of isoindole **10b** is suggested (*Scheme 4*). This structure is in accordance with all spectral and analytical data.

The molecular-weight determination (osmometry, benzene) gave 259 (± 10%). The ^{1}H-NMR ($CDCl_3$) shows the presence of $(CH_3)_2CHO$ with two diastereotopic Me groups. An additional *quartet* with J = 7.8 Hz appears at 5.15 ppm, characteristic for H–C(1). In the ^{13}C-NMR, the C-atoms of the ring system absorb as a *singlet* at low field (172.0 ppm) for C(3), six signals for the aromatic C-atoms (2 *s* and 4 *d*), and a *qd* at 69.2 ppm (^2J(C,F) = 30 Hz) for C(1).

Heating of **7b** neat or in i-PrOH to 155° in the absence of the dipolarophile led to **10b** as the sole product (*Scheme 5*). Even in a DMF/H_2O mixture after 1.5 h at 150°, no other product was formed (94% conversion, 61% **10b**).

Scheme 5



7 (R^2 = Ph) **10**

The decarboxylative cyclization of oxazolones of type **7** with R^2 = Ph turned out to be specific. Thermolysis of **7a** and **7f** at 155° in toluene (sealed tube) gave the corresponding isoindoles **10a** and **10c** in 67 and 22% yield, respectively.

The formation of the 2,5-dihydro-1,3-oxazoles *cis*- and *trans*-**9** as well as of the isoindole derivatives **10** by thermolysis of oxazolones of type **7** is in accordance with the intermediate alkoxy-substituted nitrile ylide **F** (*Scheme 6*). Using the highly polarized dipolarophile trifluoroacetophenone, the intermediate is trapped in a non-stereospecific 1,3-dipolar cycloaddition. In a competitive reaction, a 1,5-dipolar electrocyclization [15][16] (*cf.* also [3]) to **G**, followed by aromatization by 1,3-H shift led to **10**. Analogous cyclizations of photochemically generated nitrile ylides have been previously reported by *Padwa et al.* [17][18].

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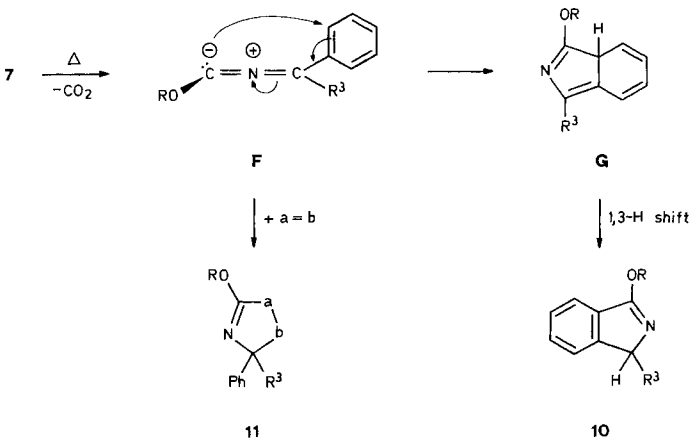
[7]) The X-ray structure analysis has been performed by Dr. *B. Vincent*; for details, see *Exper. Part.* All crystallographic data are deposited with the *Cambridge Crystallographic Data Centre*, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, England.

Scheme 6



4. Conclusions. – The synthesis of 4-alkoxy-1,3-oxazol-5(2*H*)-ones has been achieved by two different methods. In the first one, the starting material is already a 1,3-oxazol-5(2*H*)-one. Substitution of the PhS group at C(4) by an alkoxy group leads to the desired product (*Scheme 2*). This substitution can only be performed in the presence of *m*-chloroperbenzoic acid. We interprete this result with the formation of the corresponding sulfoxide as intermediate, though all attempts to its isolation failed. In the second approach, the 1,3-oxazol-5(2*H*)-ones with the desired substituents were formed directly from noncyclic precursors, namely by an acid-catalyzed condensation of ethyl 2-alkoxy-2-iminoacetates and ketones or benzaldehyde (*Scheme 3*). Although the yields of both approaches are modest-to-poor, these unusually substituted oxazolones, required for thermolytical formation of the corresponding nitrile ylides, became available by short and easy procedures.

The ability of the oxazolones to form 1-alkoxy-substituted nitrile ylides (alkoxy group at the 'nitrile C(1)-atom') was tested in some preliminary experiments. The results demonstrate clearly that 4-alkoxy-1,3-oxazol-5(2*H*)-ones are suitable precursors for this hitherto unknown type of nitrile ylides. The decarboxylation occurs on thermolysis at 155°. In the absence of dipolarophiles, the intermediate dipoles with a Ph group at the 'ylide C(3)-atom' undergo a 1,5-dipolar electrocyclization [15-18] (*Scheme 5*). The nitrile ylides can also be trapped by trifluoroacetophenone. A 1,3-dipolar cycloaddition onto the activated C=O group of this ketone leads to the formation of 2,5-dihydro-1,3-oxazoles (*Scheme 4*). The regioselectivity has been found to be the same as with Ph-, arylthio-, and amino-substituted nitrile ylides of the 'allenyl-type' **1B** (*Scheme 1*).

Cycloadditions of a series of alkoxy-substituted nitrile ylides with less polar dipolarophiles as well as computational studies of the structure of these dipoles are in progress.

Our thanks are due to the analytical services of our Institute, especially to Mr. *H. Frohofer* for elemental analyses, Mrs. *E. Patterson-Vykoukal* for running IR spectra, Mr. *M. Vöhler* for NMR spectra, Dr. *A. Lorenzi* for mass spectra, and Dr. *B. Vincent* for the X-ray analysis. Financial support by the *Swiss National Science Foundation* and by *F. Hoffmann-La Roche & Co. AG*, Basel, is gratefully acknowledged.

Experimental Part

General. See [10][19]. IR spectra in CCl_4. ^{1}H-(200 MHz) and ^{13}C-NMR (50.4 MHz) in $CDCl_3$. CI-MS with 2-methylpropene. Column chromatography on silica gel (*Kieselgel 60*, 0.040-0.063 mm; *Merck*).

