Oxo- and Imino-functionalized 1,2-Oxazetidines. An Overview

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This review article describes syntheses and reactions of 1,2-oxazetidines that have an oxo or (substituted) imino group attached to either C-3 or C-4. The rare case of a bifunctional derivative is also treated. In a final chapter, spectroscopic properties are surveyed.

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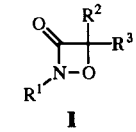
Introduction.

1,2-Oxazetidine chemistry – thus far an object of limited attention [1] – has developed within two distinct fields. The first of these can be said fluoroorganic, and studies were well advanced at the time of a previous review [2]. In the second area, target of this survey, the general systems



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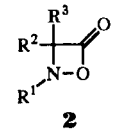

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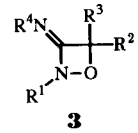

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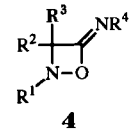

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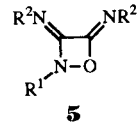

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1-4 (including the rare type **5**) are encountered. Their chemistry is of more recent date, although structures such as **1** and **2** are known since 1911 [3]. Outside these two regions remarkably few 1,2-oxazetidines exist [4] and some structural claims [5] have even been rejected [6].

The following pages, with their focus on **1-5**, are meant to be illustrative rather than encyclopedic.

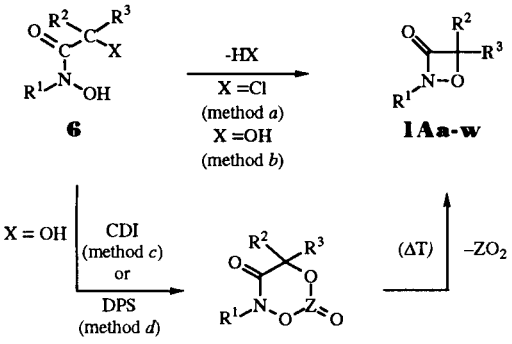
I. Synthesis.

A. 1,2-Oxazetidin-3-ones **1**.

1. Cyclization of α-Functionalized Hydroxamic Acids.

On reacting α-chlorodiphenylacetyl chloride with both *N*-alkyl- [7] and *N*-arylhydroxylamines [3,7], the respective oxazetidinones, *e.g.* **1Aa,b,d**, have been obtained

Scheme 1



6 **1Aa-w**

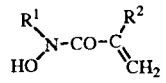
7: Z = C
7': Z = S

CDI = 1,1'-carbonyldiimidazole
DPS = 2,2'-dipyridyl sulfite

1A: $R^1/R^2/R^3$/*method*, yield (%) [reference] [a]

- **a** Ph/Ph/Ph/*a*, 100 [3], 33 [7]
- **b** Me/Ph/Ph/*a*, 90 [7]; *c*, 70 [11a]
- **c** *i*-Pr/Ph/Ph/*c*, 82 [11a]
- **d** *c*-C_6H_{11}/Ph/Ph/*a*, 30 [7]; *c*, 70 [11a], 95 [11d]
- **e** *t*-Bu/4-MeC_6H_4/4-MeC_6H_4/*c*, 96 [1d]
- **f** CH_2Ph/4-MeC_6H_4/4-MeC_6H_4/*c*, 97 [11d]
- **g** CH(Me)Ph/4-MeC_6H_4/4-MeC_6H_4/*c*, 85 [10a]
- **h** CH_2Ph/4-$MeOC_6H_4$/4-$MeOC_6H_4$/*b*, 92 [9]; *c*, 96 [10a]
- **i** $CHPh_2$/4-$MeOC_6H_4$/4-$MeOC_6H_4$/*b*, 42 [10a]
- **k** Me/2-thienyl/2-thienyl/*c*, 86 [11b]
- **l** *c*-C_6H_{11}/3-thienyl/3-thienyl/*c*, 96 [11d]
- **m** *c*-C_6H_{11}/4-ClC_6H_4/4-ClC_6H_4/*c*, 42, 95 [11d]
- **n** Me/4-ClC_6H_4/4-ClC_6H_4/*d*, 83 [12]
- **o** Me/2-thienyl/CH_2Ph/*c*, 83 [11b]
- **p** CH_2Ph/4-$MeOC_6H_4$/Me/*c*, 81 [12]
- **q** Me/*c*-C_3H_5/4-ClC_6H_4/*c*, 54 [12]; *d*, 89 [12]
- **r** Me/Ph/Me/*d*, 83 [12]
- **s** CH(*c*-C_3H_5)Me/4-ClC_6H_4/Me/*d*, 75 [12]
- **t** *c*-C_6H_{11}/Ph/*c*-C_3H_5/*d*, 82 [12]
- **u** CH_2Ph/4-$PhOC_6H_4$/Me/*d*, 79 [12]
- **v** Me/3-thienyl/H/*c*, 32 [11c]
- **w** PhC(=NOH)CMe_2/H/H/*a*, 54 [8]

[a] Underlined yield figures: addition of freshly regenerated molecular sieves (4Å) to **7**/**7'**.



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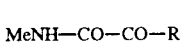
- **a** R^1 = Ph, R^2 = Me
- **b** R^1 = CH_2Ph, R^2 = 4-$MeOC_6H_4$



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- **a** R = 3-thienyl
- **b** R = 2-thienyl
- **c** R = Ph

(Scheme 1, method a). The intermediary α-chloro hydroxamic acids **6** (X = Cl) were not isolated. This kind of ring closure also led to the 4-unsubstituted derivative **1Aw** [8]. However, attempts to cyclize 2-bromo-2-methyl-*N*-phenylpropiohydroxamic acid (**6**, R^1 = Ph, R^2 = R^3 = Me, X = Br) by treatment with alkali hydroxide gave rise to the formation of compound **8a** [7]. Ring closing of α-hydroxy substituted hydroxamic acids **6** (X = OH) by intramolecular elimination of water was feasible with derivatives having for R^2 and R^3 electron-releasing ligands such as 4-$MeOC_6H_4$ (method b; **1Ah,i**); molecular sieves (4 Å) [9] and anhydrous hydrogen chloride [10a] proved effective.

Yet, a major improvement in making **1** - discovered accidentally [11a] - has turned out to be initial transformation of **6** (X = OH) into the six-membered ring **7** or **7'**. These compounds, under conditions depending upon R^2 and R^3, more or less readily loose carbon and sulfur dioxides, respectively, to give the desired oxazetidines **1** in good yield (methods c,d) [10a,11,12]. The final step bears a formal resemblance to the thermolytic ring contraction of 1,2-oxazinane-3,6-diones to β-lactams [13]. Handiness of the procedure, in conjunction with facile access to the precursors **6** (X = OH), has ultimately led to a plethora of **1**, only part of which can be mentioned here. Two main conclusions have been reached:

(i) Liberation of carbon dioxide from **7** is greatly favored by substituents R^2 and R^3 that have a +M effect. Thus, while **7b-d** [11a] and **7m** [11d] require prolonged heating to 110°, ring contraction of **7e,f,l** [11d], **7g,h** [10a] and **7k** [11b] proceeds at room temperature (substituents R^1-R^3 as in **1**). When R^2 = R^3 = 4-$MeOC_6H_4$ or 2-and 3-thienyl and also in the case R^2 = 2-thienyl/R^3 = Ph, this transformation occurs so rapidly that the intermediate **7** eludes detection [11b,d]. Since free imidazole (which is still present in the reaction mixture) causes ring expansion of the product **1Ai** particularly fast (see Section II.A.2.), this compound is not available by method c. Oxazetidines **1** that have only one electron-donating substituent such as **1Ao** [11b] and **1Ap** [12] are also formed under relatively mild conditions. This is likewise true of **1Aq** because here the activating influence of the cyclopropyl group far outweighs the opposite effect of the 4-ClC_6H_4 ligand [12].