1. Synthesis of 4-Alkoxy-1,3-oxazol-5(2*H*)-ones. – 1.1. *From 4-(Phenylthio)-1,3-oxazol-5(2*H*)-one* **2a**. 1.1.1. *4'-Ethoxyspiro[cyclohexane-1,2'-[1,3]oxazol]-5'(2'*H*)-one* (= *3-Ethoxy-1-oxa-4-azaspiro[4.5]dec-3-en-2-one*; **4a**). a) A soln. of 130 mg (0.76 mmol) *m*-chloroperbenzoic acid (*m*-CPBA) in 15 ml of $CHCl_3$, containing *ca.* 1% EtOH, was added dropwise to 200 mg (0.76 mmol) of *4'-(phenylthio)spiro[cyclohexane-1,2'-[1,3]oxazol]-5'(2'*H*)-one* (**2a**) [11] in 5 ml of $CHCl_3$ at 0° [20]. The mixture was stirred for 15 h at r.t., washed with an aq. $NaHCO_3$ soln. and H_2O, and dried (Na_2SO_4). Chromatography (EtOH/hexane 1:8) yielded 40 mg (20%) of unchanged **2a** and 36 mg (23.8%) of **4a**: white crystals. M.p. 89.3–89.4°. IR: 2990*w*, 2940*m*, 2905*w*, 2860*w*, 1796*s* (br.), 1660*s*, 1477*w*, 1450*m*, 1410*w*, 1382*m*, 1365*w*, 1340*s*, 1286*m*, 1263*m*, 1195*s*, 1145*m*, 1122*m*, 1050*m*, 1025*m*, 950*m*, 940*m*, 910*m*. ^{1}H-NMR: 4.37 (*q*, *J* = 7.1, CH_3CH_2O); 1.8–1.55 (*m*, 10 cyclohexyl H); 1.44 (*t*, *J* = 7.1, CH_3CH_2O). ^{13}C-NMR: 159.8, 156.5 (2 *s*, C(5), C(4)); 102.6 (*s*, C(2)); 66.4 (*t*, CH_3CH_2O); 36.7, 24.4, 22.6 (3 *t* (2:1:2), 5 cyclohexyl C); 13.9 (*q*, CH_3CH_2O). CI-MS: 198 ([*M* + 1]$^+$). Anal. calc. for $C_{10}H_{15}NO_3$ (197.24): C 60.89, H 7.67, N 7.10; found: C 60.57, H 7.75, N 6.88. Mol. weight (osmometr., benzene): found 215.

b) To a soln. of 520 mg (1.99 mmol) of **2a** in 16 ml of $CHCl_3$ at 0° were added 14 ml (*ca.* 240 mmol) of EtOH, 2.4 g (40 mmol) of AcOH, and a soln. of 378 mg (2.2 mmol) of *m*-CPBA in 16 ml of $CHCl_3$. After 1 h at 0° and 36 h at r.t., workup according to *a* yielded 230 mg (44%) of **2a** and 120 mg (31.8%) of **4a**.

c) In an analogous experiment, a soln. of **2a** in a mixture of AcOH/EtOH/$CHCl_3$ (0.3:1:1) was stirred for 4 h at r.t. After that time, no **4a** has been formed (TLC, GLC). Addition of 1 equiv. of *m*-CPBA to the mixture at 0° and stirring for 15 h at r.t. yielded 39.8% of **2a** and 40.2% of **4a**.

1.1.2. *4'-Methoxyspiro[cyclohexane-1,2'-[1,3]oxazol]-5'(2'*H*)-one* (=*3-Methoxy-1-oxa-4-azaspiro[4.5]dec-3-en-2-one*; **4b**). A soln. of 34.5 mg (0.2 mmol) *m*-CPBA in 3 ml of CH_2Cl_2 was added to 50 mg (0.19 mmol) of **2a** in 4 ml of CH_2Cl_2 and 2 ml of MeOH at 0°. After stirring at r.t. overnight, another portion of 43.5 mg (0.25 mmol) of *m*-CPBA was added and the mixture stirred for 8 h. Workup according to *1.1.1* yielded 20 mg (56%) of **4b**. IR: 2990*w*, 2950*m*, 2905*w*, 2860*w*, 1812*s*, 1796*s*, 1663*s*, 1446*m*, 1378*w*, 1358*w*, 1346*m*, 1288*m*, 1262*m*, 1205*m*, 1192*s*, 1142*w*, 1108*w*, 1050*m*, 1033*w*, 1007*w*, 992*w*, 980*w*, 950*m*, 940*m*, 910*w*. ^{1}H-NMR: 4.02 (*s*, CH_3O); 1.9–1.6 (*m*, 10 cyclohexyl H). ^{13}C-NMR: 161.3, 156.9 (2*s*, C(5), C(4)); 102.7 (*s*, C(2)); 57.0 (*q*, CH_3O); 36.7, 24.4, 22.6 (3*t* (2:1:2), 5 cyclohexyl C).

1.1.3. *4'-Isopropoxyspiro[cyclohexane-1,2'-[1,3]oxazol]-5'(2'*H*)-one* (= *3-Isopropoxy-1-oxa-4-azaspiro[4.5]dec-3-en-2-one*; **4c**). A soln. of 52 mg (0.3 mmol) of *m*-CPBA in 3 ml of CH_2Cl_2 was added dropwise to 59 mg (0.23 mmol) of **2a** in 2 ml of CH_2Cl_2 and 2.1 ml (28 mmol) of i-PrOH at 0°. After stirring at r.t. for 2 d, CH_2Cl_2 and i-PrOH were evaporated, the residue dissolved in CH_2Cl_2, washed with aq. $NaHCO_3$ soln. and H_2O, and dried (Na_2SO_4). Chromatography (Et_2O/hexane 1:9) gave 38.2 mg (64.8%) of **2a** and 2.0 mg (4.1%) of **4c**. For spectral data, see *1.2.2.2.*

1.2. *By Condensation of Imino-acetates with Ketones.* 1.2.1. *Synthesis of Imino-acetates.* 1.2.1.1. *Ethyl 2-Ethoxy-2-iminoacetate* (**6a**) [14]. Dry HCl gas was bubbled through a mixture of 3.96 g (40 mmol) of ethyl cyanoformate and 2.3 ml (1.84 g, 40 mmol) of EtOH in 20 ml of Et_2O at 0° for 7 h. The solvent was evaporated, the residue washed with dry Et_2O, and dried i.v.: 6.56 g (90.3%) of **6a** · HCl (= **5a**). A suspension of this material in 20 ml of Et_2O was treated with 5.6 ml of Et_3N for 2 h. After filtration, the solvent was evaporated and the residue distilled at 125°/30 Torr: 3.2 g (55.2%) of **6a**. Colourless oil. IR: 3345*w*, 3318*w*, 2985*m*, 2940*w*, 2910*w*, 2875*w*, 1760*s*, 1740*s*, 1652*s*, 1478*w*, 1465*w*, 1448*w*, 1380*m*, 1345*m*, 1302*w*, 1220*s* (br.), 1190*m*, 1175*m*, 1160*w*, 1120*m*, 1095*s*, 1020*m*, 910*m*, 875*m*. ^{1}H-NMR (90 MHz, $CDCl_3$): 8.80 (br. *s*, NH); 4.30 (br. *q*, *J* = 6.5, 2 CH_3CH_2O); 1.38 (br. *t*, *J* = 6.5, 2 CH_3CH_2O). ^{13}C-NMR: 159.3, 158.0 (2*s*, C=O, C=N); 63.3, 62.9 (2*t*, 2 CH_3CH_2O); 13.9, 13.8 (2*q*, 2 CH_3CH_2O).

1.2.1.2. *Ethyl 2-Imino-2-isopropoxyacetate* (**6b**). In analogy to *1.2.1.1* 7.93 g (80 mmol) of ethyl cyanoformate and 4.80 g (80 mmol) of i-PrOH in 50 ml of Et_2O reacted to give 15.4 g (98.4%) of **6b** · HCl (= **5b**). After treatment of a suspension of this material in 20 ml of Et_2O with 8.2 g of Et_3N for 24 h at r.t., filtration, evaporation of Et_2O, and distillation at 125°/15 Torr, 11.0 g (86.2%) of **6b** were isolated. Colourless oil. IR: 3345*w*, 3318*w*, 2983*m*, 2940*w*, 2910*w*, 2875*w*, 1758*s*, 1740*s*, 1658*s*, 1468*w*, 1455*w*, 1445*w*, 1410*w*, 1383*m*, 1372*w*, 1340*w*, 1325*m*, 1300*w*, 1223*s* (br.), 1182*w*, 1145*w*, 1118*m*, 1090*s*, 1025*m*, 930*w*, 910*w*, 880*w*, 865*w*. ^{1}H-NMR: 8.77 (br. *s*, NH); 5.15 (*sept.*, *J* = 6.2, $(CH_3)_2CHO$); 4.32 (*q*, *J* = 7.1, CH_3CH_2O); 1.37 (*t*, *J* = 7.1, CH_3CH_2O); 1.36 (*d*, *J* = 6.2, $(CH_3)_2CHO$). ^{13}C-NMR: 157.9, 157.6 (2*s*, C=O, C=N); 69.3 (*d*, $(CH_3)_2CHO$); 61.9 (*t*, CH_3CH_2O); 20.5 (*q*, $(CH_3)_2CHO$); 13.2 (*q*, CH_3CH_2O). CI-MS: 160 ([*M* + 1]$^+$).

1.2.1.3. *Ethyl 2-Imino-2-phenoxyacetate* (**6c**). In analogy to *1.2.1.1*, a soln. of 3.96 g (40 mmol) of ethyl cyanoformate and 3.76 g (40 mmol) of phenol in 20 ml of Et_2O was treated with HCl gas during 8 h at 0°: 6.57 g (72%) of **5c**. IR: 3610*w*, 3500–3200*w* (v.br.), 3045*w*, 2990*w*, 1756*s*, 1715*s*, 1608*s*, *1598s*, 1537*w*, 1500*s*, 1470*s*, 1380*w*, 1357*w*, 1342*w*, 1258*s*, 1230*s* (br.), 1180*s*, 1168*s*, 1152*s*, 1070*w*, 1020*m*, 1000*w*, 883*w*, 802*w*, 690*s*. ^{1}H-NMR: 7.3–7.15 (*m*, 2 arom. H); 7.0–6.8 (*m*, 3 arom. H); 4.57 (*q*, *J* = 7.2, CH_3CH_2O); 1.47 (*t*, *J* = 7.2, CH_3CH_2O). ^{13}C-NMR: 166.8, 161.3 (2*s*, C=O, C=N); 155.5 (*s*, 1 arom. C); 129.6, 120.6, 115.3 (3*d*, 5 arom. C); 64.1 (*t*, CH_3CH_2O); 14.0 (*q*, CH_3CH_2O).

A suspension of 6.0 g (26.3 mmol) of **5c** in 5 ml of Et_2O was treated with 2.5 ml of Et_3N. After 3 h, $Et_3N \cdot HCl$ was filtrated and the solvent evaporated: 3.67 mg (72.8%) of crude free base **6c**. IR: 3500–3200*w* (v.br.), 3045*w*, 2980*w*, 1763*m*, 1720*m*, 1650*w*, 1608*s*, 1598*s*, 1500*s*, 1470*s*, 1370*w*, 1342*w*, 1250*s* (br.), 1218*s*, 1180*m*, 1168*m*, 1152*m*, 1070*w*, 1025*w*, 1000*w*, 910*w*, 883*w*, 691*w*. ^{1}H-NMR (90 MHz, $CDCl_3$): 7.90 (br. *s*, NH); 7.35–7.1 (*m*, 2 arom. H); 7.0–6.75 (*m*, 3 arom. H); 3.70 (*q*, *J* = 7, CH_3CH_2O); 1.07 (*t*, *J* = 7, CH_3CH_2O). ^{13}C-NMR: 156.5 (*s*, C=O, C=N, 1 arom. C); 129.5, 119.8, 115.7 (3*d*, 5 arom. C); 45.2 (*t*, CH_3CH_2O); 9.6 (*q*, CH_3CH_2O). Distillation of **6c** at 160°/20 Torr lead to partial decomposition of the material.

1.2.2. *Synthesis of 1,3-Oxazol-5(2*H*)-ones*. 1.2.2.1. *Synthesis of* **4a**. To a soln. of 460 mg (3.2 mmol) of **6a** and 3 drops of $TiCl_4$ in 2.5 ml of Et_2O at 0° was added a soln. of 470 mg (4.8 mmol) of cyclohexanone in 1.5 ml of Et_2O and 2 drops of $BF_3 \cdot Et_2O$. The mixture was stirred for 12 h at r.t. under Ar, washed with aq. $NaHSO_3$, $NaHCO_3$, and H_2O, and dried (Na_2SO_4). Purification by chromatography (see *1.1.1*) yielded 70 mg (11.3%) of **4a**, identical with the material from *1.1.1*. Some other fractions also contained small amounts of **4a**.