(ii) Replacing carbon with sulfur in the structural unit -O-C(O)-O- of **7** renders the six-membered heterocycle

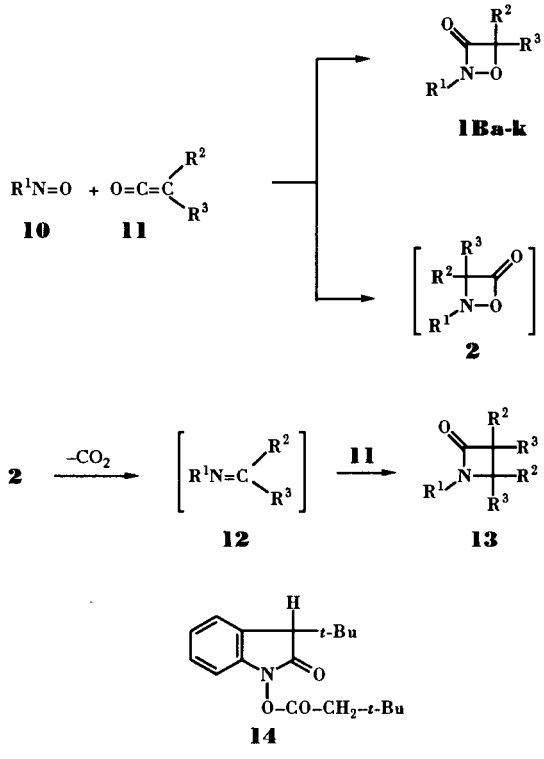
much more prone to ring contraction [12]. In contrast to **7m** (see above), the (elusive) intermediate **7'n** reacts within several minutes at room temperature [12]. Moreover, an oxazetidine such as **1Ar** - whose preparation failed by method c (because of thermal stability of **7r**) [11a] - could readily be obtained *via* the sulfite **7'r**; only a strong electron-withdrawing group such as 4-$O_2NC_6H_4$ at ring carbon of **7'** proved an obstacle to oxazetidine formation [12]. A further advantage of method d is the non-basic reaction medium. This, in contrast to variant c, allows the synthesis of 2-benzhydryl substituted members **1** (**1Ai** and congeners) [12]. On the other hand, acidic workup may give rise to ring opening as observed with **1Ap** which under the conditions of method d gave the amide **8b** [12].

4-Monosubstituted oxazetidines of the **1A** series have been prepared only once, **1Av**, and here a considerable amount of the α-oxoamide **9a** was found as by-product (the latter has been shown not to arise from the four-membered ring) [11c]. Interestingly, analogous amides, *viz.* **9b** [11c] and **9c** [14] were the sole materials isolated on thermolysis of the appropriate heterocycles **7**. The preparation of 2-aryl substituted oxazetidines **1** by either method c or d has not been reported yet. As regards the mechanism, the transformation of **7** into **1** has been discussed at length [9]. Beyond hydrogen chloride and imidazole, molecular sieves have been found to act as catalyst. Use has been made of the latter which allows certain ring contractions of **7**/**7'** to occur under milder conditions (*i.e.* in the case of **7** at ambient temperature) [11d,12]. A conspicuous example is **1Am** which on employment of method c largely underwent [2+2] cycloreversion (*cf.* Section II.A.1.) [11d]. Ethanolysis of **7b** at 20° to give **1Ab** as another mild process has been mentioned but this variant has not been pursued any further [14].

2. [2+2] Cycloaddition of Nitroso Compounds to Ketenes.

Aromatic nitroso compounds **10** (R^1 = Ph, 4-RC_6H_4) are long known to react readily at room temperature with diphenylketene **11** (R^2 = R^3 = Ph), thereby producing the cycloadducts **1B** along with their isomers **2** (the latter decompose spontaneously; Scheme 2). Early workers [3,15] have realized the low regioselectivity of this reaction only when submitting unsubstituted nitrosobenzene; on employment of 4-substituted derivatives, they obtained either oxazetidin-3-ones, *e.g.* **1Bb,d**, or β-lactams such as **13c,d**. However, a more recent study [16] has expectedly revealed that also in those cases the title reaction proceeds in *both* directions. So, the isomers **1B** and **2** (R^2 = R^3 = Ph) were found to have been formed in the ratio 84:16 (R^1 = Ph), 87:13 (R^1 = 4-MeC_6H_4), 79:21 (R^1 = 4-$MeOC_6H_4$), 32:68 (R^1 = 4-$Me_2NC_6H_4$) and 72:28 (R^1 = 4-$MeO_2CC_6H_4$), respectively; the proportions of the elusive compounds **2** were based on the final products **13** [16].

Scheme 2



1B:	$R^1/R^2/R^3$/yield (%) [reference]
a	Ph/Ph/Ph/63-65 [3], 45 [15], 60 [16]
b	4-ClC_6H_4/Ph/Ph/48 [15]
c	4-ClC_6H_4/4-ClC_6H_4/Ph/38 [15]
d	4-MeC_6H_4/Ph/Ph/38 [15]
e	4-$MeOC_6H_4$/Ph/Ph/– [16]
f	4-$Me_2NC_6H_4$/Ph/Ph/– [16] [a]
g	4-$MeO_2CC_6H_4$/Ph/Ph/(72) [16] [b]
h	*t*-Bu/*t*-Bu/H/61 [17]
i	Ph/*t*-Bu/H/11 [17]
k	CF_3/Ph/Ph/– [18]

[a] Formation detectable through [2+2] cycloreversion products **38**/**39** only (see Scheme 12). [b] Yield normalized to 100% (*cf.* **13e**).

13:	$R^1/R^2/R^3$/yield (%) [reference]
a	Ph/Ph/Ph/- [3,15], 13 [16] [a]
b	4-MeC_6H_4/Ph/Ph/13 [16]
c	4-$MeOC_6H_4$/Ph/Ph/40 [15], 22 [16]
d	4-$Me_2NC_6H_4$/Ph/Ph/65 [3], 61 [16]
e	4-$MeO_2CC_6H_4$/Ph/Ph/(28) [16] [b]

[a] In ref. [15]: precursor **12** (**13** not observed). [b] Yield normalized to 100% (*cf.* **1Bg**).

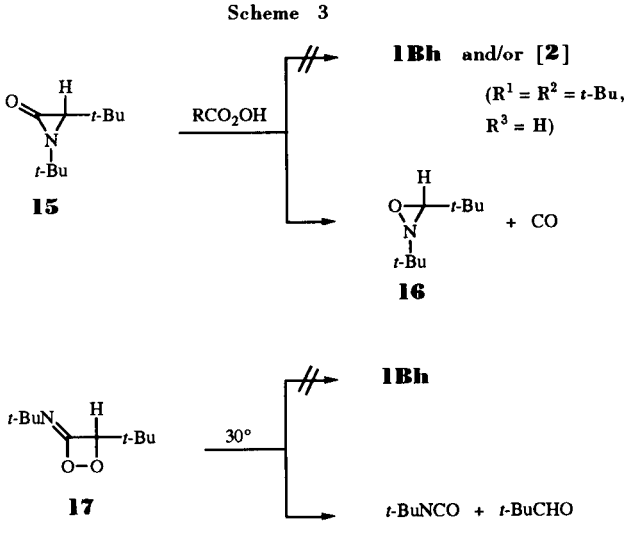
In contrast to the foregoing, cycloadditions with *tert*-butylketene **11** (R^2 = *t*-Bu, R^3 = H) occur regiospecifically, → **1Bh,i**, [17]. This excludes operation of the 'near-concerted' mechanism suggested to accommodate the above results with diphenylketene [16]. Apart from **1Bi**, the indolone derivative **14** (15% yield) and a 1:1 mixture

of nitrobenzene and azoxybenzene (totally 20%) have been isolated [17], while in the reaction of trifluoronitrosomethane **10** ($R^1 = CF_3$) with **11** ($R^2 = R^3 = Ph$) the oxazetidine **1Bk** has been the only product mentioned [18]. Attempts to add **10** ($R^1 = Ph$) onto the parent ketene **11** ($R^2 = R^3 = H$) have been reported unsuccessful [15].

3. Ineffectual Approaches.

A 1,2-oxazetidine has been invoked as one of the possible intermediates to account for the fragmentation products formed in the reaction of *cis*-1,2,3-triphenylaziridine with 3-chloroperbenzoic acid [19]. However, when this reaction was applied to the α-lactam **15**, instead of the four-membered ring **1Bh** [and/or derivatives of its unstable isomer **2** ($R^1 = R^2 = t$-Bu, $R^3 = H$)], the oxaziridine **16** and carbon monoxide were found (Scheme 3) [20a]. As for the

Scheme 3



mechanism of this transformation, a recent study on chiral **15** has demonstrated that loss of carbon monoxide is the *first* step; the resultant imine is then oxidized to **16** [20b]. This belies the 'aziridinone *N*-oxide theory' previously adhered to [20a].

1,2-Dioxetan-3-imines, which arise from photooxygenation of ketenimines [21], may be regarded as precursors to the oxazetidin-3-ones **1**. Yet, their instability does not allow for the necessary Dimroth rearrangement, → **1**, but rather results in [2+2] cycloreversion. This is shown here for the derivative **17** which on gentle warming gave *tert*-butyl isocyanate and pivalaldehyde (Scheme 3) [21b].

B. 1,2-Oxazetidin-4-ones **2**.

1. [2+2] Cycloaddition of Nitroso Compounds to Ketenes.

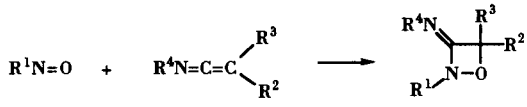
These oxazetidines are formed jointly with their isomers **1** and have therefore already been treated in Section I.A.2.

C. 1,2-Oxazetidin-3-imines **3**.

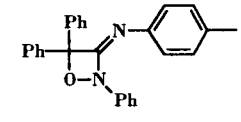
1. [2+2] Cycloaddition of Nitroso Compounds to Ketenimines.

In contrast with diphenylketene [16], ketenimines **18** have been found to add onto nitroso compounds **10** regiospecifically, thereby affording the oxazetidines **3** in moderate to fair yield (Scheme 4) [23-26]. In no case has an

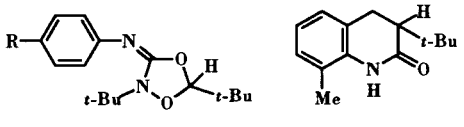
Scheme 4

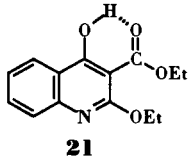


3:	$R^1/R^2/R^3/R^4$/yield (%) [reference]
a	Ph/Ph/Ph/Ph/- [22]
b	Ph/Ph/Ph/4-MeC_6H_4/60 [23a, 24]
c	4-BrC_6H_4/Ph/Ph/4-BrC_6H_4/60 [23a]
d	4-IC_6H_4/Ph/Ph/4-MeC_6H_4/33 [23b]
e	4-$O_2NC_6H_4$/Ph/Ph/4-MeC_6H_4/71 [23a]
f	Ph/Ph/Ph/4-$O_2NC_6H_4$/60 [24]
g	Ph/Ph/Ph/Q/53 [23c]
h	4-$Me_2NC_6H_4$/Ph/Ph/4-MeC_6H_4/- [23b] [a]
i	4-$Me_2NC_6H_4$/Ph/Ph/4-$O_2NC_6H_4$/- [24] [a]
k	*t*-Bu/Ph/Ph/4-MeC_6H_4/83 [24]
l	*t*-Bu/Ph/Ph/4-$O_2NC_6H_4$/73 [24]
m	*t*-Bu/*t*-Bu/H/Ph/24 [25]
n	*t*-Bu/*t*-Bu/H/4-MeC_6H_4/19 [25]
o	*t*-Bu/*t*-Bu/H/4-$MeOC_6H_4$/2 [25]
p	*t*-Bu/*t*-Bu/H/4-ClC_6H_4/35 [25]
q	*t*-Bu/*t*-Bu/H/4-$O_2NC_6H_4$/29 [25]
r	*t*-Bu/*t*-Bu/H/2,6-$Me_2C_6H_3$/19 [25]
s	Ph/*t*-Bu/H/2,6-$Me_2C_6H_3$/- [25] [a]
t	Ph/Ph/Me/Me_2(*t*-Bu)Si/- [26] [a]

Q = 

[a] Formation detectable through [2+2] cycloreversion products **39**/**46** only (see Scheme 17).