1.2.2.2. *Synthesis of* **4c**. a) To a soln. of 398 mg (2.5 mmol) of **6b**, 245 mg (2.5 mmol) of cyclohexanone, and 3 drops of Et_3N in 5 ml of Et_2O were added 5 drops of $BF_3 \cdot Et_2O$. After 24 h stirring at r.t., again 5 drops of $BF_3 \cdot Et_2O$ were added. After another 48 h, the mixture was filtrated, the solvent evaporated, and the residue chromatographed (Et_2O/hexane): 116 mg (31.1%) of *triethyl 1,3,5-triazine-2,4,6-tricarboxylate* (**8**) [14] (for spectral data, see *2*) and 384 mg of a crude oil which was again chromatographed: 115 mg (21.8%) of **4c**. White crystals. M.p. 50.7–51.1°. IR: 2982*w*, 2940*m*, 2900*w*, 2860*w*, 1797*s*, 1655*s*, 1468*w*, 1450*w*, 1400*w*, 1387*w*, 1375*w*, 1360*w*, 1332*w*, 1285*m*, 1263*m*, 1195*s*, 1150*w*, 1140*w*, 1109*m*, 1050*w*, 950*w*, 927*m*, 910*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 5.04 (*sept.*, *J* = 6.2, $(CH_3)_2CHO$); 1.85–1.6 (*m*, 10 cyclohexyl H); 1.40 (*d*, *J* = 6.2, $(CH_3)_2CHO$). ^{13}C-NMR: 160.1, 155.7 (2*s*, C(5), C(4)); 102.5 (*s*, C(2)); 74.4 (*d*, $(CH_3)_2CHO$); 36.7, 24.4, 22.6 (3*t* (2:1:2), 5 cyclohexyl C); 21.2 (*q*, $(CH_3)_2CHO$). CI-MS: 212 (100, $[M+1]^+$), 170 (31), 124 (19), 81 (18). Anal. calc. for $C_{11}H_{17}NO_3$ (211.26): C 62.54, H 8.11, N 6.63; found: C 62.94, H 8.16, N 6.37.

b) To 4.42 g (22.57 mmol) of **5b** in 50 ml of dry Et_2O at –10° were added 2.23 g (22 mmol) of Et_3N, 3.32 g (33.8 mmol) of cyclohexanone, and 5 drops of $BF_3 \cdot Et_2O$. The mixture was stirred for 2 d at –10° and 20 d at r.t. Workup according to *1.2.1.1* yielded 1.2 g (25.8%) of **4c**. The yield of **8** was not determined.

1.2.2.3. *4'-Isopropoxyspiro[cyclopentane-1,2'-[1,3]oxazol]-5'(2'*H*)-one* (= *3-Isopropoxy-1-oxa-4-azaspiro[4.4]non-3-en-2-one*; **4d**). To a suspension of 978 mg (5 mmol) of **5b** in 15 ml of Et_2O at r.t. was added a soln. of 631 mg (7.5 mmol) of cyclopentanone and 5 drops of $BF_3 \cdot Et_2O$. After dropwise addition of 506 mg (5 mmol) of Et_3N in 15 ml of Et_2O, the mixture was stirred overnight, again 5 drops of $BF_3 \cdot Et_2O$ were added and the mixture stirred for 2 d. Filtration, washing with H_2O, and repeated chromatography (Et_2O/hexane 1:20) gave in addition to ethyl 2-propyl oxalate and **8**, 32 mg (3.2%) of **4d**. IR: 2980*w*, 2940*w*, 2875*w*, 2860*w*, 1800*s*, 1650*s*, 1467*w*, 1452*w*, 1433*w*, 1395*w*, 1385*w*, 1373*w*, 1325*w*, 1227*m*, 1182*w*, 1138*m*, 1110*m*, 972*w*, 930*w*. ^{1}H-NMR: 5.05 (*sept.*, *J* = 6.2, $(CH_3)_2CHO$); 2.2–1.8 (*m*, 8 cyclopentyl H); 1.41 (*d*, *J* = 6.2, $(CH_3)_2CHO$). CI-MS: 198 ($[M+1]^+$).

1.2.2.4. *4-Ethoxy-2-phenyl-2-(trifluoromethyl)-1,3-oxazol-5(2*H*)-one* (**7a**). To a soln. of 442 mg (3.04 mmol) of **6a** in 5 ml of Et_2O was added dropwise a mixture of 900 mg (5.17 mmol) of trifluoroacetophenone and 3 drops of $BF_3 \cdot Et_2O$ in 10 ml of Et_2O at r.t. After stirring for 15 h, filtration (colourless crystals of **8**), evaporation of the solvent, and chromatography (Et_2O/hexane) yielded 116 mg (14%) of **7a**. Colourless oil. IR: 3070*w*, 3040*w*, 2990*w*, 2960*w*, 2940*w*, 2905*w*, 1830*s*, 1723*w*, 1660*s*, 1500*w*, 1475*w*, 1450*m*, 1418*w*, 1385*m*, 1352*m*, 1290*m*, 1260*w*, 1205*s*, 1195*s*, 1180*m*, 1168*s*, 1160*m*, 1093*w*, 1076*m*, 1020*s*, 1010*s*, 962*s*, 940*w*, 920*w*, 902*w*, 865*w*, 725*s*, 695*m*, 665*m*. ^{1}H-NMR: 7.75–7.65 (*m*, 2 arom. H); 7.6–7.4 (*m*, 3 arom. H); 4.65–4.5 (*ABX*$_3$, CH_3CH_2O); 1.50 (*t*, *J* = 7.1, CH_3CH_2O). ^{13}C-NMR: 159.8, 157.5 (2*s*, C(5), C(4)); 131.4 (*s*, 1 arom. C); 130.6, 128.5, 127.6 (3*d*, 5 arom. C); 121.4 (*q*, ^1J(C,F) = 285, CF_3); 97.2 (*q*, ^2J(C,F) = 30, C(2)); 68.3 (*t*, CH_3CH_2O); 13.8 (*q*, CH_3CH_2O). MS: 273 (2, M^+), 205 (7), 204 (57), 200 (27), 176 (6), 150 (10), 127 (6), 106 (8), 105 (100), 104 (5), 103 (6), 77 (28). Anal. calc. for $C_{12}H_{10}F_3NO_3$ (273.21): C 52.75, H 3.69, F 20.86, N 5.13; found: C 52.57, H 3.95, F 20.80, N 4.92.