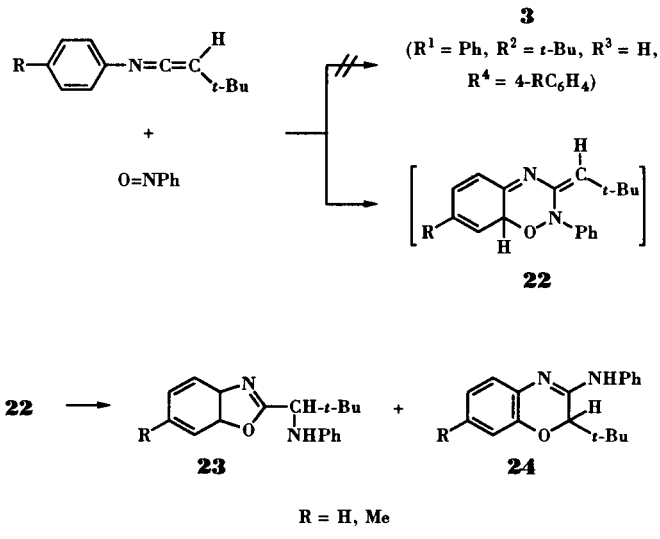
isomer **4** been detected. This specificity - unexpected in view of classical bond polarities - has been explained by photosensitization experiments (which showed a triplet nitroso species to be involved) [23b] as well as by FMO considerations [24,27]. Hence, doubt arises whether the oxazetidine **4a** (see below Scheme 8) [28] is formed *via* the ketenimine route (path b) which has been put forward in ref [29] as the sole pathway.

The ease of the above cycloadditions depends on both the nitroso component **10** and the ketenimine **18**. For example, the reactivity of **10** towards *N*-(4-nitrophenyl)diphenylketenimine **18** (R^2 = R^3 = Ph, R^4 = 4-$O_2NC_6H_4$) has been found to decrease in the order R^1 = 4-$Me_2NC_6H_4$ > Ph > *t*-Bu (relative rate of oxazetidine formation: **3i** > **3f** > **3l**) [24]. This behavior matches observations in the ketene series including the fact that *N*-nitroso compounds do not react at all [3,17,24]. When comparing the cycloaddition of 2-methyl-2-nitrosopropane **10** (R^1 = *t*-Bu) onto various *N*-aryl-*tert*-butylketenimines **18** (R^2 = *t*-Bu, R^3 = H, R^4 = 4-RC_6H_4) - which, in contrast to the aforementioned reactions, requires elevated temperatures -, the reactivity sequence is R = NO_2 > H > MeO (relative rate of oxazetidine formation: **3q** > **3m** > **3o**) [25]. The low yield of **3o** is due to enhanced instability with respect to [2+2] cycloreversion (see Section II.C.1.).

As by-products deserve especial mention: (i) 1,4,2-dioxazolidin-3-imines **19** (R = H, Me, Cl) which may occur during the preparation of **3m,n,p** (but which do not arise from these oxazetidines) [30], and (ii) the dihydroquinolone derivative **20** in the case of **2r** [25]. This compound is an oxidation product of the respective ketenimine **18** (R^2 = *t*-Bu, R^3 = H, R^4 = 2,6-$Me_2C_6H_3$), but attempts to generate it by treating the ketenimine with oxidizing agents such as activated manganese(IV) and silver(I) oxides, 3-chloroperbenzoic acid, an azomethine *N*-oxide or 2-methyl-2-nitropropane remained unrewarded [31].

Cycloaddition experiments with *N*-alkylketenimines proved to be entirely unsatisfactory, **18** (R^2 = *t*-Bu or Ph, R^3 = H, R^4 = *c*-C_6H_{11}/R^2 = Ph, R^3 = H, R^4 = *t*-Bu/R^2 = R^3 = Ph, R^4 = *c*-C_6H_{11}), as well as with dimethyl-*N*-phenylketenimine **18** (R^2 = R^3 = Me, R^4 = Ph) [24], and in an attempt to react bis(ethoxycarbonyl)-*N*-phenylketenimine **18** (R^2 = R^3 = CO_2Et, R^4 = Ph), the 'rearranged ketenimine' **21** was the only product [24,32]. Finally, the desired oxazetidines **3** did not result from nitrosobenzene and *tert*-butyl-*N*-phenylketenimines that have a free *ortho* position in the phenyl ligand. The respective benzoxazole **23** and benzoxazine **24** which were obtained instead (Scheme 5; low yield) are likely to arise from a transient [4+2] cycloadduct **22** as shown in ref [25].

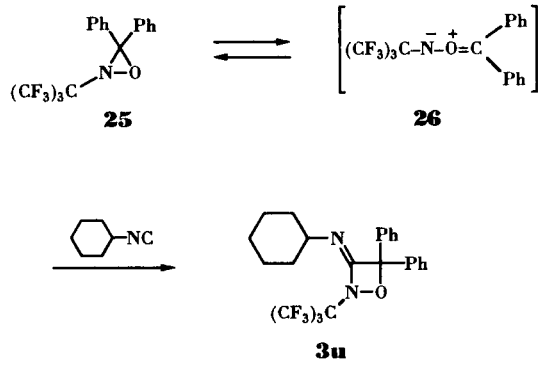
Scheme 5



2. [1+3] Cycloaddition of Isocyanides to Carbonyl Imines [33].

This approach to compounds of type **3** as exemplified in Scheme 6 [34] is rather an exception in that ring opening of oxaziridines occurs either at the N-O or the C-O bond. The formation of **3u** has been mistakenly commented on elsewhere [1b].

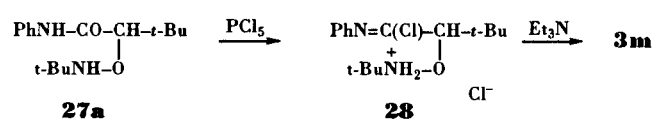
Scheme 6



3. Cyclization of α-(Aminooxy)imidoyl Chlorides.

Ring closure by C-N bond forming of a linear precursor such as **28** has been reported only once (Scheme 7) [25].

Scheme 7



The reaction might gain importance for the synthesis of 2-phenyl substituted derivatives akin to **3m** which are inaccessible by the method outlined in Section I.C.1. The

starting anilinooxy compounds related to **27a** should be conveniently prepared by aminolysis of appropriate oxazetidinones such as **1Bi** (*cf.* Scheme 15) - provided there is no N-O bond breaking as shown in Scheme 13.

A C-N bond building reaction to be performed with α-(aminooxy) acids has likewise been proposed as an entry to **1** but not verified until now [7].

D. 1,2-Oxazetidin-4-imines **4**.

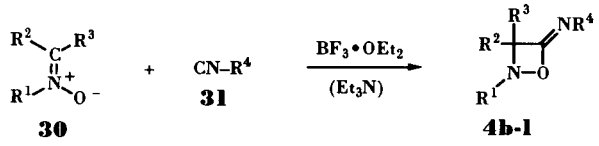
1. Reaction of 3-Methylene-1,2-oxazetidines with Nitroso Compounds.

On heating the perfluoro substituted 3-methyleneoxazetidine **29** with trifluoronitrosomethane, the oxazetidin-4-imine **4a** has been obtained (Scheme 8) [28]. Its formation may proceed through either pathway a or b, the latter being at variance with Section I.C.1. Since **29** arises from [2 + 2] cycloaddition of the nitroso compound to tetrafluoroallene [28], one might envisage a general route to **4** starting from allenes. However, attempts to obtain analogs of **29** (or the respective compounds **4** even directly) failed with the parent allene and trifluoronitrosomethane [35a] as well as with the educt couple nitrosobenzene/tetramethylallene [35b].

2. [1 + 3] Cycloaddition of Isocyanides to Azomethine *N*-Oxides (Nitrones) [33].

Using equimolar amounts of boron trifluoride etherate as catalyst, azomethine *N*-oxides **30** undergo cyclization with isocyanides **31** to afford the oxazetidines **4** (Scheme 9) [36-39]. Compounds **4b-f** are unstable oils that could not be purified. The reaction occurs momentaneously even at −40° when $R^1 = R^2$ = alkyl, R^3 = H and R^4 = alkyl, and proceeds only a little less fast for R^4 = Ph. Experiments with **30** where $R^3 \neq$ H have not been reported. Triethylamine quenches the catalyst which is also capable of ring opening the product (see Section II.D.2.). Mixtures

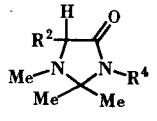
Scheme 9



30 **31** **4b-l**

	$R^1/R^2/R^3/R^4$/yield (%) [reference]
4b	Me/*t*-Bu/H/*c*-C_6H_{11}/– [36a]
c	Me/*t*-Bu/H/Ph/– [36b, 37]
d	Et/*i*-Pr/H/*c*-C_6H_{11}/– [36b, 37]
e	*t*-Bu/H/H/*c*-C_6H_{11}/– [37]
f	*t*-Bu/*t*-Bu/H/*t*-Bu/– [37]
g	*t*-Bu/*t*-Bu/H/*c*-C_6H_{11}/67 [38]
h	*t*-Bu/*t*-Bu/H/CH_2Ph/47 [38]
i	*t*-Bu/*t*-Bu/H/Ph/25 [38]
k	*t*-Bu/*t*-Bu/H/4-$O_2NC_6H_4$/20 [39] [a]
l	*t*-Bu/*t*-Bu/H/2,4,6-$Br_3C_6H_2$/– [39] [b]

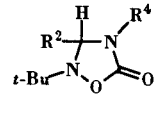
[a] Besides **32a**. [b] Besides **32b**.



32

R^2/R^4:

a *t*-Bu/4-$O_2NC_6H_4$
b *t*-Bu/2,4,6-$Br_3C_6H_2$
c Ph/*t*-Bu



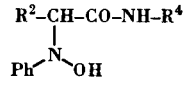
33

R^2/R^4:

a Ph/4-$O_2NC_6H_4$
b *t*-Bu/4-$Me_2NC_6H_4$

R^2–CO–CO–NH–R^4

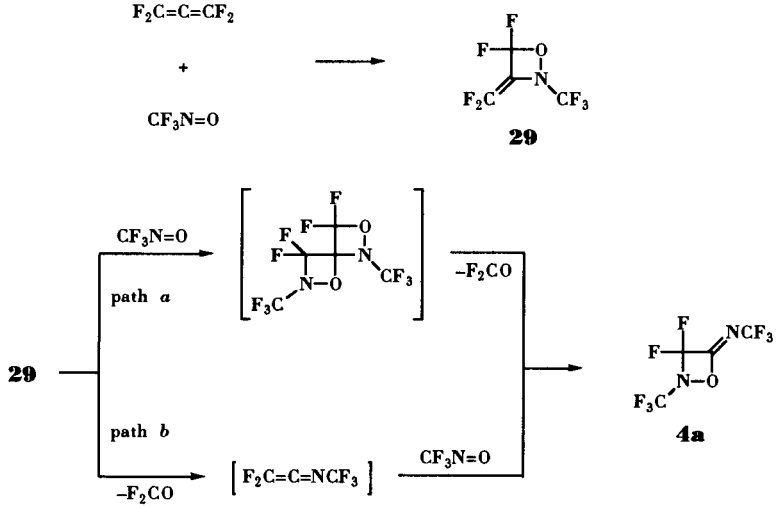
9d



34

R^2 = 4-ClC_6H_4, R^4 = *c*-C_6H_{11}

Scheme 8



containing less reactive isocyanides **31** (R^4 = 4-$O_2NC_6H_4$ or 2,4,6-$Br_3C_6H_2$) require prolonged exposure to the catalyst and thus, on employment of **30** (R^1 = R^2 = *t*-Bu, R^3 = H), the ring expanded products **32a,b** were formed, respectively [39]. A compound of this type, *viz.* **32c**, also resulted from the reaction of **30** (R^1 = *t*-Bu, R^2 = Ph, R^3 = H) [39] or the corresponding oxaziridine [37] with **31** (R^4 = *t*-Bu), the four-membered ring **4** remaining undetected in this case.

Further attempts to obtain oxazetidines **4** from aryl substituted educts **30** (including *C,N*-diaryl and *C*-aroyl-*N*-aryl derivatives) were likewise unsatisfactory [37] and gave products (if any) of different type, *e.g.* **33a** [39] and **9d/34** [40]. Their actual mode of formation, also that of **33b**, seems open to discussion [39].

3. Cyclization of α-(Hydroxyamino)nitriles.

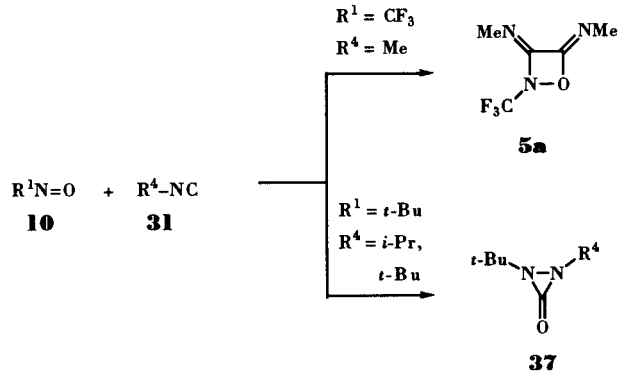
A C-O bond building process to give a transient oxazetidine structure has been invoked to account for the formation of the α-oxoamide **9e**. This compound has been prepared from the nitrile **35** as shown in Scheme 10 [41]. As regards ring opening of **4m**, it is interesting to note that an *a*-oxoamide is not produced as a consequence of N-O bond cleavage in the case of **4g** and congeners (see Section II.D.2.) [38,39].

E. 1,2-Oxazetidine-3,4-diimines **5**.

1. [1+1+2] Cycloaddition of Isocyanides to Nitroso Compounds [33].

There is an isolated example of this process, giving the unique structure **5a** (Scheme 11) [18]. The result is perhaps owing to the particular nitroso component **10** (R^1 = CF_3) since 2-methyl-2-nitrosopropane **10** (R^1 = *t*-Bu) reacts with **31** in a 1:1 fashion to yield the diaziridinones **37** along with some nitroalkane and carbodiimide [42].

Scheme 11



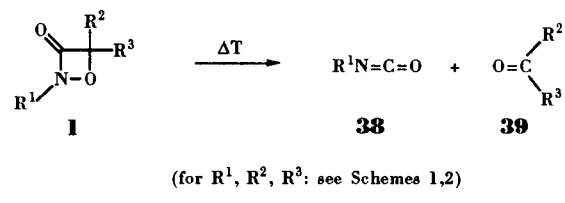
II. Reactions.