1.2.2.5. *4-Isopropoxy-2-phenyl-2-(trifluoromethyl)-1,3-oxazol-5(2*H*)-one* (**7b**). a) To a soln. of 955 mg (6.0 mmol) of **6b** and 1.04 g (6.0 mmol) of trifluoroacetophenone in 15 ml of Et_2O at r.t. were added 3 drops of $BF_3 \cdot Et_2O$. After 24 h, the soln. was filtrated (colourless **8**), the solvent removed, and the residue chromatographed (Et_2O/hexane 1:15): 487 mg (28.3%) of **7b**. Colourless oil. IR: 3033*w*, 2990*w*, 2940*w*, 1829*s*, 1725*w*, 1660*s*,

1500*w*, 1465*w*, 1450*w*, 1410*w*, 1388*w*, 1375*w*, 1338*w*, 1290*m*, 1260*w*, 1205*s*, 1193*s*, 1180*s*, 1168*s*, 1158*s*, 1105*m*, 1077*w*, 1013*s*, 962*m*, 940*w*, 921*w*, 915*w*, 725*s*, 695*w*, 665*w*. ^{1}H-NMR: 7.8–7.7 (*m*, 2 arom. H); 7.6–7.4 (*m*, 3 arom. H); 5.27 (*sept.*, *J* = 6.2, $(CH_3)_2CHO$); 1.50, 1.46 (2*d*, *J* = 6.2, $(CH_3)_2CHO$). ^{13}C-NMR: 159.0, 157.9 (2*s*, C(5), C(4)); 131.5 (*s*, 1 arom. C); 130.6, 128.5, 127.6 (3*d*, 5 arom. C); 121.5 (*q*, ^1J(C,F) = 285, CF_3); 97.4 (*q*, ^2J(C,F) = 32, C(2)); 77.0 (*d*, $(CH_3)_2CHO$); 21.1 (*q*, $(CH_3)_2CHO$). MS: 287 (2, M^+), 219 (8), 218 (67), 201 (6), 200 (46), 177 (10), 176 (100), 150 (8), 127 (6), 106 (6), 105 (75), 104 (21), 103 (15), 77 (33), 76 (7), 51 (11), 43 (77). Anal. calc. for $C_{13}H_{12}F_3NO_3$ (287.24): C 54.36, H 4.21, F 19.84, N 4.88; found: C 54.50, H 4.45, F 19.73, N 5.06.

b) A suspension of 468 mg (2.4 mmol) of **5b** and 417 mg (2.4 mmol) of trifluoroacetophenone in 20 ml of Et_2O was stirred for 4 d. According to TLC and IR, no oxazolone has been formed. After addition of 0.5 ml (*ca.* 5.6 mmol) of Et_3N, stirring for 2 h, addition of 10 drops of $BF_3 \cdot Et_2O$, and stirring overnight, the soln. was filtrated (colourless **8**), the solvent removed, and the residue chromatographed: 136 mg (20%) of **7b**.

1.2.2.6. *4-Isopropoxy-2,2-bis(trichloromethyl)-1,3-oxazol-5(2*H*)-one* (**7c**). To a soln. of 955 mg (6 mmol) of **6b** in 10 ml of Et_2O were added at r.t. a soln. of 2.38 g (9 mmol) of hexachloroacetone and 3 drops of $BF_3 \cdot Et_2O$. After stirring for 4 d and usual workup, chromatography yielded 107 mg (4.7%) of **7c**. White crystals. M.p. 86.2–87.0°. IR: 3060*w*, 2990*w*, 2940*w*, 2870*w*, 1855*m*, 1835*s*, 1655*s*, 1465*w*, 1412*w*, 1388*w*, 1378*w*, 1337*m*, 1162*s*, 1102*s*, 1040*m*, 930*s*, 905*m*, 862*s*, 688*w*, 670*s*. ^{1}H-NMR: 5.29 (*sept.*, *J* = 6.2, $(CH_3)_2CHO$); 1.51 (*d*, *J* = 6.2, $(CH_3)_2CHO$). ^{13}C-NMR: 162.1, 157.3 (2*s*, C(5), C(4)); 102.3 (*s*, C(2)); 98.5 (*s*, 2 CCl_3); 78.7 (*d*, $(CH_3)_2CHO$); 21.2 (*q*, $(CH_3)_2CHO$). MS: 262 (5, 379 – CCl_3), 261 (2), 260 (12, 377 – CCl_3), 259 (2), 258 (13, 375 – CCl_3), 257 (1), 234 (2), 232 (7), 230 (7), 220 (19), 218 (39), 216 (35), 192 (22), 190 (68), 188 (70), 147 (9), 145 (9), 126 (8), 121 (12), 119 (37), 117 (38), 110 (8), 84 (7), 82 (10), 69 (11), 63 (9), 44 (24), 43 (100), 42 (23), 41 (99). Anal. calc. for $C_8H_7Cl_6NO_3$ (377.87): C 25.43, H 1.87, Cl 56.29, N 3.71; found: C 25.66, H 2.00, Cl 56.27, N 3.99.