A. 1,2-Oxazetidin-3-ones **1**.

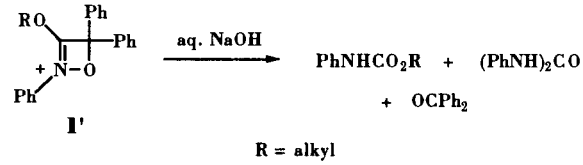
1. [2+2] Cycloreversion.

Like all 1,2-oxazetidines, compounds of type **1** are capable of undergoing thermal decomposition with N-O and

Scheme 12

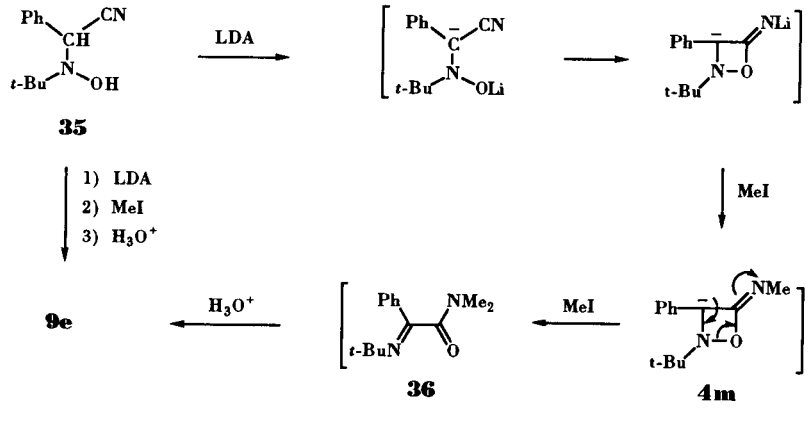


(for R^1, R^2, R^3: see Schemes 1,2)



R = alkyl

Scheme 10



Ph-CO-CO-NMe_2

9e

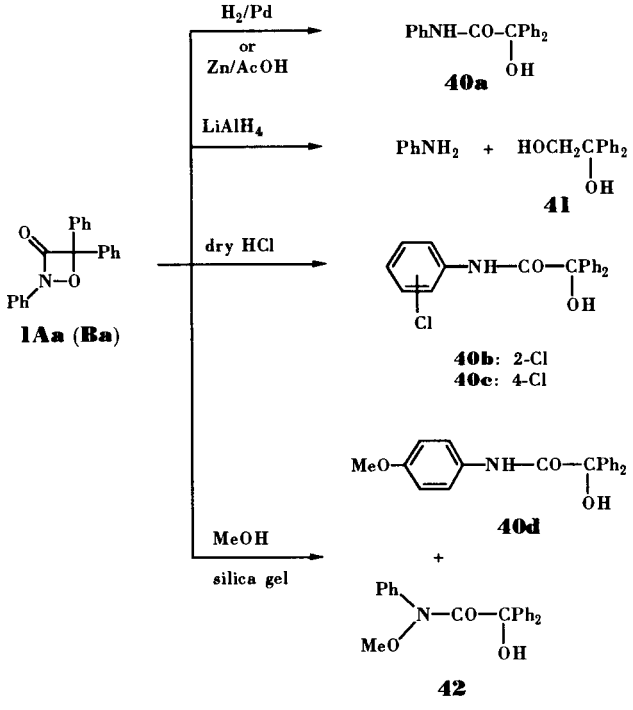
C-C bond cleavage to give the products **38** and **39** (Scheme 12). The reaction is known since the discovery of class **1** [3] and has been encountered several times by later workers in the field [9,11d,16-18, 43]. It has also been the object of a theoretical study, which confirms the preference of N-O/C-C over C-N/C-O bond breaking [44]. The ease of fragmentation is greatly influenced by the *N*-substituent: **1Bi** is more reactive than **1Bh** [17], and in the case of **1Ba,d-f**, the order is **1Bf** > **1Be** > **1Bd** > **1Ba** [16].

A formally related decomposition has been observed on alkaline hydrolysis of the onium structure in **1'** [43].

2. Ring Opening at N-O Bond.

Oxazetidines **1** having R^1 = aryl, *e.g.* **1Aa(Ba)**, can be converted into α-hydroxycarboxamides (Scheme 13). This has been accomplished by:

Scheme 13



(i) Mild hydrogenation which gives α-hydroxybenzilanilide (**40a**) [7,15] (with lithium aluminum hydride, however, the reduction proceeds to aniline and the glycol **41** [7], while with sodium borohydride azoxybenzene was isolated [15]).

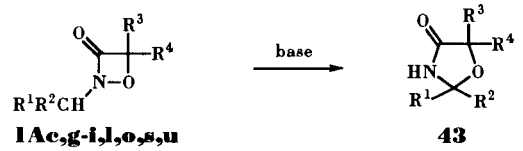
(ii) Anhydrous hydrogen chloride which furnishes 2- and 4-chloroanilides such as **40b,c** [7] (the isomer **40b** has been shown [7] to be the material previously obtained from **1Aa(Ba)** but erroneously thought to be α-chlorobenzilanilide [3]).

(iii) Methanolysis which affords a 1:3 mixture of compounds **40d** and **42** [16].

The results shown under (ii) and (iii) clearly point to a nitrenium ion-like intermediate [16].

Oxazetidinones **1** that have at least one hydrogen ligand attached to the α-position of the *N*-substituent can undergo base-induced ring enlargement to give the oxazolidinones **43** (Scheme 14) [9,10,45]. This transformation has a

Scheme 14

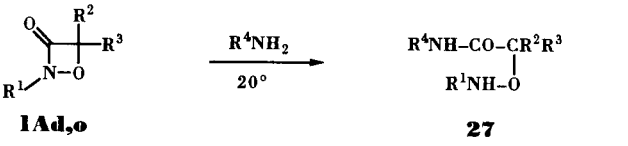


R^1/R^2 // R^3/R^4:

1Ac	**43a**	Me/Me // Ph/Ph
g	**b**	Ph/Me // 4-MeC_6H_4/4-MeC_6H_4
h	**c**	Ph/H // 4-$MeOC_6H_4$/4-$MeOC_6H_4$
i	**d**	Ph/Ph // 4-$MeOC_6H_4$/4-$MeOC_6H_4$
l	**e**	–$[CH_2]_5$– // 3-thienyl/3-thienyl
o	**f**	H/H // 2-thienyl/CH_2Ph
s	**g**	*c*-C_3H_5/Me // 4-ClC_6H_4/Me
u	**h**	Ph/H // 4-$PhOC_6H_4$/Me

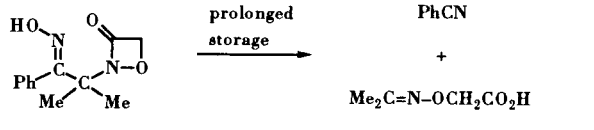
close parallel in 1,2-diazetidin-3-one chemistry [46] and, in addition, bears a formal resemblance to the conversion of **4k,l** into **32a,b** (see below Scheme 22) [39]. The nature of R^1 and R^2 in the starting oxazetidines **1** has a tremendous effect on the ease of this ring expansion whereas R^3 and R^4 are of little or no moment. So, **1Ag-i** are increasingly prone for giving the respective products **43b-d, 1Ai** reacting even at room temperature [9,10a]. Bases used for this ring enlargement were benzylamine [9] and imidazole [10a]. Quite remarkably, the primary amine did not convert **1Ag-i** into the expected *N*-benzylcarboxamides of type **27** (see following Section) [9]. The same applies to isopropylamine which transformed **1u** into **43h** [45]. Ring transformations of **1Ac,l,o,s** (*i.e.* of derivatives lacking a phenyl group on the *N*-substituent) failed with imidazole but could be effected by DBU in boiling benzene to give

Scheme 15



$R^1/R^2/R^3/R^4$:

b *c*-C_6H_{11}/Ph/Ph/CH_2Ph
c Me/2-thienyl/CH_2Ph/*i*-Pr



43a,e,f [10b] and **43g** [45], the 2-methyloxazetidine **1Ao** reacted faster than **1Ac** or **1Al**. Yields are generally good with this kind of interconversion.

3. Ring Opening at C-N Bond.

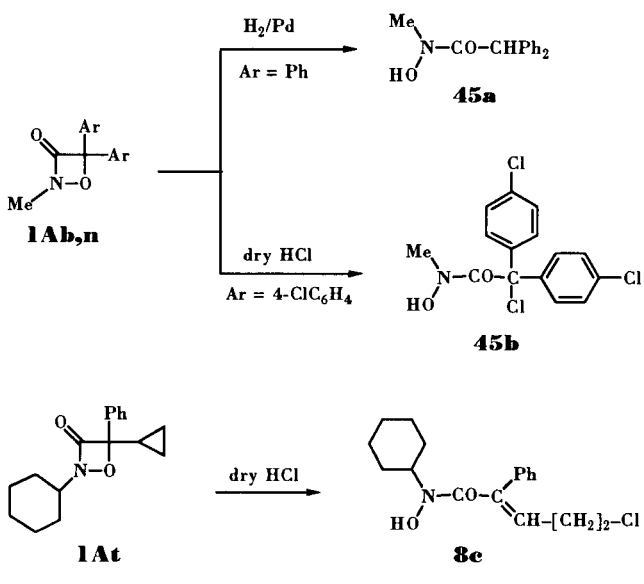
Treatment of 2-alkyl-1,2-oxazetidin-3-ones such as **1Ad,o** with a primary amine led to α-(aminooxy)carboxamides **27** (Scheme 15) [11b,d]. The reaction is hampered by bulky substituents on the four-membered ring. Thus, **27b** was formed in significantly lower yields than **27c** (28% *vs.* 92%), and representatives such as **1Ae** or those having two *o*-tolyl groups in position 4 did not react at all [11d] (see, however, the conversion of **3n** into **27d** as shown in Scheme 18 [25]).

A different sort C-N bond breaking has been observed with the elaborately substituted oxazetidine **1Aw**: the formation of benzonitrile along with the open-chain product **44** [8] reminds of the Beckmann fragmentation.

4. Ring Opening at C-O Bond.

In contrast to 2-aryl-1,2-oxazetidin-3-ones such as **1Aa(Ba)**, the N-O bond of 2-*alkyl* derivatives remains unaffected on hydrogenation or treatment with hydrogen chloride. This is exemplified by the behavior of compounds **1Ab,n,t** which gave the ring open products **45a** [7], **45b** (recyclized on silica gel) [45] and **8c** [45], respectively (Scheme 16). A related case of ring cleavage, the formation of **8b** [12], has already been mentioned in Section I.A.1.

Scheme 16



1Ab,n **45a** **45b** **1At** **8c**

B. 1,2-Oxazetidin-4-ones **2**.

1. [2+2] Cycloreversion.

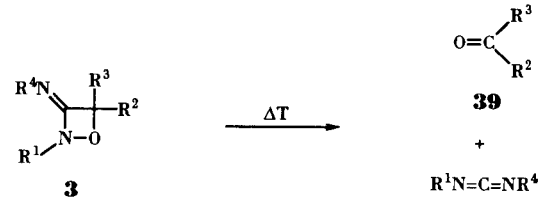
As pointed out in Section I.A.2., compounds of type **2** rapidly decompose after their formation to give carbon dioxide and an azomethine **12** [3,15,16].

C. 1,2-Oxazetidin-3-imines **3**.

1. [2+2] Cycloreversion.

As a rule, the title oxazetidines **3** can revert into a carbodiimide **46** and a carbonyl compound **39** (Scheme 17).

Scheme 17



3 **39** + $R^1N{=}C{=}NR^4$ **46**

(for R^1,R^2,R^3,R^4: see Scheme 4)

This reaction which in certain cases vitiates the synthetic approach to **3** (see Section I.C.1.) has been mentioned by all workers in the field [22-26,34]. Ring opening commences with N-O bond breaking to leave a nitrenium-like intermediate (*cf.* ref [16]). Therefore substituents that are capable of stabilizing a positive charge on the former ring nitrogen favor the cycloreversion. The crucial ligands are R^1 and R^4:

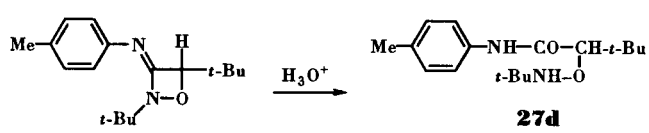
(i) The propensity for giving **39** and **46** increases in the order **3k** < **3b** < **3h**. Compound **3b** decomposed in boiling chloroform [24] (as did **3a** [22]), while **3h** proved entirely elusive already at lower temperature [23b].

(ii) Comparing the ease of cycloreversion of **3m-r**, the sequence **3q** < **3p** < **3m,n** < **3r** < **3o** was observed [25]. A 2,6-xylyl [25] or a silyl group [26] attached to the exocyclic nitrogen, in connection with a phenyl group at N-2, confers instability upon the respective oxazetidines **3s,t** even at room temperature.

2. Ring Opening at C-N Bond.

The semicyclic amidine function of 2,4-dialkyl-1,2-oxazetidin-3-imines as in **3n** is readily hydrolyzed by mineral acid to give the carboxamide **27d** in high yield (Scheme 18) [25]. Analogs of **3n** as listed in Scheme 4 behave similarly [24]. The amide type **27** also arises on aminolysis of **1** (see Section II.A.3.) [11b,d].