1.2.2.7. *4-Phenoxy-2,2-bis(trichloromethyl)-1,3-oxazol-5(2*H*)-one* (**7d**). To a suspension of 6.5 g (28 mmol) of **5c** in 20 ml of Et_2O were added 8.2 g (30.8 mmol) of hexachloroacetone and 5 drops of $BF_3 \cdot Et_2O$. After cooling to –10°, 2.83 g (28 mmol) of Et_3N in 10 ml of Et_2O were slowly added, the mixture stirred for 36 h at –10°, filtrated, washed with 2N NaOH and H_2O, and dried (Na_2SO_4). Evaporation of the solvent and chromatography (Et_2O/hexane 1:20) yielded 480 mg (4.2%) of **7d**. White crystals. M.p. 132°. IR: 3045*w*, 3030*w*, 3020*w*, 1835*s*, 1764*w*, 1658*s*, 1600*w*, 1588*m*, 1490*m*, 1458*w*, 1392*s*, 1245*w*, 1185*s*, 1170*m*, 1150*m*, 1072*w*, 1032*m*, 1025*m*, 930*m*, 904*m*, 864*s*, 832*m*, 692*w*, 682*w*, 670*m*. ^{1}H-NMR: 7.55–7.3 (*m*, 5 arom. H). ^{13}C-NMR: 161.8, 156.8 (2*s*, C(5), C(4)); 152.3 (*s*, 1 arom. C); 130.0, 127.2, 119.6 (3*d*, 5 arom. C); 102.3 (*s*, C(2)); 98.0 (*s*, 2 CCl_3). CI-MS: 419 (7), 418 (5), 417 (10), 416 (5), 415 (32), 414 (22), 413 (65), 412 (35), 411 (59), 410 (13), 409 (2), 408 (2). MS: 415 (5), 413 (11), 411 (13), 409 (6), 296 (9), 294 (29), 292 (29), 268 (9), 266 (30), 264 (30), 240 (7), 238 (22), 236 (23), 230 (8), 205 (27), 203 (43), 199 (31), 178 (10), 177 (13), 175 (19), 161 (9), 159 (27), 157 (25), 152 (9), 120 (8), 119 (33), 117 (31), 112 (12), 110 (14), 94 (96), 77 (100). Anal. calc. for $C_{11}H_5Cl_6NO_3$ (411.89): C 32.08, H 1.22, Cl 51.64, N 3.40; found: C 32.34, H 1.47, Cl 51.98, N 3.66.

1.2.2.8. *2,2-Dimethyl-4-isopropoxy-1,3-oxazol-5(2*H*)-one* (**7e**). A soln. of 955 mg (6 mmol) of **6b**, 522 mg (9 mmol) of acetone, and 5 drops of $BF_3 \cdot Et_2O$ in 25 ml of Et_2O was stirred for 10 d at r.t. After filtration and washing with H_2O, the mixture was dried (Na_2SO_4), the solvent removed, and the residue chromatographed (Et_2O/hexane 1:15): 340 mg of **8**, *ca.* 30 mg of dialkyl oxalate, and 22 mg (2.0%) of **7e**. IR: 2960*s*, 2930*s*, 2875*m*, 2860*m*, 1795*s*, 1653*s*, 1468*w*, 1452*w*, 1383*w*, 1372*w*, 1310*w*, 1246*m*, 1340*w*, 1243*m*, 1190*m*, 1155*w*, 1105*w*, 1095*m*, 910*w*. ^{13}C-NMR: 160.2, 158.8 (2*s*, C(5), C(4)); 101.4 (*s*, C(2)); 74.7 (*d*, $(CH_3)_2CHO$); 27.1 (*q*, 2 CH_3–C(2)); 21.3 (*q*, $(CH_3)_2CHO$).

1.2.2.9. *4-Isopropoxy-2-phenyl-1,3-oxazol-5(2*H*)-one* (**7f**). A soln. of 1.0 g (6.28 mmol) of **6b** in 10 ml of Et_2O was added dropwise at r.t. to a soln. of 0.66 g (6.28 mmol) of benzaldehyde and 2 drops of $BF_3 \cdot Et_2O$ in 20 ml of Et_2O. After stirring under N_2 for 7 d, GLC analysis indicated formation of 13.5% of **7f**. Usual workup after 8 d and chromatography (Et_2O/hexane 1:20 and 1:10) yielded 100 mg (7.3%) of **7f**. Colourless crystals. M.p. 42.0–43.4°. IR: 3065*w*, 3035*w*, 2982*w*, 2938*w*, 1810*s*, 1730*w*, 1655*s*, 1495*w*, 1465*w*, 1453*w*, 1398*w*, 1385*m*, 1375*w*, 1325*w*, 1290*m*, 1183*w*, 1135*s*, 1110*s*, 1068*w*, 1030*w*, 980*w*, 955*w*, 920*m*, 862*w*, 845*w*, 730*w*, 695*m*, 635*w*. ^{1}H-NMR: 7.5–7.4 (*m*, 5 arom. H); 6.75 (*s*, H–C(2)); 5.20 (*sept.*, *J* = 6.2, $(CH_3)_2CHO$); 1.49, 1.47 (2*d*, *J* = 6.2, $(CH_3)_2CHO$). ^{13}C-NMR: 160.0, 157.4 (2*s*, C(5), C(4)); 134.9 (*s*, 1 arom. C); 129.7, 128.8, 126.5 (3*d*, 5 arom. C); 95.6 (*d*, C(2)); 75.4 (*d*, $(CH_3)_2CHO$); 21.4 (*q*, $(CH_3)_2CHO$). MS: 219 (6, M^+), 180 (5), 177 (6), 165 (12), 133 (11), 132 (100), 117 (6), 105 (20), 104 (9), 78 (5), 77 (34), 51 (15), 44 (10), 43 (34), 41 (18), 40 (30).

2. Synthesis of Triethyl 1,3,5-Triazine-2,4,6-tricarboxylate (**8**) [14]. – According to [14], dry HCl gas was bubbled through 200 mg (2.0 mmol) of ethyl cyanoformate at 0° during 20 min. After 3 d at r.t., the formed crystals were separated by filtration, washed with Et_2O, and recrystallized from EtOH: 125 mg (63.1%) of **8**. Colourless crystals. M.p. 165°. IR: 3015*w*, 3002*w*, 2980*w*, 2940*w*, 2904*w*, 1750*s*, 1535*s*, 1465*w*, 1435*w*, 1425*w*, 1400*w*, 1380*m*, 1353*w*, 1298*w*, 1235*s* (br.), 1095*w*, 1017*s*, 860*w*, 710*w*, 665*w*. ^{1}H-NMR: 4.59 (*q*, *J* = 7.1, CH_3CH_2O); 1.49

(*t*, *J* = 7.1, CH_3CH_2O). ^{13}C-NMR: 166.9, 161.2 (2*s*, C=O, arom. C); 64.0 (*t*, CH_3CH_2O); 14.0 (*q*, CH_3CH_2O). CI-MS: 298 ([M^++1]).

Compound **8** was obtained in all experiments, when mixtures of imino-esters **6a-c** and ketones were treated with $BF_3 \cdot Et_2O$ (identified by IR, NMR, or MS).

3. Thermolysis of 4-Alkoxy-2-phenyl-1,3-oxazol-5(2*H*)-ones. – 3.1. *Thermolysis of* **7b**. 3.1.1. *In the Presence of Trifluoroacetophenone.* In a degassed and sealed tube, a mixture of 100 mg (0.35 mmol) of **7b** and 140 mg (0.8 mmol) of trifluoroacetophenone was heated to 155° for 30 min. After evaporation of remaining trifluoroacetophenone at 50°, the yellow oil was chromatographed (Et_2O/hexane 1:40): 31 mg (21.3%) of trans-*2,5-dihydro-4-isopropoxy-2,5-diphenyl-2,5-bis(trifluoromethyl)-1,3-oxazole* (*trans*-**9**), 28 mg (19.3%) of *cis*-**9**, 5 mg (6%) of *3-isopropoxy-1-(trifluoromethyl)-1*H*-isoindole* (**10b**), and 50 mg (50%) of **7b**.

Data of trans-**9**: white crystals. M.p. 82.4–83.0°. IR: 2980*w*, 1665*m*, 1500*w*, 1468*w*, 1450*w*, 1385*w*, 1375*w*, 1330*w*, 1272*w*, 1255*w*, 1192*s*, 1135*m*, 1105*w*, 1070*w*, 1058*m*, 1035*w*, 1018*w*, 960*w*, 948*w*, 915*w*, 728*m*, 698*w*, 670*w*. ^{1}H-NMR: 7.85–7.75 (*m*, 4 arom. H); 7.5–7.4 (*m*, 6 arom. H); 5.28 (*sept.*, *J* = 6.2, $(CH_3)_2CHO$); 1.45, 1.43 (2*d*, *J* = 6.2, $(CH_3)_2CHO$). ^{13}C-NMR: 165.0 (*s*, C(4)); 135.1, 131.5 (2*s*, 2 arom. C); 129.5, 129.4, 128.2, 128.0, 127.2, 126.4 (6*d*, 10 arom. H); 122.7, 122.2 (2*q*, ^1J(C,F) = 286, 2 CF_3); 104.5 (*q*, ^2J(C,F) = 32, C(2)); 86.9 (*q*, ^2J(C,F) = 32, C(5)); 76.4 (*d*, $(CH_3)_2CHO$); 24.1, 21.2 (2*q*, $(CH_3)_2CHO$). MS: 417 (<1, M^+), 348 (30), 306 (77), 200 (12), 198 (11), 105 (100), 104 (30), 103 (20), 97 (18), 94 (38), 85 (19), 83 (20), 77 (61), 73 (13), 71 (29), 69 (29), 57 (59), 55 (38), 51 (20), 45 (21), 44 (36), 43 (95), 41 (50). Anal. calc. for $C_{20}H_{17}F_6NO_2$ (417.35): C 57.56, H 4.11, F 27.31, N 3.36; found: C 58.50, H 4.43, F 26.11, N 3.38.

Data of cis-**9**: white crystals. M.p. 77.4–78.0°. IR: 3025*w*, 2983*w*, 2960*w*, 2940*w*, 1668*s*, 1498*w*, 1468*w*, 1450*w*, 1395*w*, 1385*m*, 1375*w*, 1330*w*, 1300*m*, 1280*w*, 1255*w*, 1200*s*, 1185*s*, 1135*m*, 1105*w*, 1070*w*, 1060*m*, 1035*w*, 1018*m*, 960*w*, 948*m*, 918*w*, 910*w*, 728*m*, 695*m*, 665*w*. ^{1}H-NMR: 7.7–7.55 (*m*, 4 arom. H); 7.3–7.15 (*m*, 6 arom. H); 5.33 (*sept.*, *J* = 6.2, $(CH_3)_2CHO$); 1.52, 1.46 (2*d*, *J* = 6.2, $(CH_3)_2CHO$). ^{13}C-NMR: 165.1 (*s*, C(4)); 135.4, 131.9 (2*s*, 2 arom. C); 129.4, 128.1, 127.8, 127.4, 126.6 (5*d*, 10 arom. C); 122.5, 122.0 (2*q*, ^1J(C,F) = 285, 2 CF_3); 104.4 (*q*, ^2J(C,F) = 32, C(2)); 87.1 (*q*, ^2J(C,F) = 32, C(5)); 76.6 (*d*, $(CH_3)_2CHO$); 21.4, 21.2 (2*q*, $(CH_3)_2CHO$). MS: 417 (1, M^+), 348 (74), 306 (100), 200 (30), 150 (10), 127 (11), 105 (100), 104 (60), 103 (28), 77 (80), 69 (11), 51 (16), 43 (73), 41 (28). Anal. calc. for $C_{20}H_{17}F_6NO_2$ (417.35): C 57.56, H 4.11, F 27.31, N 3.36; found: C 58.40, H 4.54, F 26.80, N 3.39.

Data of **10b**: colourless oil. For spectral data, see *3.1.2*.

3.1.2. *In the Absence of Trifluoroacetophenone.* a) In a degassed and sealed tube, 60 mg (0.21 mmol) of **7b** were heated 1 h to 155°. The yellow, semisolid material was dissolved in Et_2O/acetone and chromatographed (Et_2O/hexane 1:20): 10 mg (16%) of **7b** and 20 mg (39%) of **10b**. IR: 3060*w*, 2980*w*, 2935*w*, 2870*w*, 1825*w*, 1722*w*, 1665*w*, 1623*m*, 1600*m*, 1574*s*, 1465*w*, 1450*w*, 1405*s*, 1385*m*, 1373*w*, 1338*m*, 1320*m*, 1270*m*, 1214*w*, 1188*m*, 1165*s*, 1124*s*, 1110*m*, 1098*m*, 1052*w*, 1015*w*, 922*w*, 910*w*, 883*w*, 855*w*, 835*w*, 700*s*. ^{1}H-NMR: 7.7–7.55 (*m*, 2 arom. H); 7.55–7.45 (*m*, 2 arom. H); 5.39 (*sept.*, *J* = 6.2, $(CH_3)_2CHO$); 5.15 (*q*, ^3J(H,F) = 7.8, H–C(1)); 1.45, 1.44 (2*d*, *J* = 6.2, $(CH_3)_2CHO$). ^{13}C-NMR: 172.0 (*s*, C(3)); 144.4, 134.5 (2*s*, C(7a), C(3a)); 129.9, 129.0 (2*d*, 2 arom. C); 124.9 (*q*, ^1J(C,F) = 279, CF_3); 123.5, 121.1 (2*d*, 2 arom. C); 72.1 (*d*, $(CH_3)_2CHO$); 69.1 (*q*, ^2J(C,F) = 30, C(1)); 21.9, 21.7 (2*q*, $(CH_3)_2CHO$). CI-MS: 245 (30), 244 (100, [M + 1]$^+$), 202 (51). Anal. calc. for $C_{12}H_{12}F_3NO$ (243.23): C 59.26, H 4.97, F 23.43, N 5.76; found: C 59.63, H 5.01, F 22.87, N 5.88. Mol.weight (osmometr., benzene): found 259.

b) A soln. of 53 mg (0.18 mmol) of **7b** in 1 ml of i-PrOH was heated for 1 h to 155° (sealed tube). Workup according to *a* yielded 16 mg (30%) of **7b** and 12 mg (27.4%) of **10b**.

c) A soln. of 40 mg (0.14 mmol) of **7b** in 2 ml of DMF containing *ca.* 30 mg of H_2O was heated to 150°. Evaporation and chromatography gave 27 mg (79%) of **10b**.

3.2. *Thermolysis of* **7a**. A soln. of 109 mg (0.4 mmol) of **7a** in 1 ml of toluene was heated for 3 h to 155° (sealed tube). According to GLC, the mixture consisted of 20% of **7a** and 74% of *3-ethoxy-1-(trifluoromethyl)-1*H*-isoindole* (**10a**). Chromatography (Et_2O/hexane 1:30) yielded 11 mg (10.1%) of **7a** and 62 mg (67.7%) of **10a**. Colourless oil. IR: 2990*w*, 2960*w*, 2930*w*, 1625*m*, 1602*w* *1578s*, 1480*w*, 1445*w*, 1415*m*, 1382*m*, 1351*s*, 1335*m*, 1318*w*, 1270*s*, 1212*w*, 1190*w*, 1167*s*, 1125*s*, 1098*w*, 1055*w*, 1018*w*, 910*w*, 882*w*, 855*w*, 730*w*, 700*m*. ^{1}H-NMR: 7.7–7.55 (*m*, 2 arom. H); 7.55–7.45 (*m*, 2 arom. H); 5.14 (*sept.*, ^3J(H,F) = 7.8, H–C(1)); 4.65–4.45 (*ABX*$_3$, CH_3CH_2O); 1.47 (*t*, *J* = 7.1, CH_3CH_2O). ^{13}C-NMR: 172.7 (*s*, C(3)); 144.4, 134.0 (2*s*, C(7a), C(3a)); 130.0, 129.1 (2*d*, 2 arom. C); 125.2 (*q*, ^1J(C,F) = 279, CF_3); 123.6, 121.1 (2*d*, 2 arom. C); 69.0 (*q*, ^2J(C,F) = 31, C(1)); 64.8 (*t*, CH_3CH_2O); 14.3 (*q*, CH_3CH_2O). MS: 229 (14, M^+), 202 (7), 201 (11), 166 (7), 165 (26), 132 (100), 104 (14), 103 (5), 102 (5), 77 (15), 76 (10), 75 (5), 51 (7), 50 (7).

3.3. *Thermolysis of* **7f**. A soln. of 62 mg (0.28 mmol) of **7f** in 2 ml of toluene was heated for 30 min to 155° (sealed tube). The dark-brown mixture was chromatographed with Et_2O/hexane 1:20 to 1:5: 11 mg (22.5%) of

3-isopropoxy-1H-isoindole (**10c**). Yellow oil. IR: 2980*w*, 2935*w*, 2910*w*, 1622*m*, 1602*m*, 1571*s*, 1525*w*, 1468*w*, 1395*m*, 1382*m*, 1372*m*, 1340*w*, 1328*m*, 1317*m*, 1190*w*, 1140*w*, 1113*m*, 1095*w*, 1026*w*, 1014*w*, 925*w*, 725*m*, 662*w*. ^{1}H-NMR: 7.65–7.3 (*m*, 4 arom. H); 5.31 (*sept.*, J = 6.2, $(CH_3)_2CHO$); 4.61 (*s*, 2 H–C(1)); 1.44 (*d*, J = 6.2, $(CH_3)_2CHO$). ^{13}C-NMR: 169.3 (*s*, C(3)); 150.4, 133.5 (2*s*, C(7a), C(3a)); 128.8, 126.9, 122.2, 120.6 (4*d*, 4 arom. C); 70.8 (*d*, $(CH_3)_2CHO$); 58.2 (*t*, C(1)); 22.0 (*q*, $(CH_3)_2CHO$). MS: 175 (3, M^+), 135 (10), 134 (100), 133 (20), 132 (35), 118 (6), 117 (34), 116 (13), 106 (5), 105 (39), 104 (28), 91 (6), 90 (9), 89 (9), 78 (7), 77 (23), 76 (7), 63 (5), 57 (6), 51 (10), 50 (5), 43 (7), 41 (13), 39 (8).

4. X-Ray Structure Determination of *cis*-9. – Crystals of *cis*-**9** (*Scheme 4*), obtained from hexane, were used for X-ray structure determination. Data were collected on a *Nicolet-R3* diffractometer fitted with a graphite monochromator in the ω-scan mode with Mo$K\alpha$ radiation ($2\theta_{max}$ = 50°) at 294 K. From 3447 unique reflections, 2090 with $I > 2.5\,\sigma(I)$ have been used in the refinement; 298 least-square parameters. The usual corrections except for absorptions were applied. The structure was determined by direct methods and refined by blocked-cascade refinements with *ca.* 100 variables per block. The complete heavy-atom network was revealed from the best E map from SHELXTL version 5.1 [21]. The 17 H-atoms were the largest peaks in a difference *Fourier* map calculated with anisotropic refinement. R = 0.041 (R_w = 0.038); $w = 1/(\sigma^2(F) + 0.00009F^2)$.

Crystallographic Data. Formula: $C_{20}H_{17}F_6NO_3$ (417.354). Cell dimensions[8]): a = 9.730(2), b = 12.561(3), c = 8.956(3) Å, α = 106.38(2), β = 105.43(2), γ = 74.43(2)°; V = 989.9(5) Å^3. Calculated density: 1.400 Mg · m^{-3}. Space group: $P\bar{1}$, triclinic, centrosymmetric; Z = 2.

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