Scheme 18



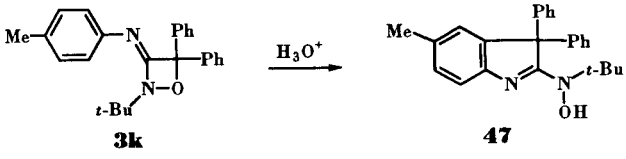
3n **27d**

3. Ring Opening at C-O Bond.

In contrast to the oxazetidine **3n**, the 4,4-diphenyl congener **3k** undergoes C-O bond rupture when treated with

mineral acid under comparable conditions. The putative carbenium intermediate stabilizes by linking to the *p*-tolyl substituent (Scheme 19) [24]. Attempts to obtain the analog of **47** from the 2-phenyl derivative **3b** met with failure [24].

Scheme 19



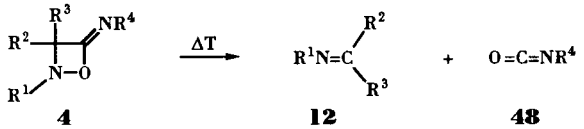
3k **47**

D. 1,2-Oxazetidin-4-imines **4**.

1. [2+2] Cycloreversion.

Quite expectedly, thermolysis of compounds **4** gives rise to the formation of an azomethine **12** and an isocyanate **48** (Scheme 20) [28,36a,37,38]. However, this straightforward reaction may be accompanied by a side process involving

Scheme 20



4 **12** **48**

(for R^1, R^2, R^3, R^4: see Scheme 9)

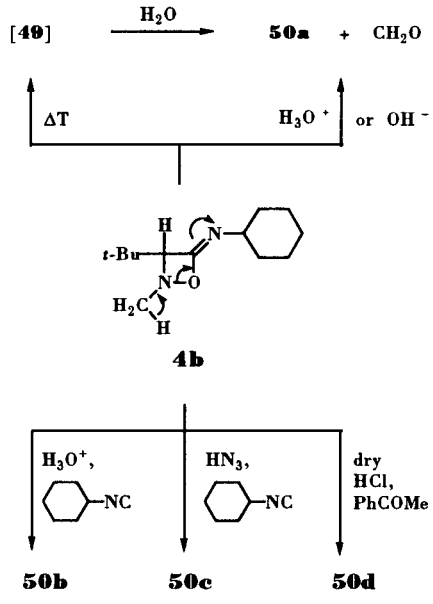
the 2-substituent of **4**. A typical example is shown below in Scheme 21 [37].

2. Ring Opening at N-O Bond.

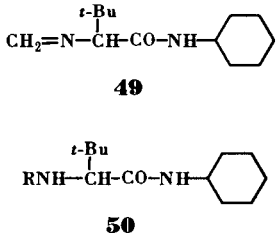
The *O*-imidoylhydroxylamine function present in **4b** has a pronounced tendency to form the stable amide grouping. Deprotonation which follows N-O bond breaking occurs regiospecifically on the methyl group, the hydrogen atom on C-3 remaining unaffected (Scheme 21). This transformation is achieved both thermally [37] and by acid [36a] and base [37]. The primary product **49** is usually not found; so, in the case of thermolysis, besides the urea **50e** the 'parent' amide **50a** and formaldehyde were obtained [37]. In acidic media, **4b** behaves like the protonated azomethine **49** and can therefore be converted into derivatives such as **50b,c** [36a] and **50d** [37]. The smooth conversion of **4b** into the diamide **50b**, in conjunction with the fact that the [1+3] cycloaddition of Section I.D.2. is also proton-catalyzed [37], led to an understanding [36,37] of the puzzling one-pot synthesis of this compound from *N*-methylhydroxylamine, pivalaldehyde and cyclohexyl isocyanide in aqueous mineral acid (Ugi reaction) [47].

Remarkably, compound **4g** on treatment with dilute acid exactly follows the rearrangement pattern of **4b**, *i.e.*, hydrogen on C-3 is not abstracted, but a methyl group of the 2-*tert*-butyl substituent migrates to the adjacent nitrogen [37-39]; ensuing hydrolysis then gives acetone and the amide **50f** (Scheme 22 [48]). In summary, the fate

Scheme 21



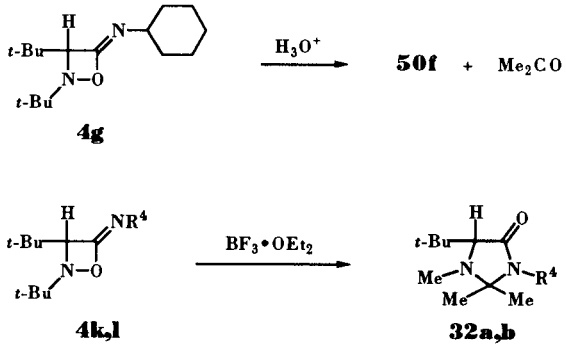
4b **50b** **50c** **50d**



49 **50**

a R = H
b R = *c*-$C_6H_{11}NHCOCH_2$
c R = *c*-C_6H_{11}N(CH$_2$)(N=N-N)
d R = $PhCOCH_2CH_2$
e R = *c*-$C_6H_{11}NHCO$
f R = Me

Scheme 22



4g **50f** **4k,l** **32a,b**

(for R^4: see Scheme 9)

of 2-alkyl groups of ring opened compounds **4** directly refers to long known observations in oxaziridine chemistry [49]. As regards action of alkali hydroxide, the behavior of **4g** has not been described; in the case of **4a**, fluoride ion (along with some unreacted starting material) was the only product mentioned [28]. Attempts to photolyze or photochlorinate **4a** failed while treatment with anhydrous hydrogen fluoride readily produced a secondary amine of undetermined structure [28].

Boron trifluoride etherate has been found to cause ring transformation of **4k,l** into the imidazolidinones **32a,b** (*cf.* Section I.D.2.) [39]. However, on attempting this interconversion with the oxazetidines **4g-i**, the amide **50f** and its respective analogs were formed instead [39].

Examples of ring opening at the N-O bond *without* affecting the 2-substitutent include the supposed intermediate **4m** depicted in Scheme 10 (see above) [41] and a likewise putative derivative **4** (R^1 = Ph, R^2 = 4-ClC_6H_4, R^3 = H, R^4 = *c*-C_6H_{11}) which has been regarded the precursor of **9d** (Scheme 9) [40].

3. Ring Opening at C-O Bond.

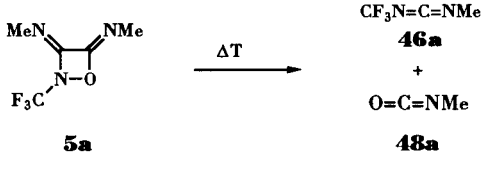
There is no definite instance as yet because the formation of compound **34** (Scheme 9) [40] does not necessarily proceed through the suggested oxazetidine stage as has been demonstrated in detail elsewhere [39].

E. 1,2-Oxazetidine-3,4-diimines **5**.

1. [2+2] Cycloreversion.

Thermal decomposition of **5a**, the only member of this class known, has been performed *in vacuo* at 350-400° to yield the carbodiimide **46a** and methyl isocyanate (**48a**) (Scheme 23) [18].

Scheme 23



5a

III. Spectroscopic Properties.

Literature data on spectroscopic behavior are available in the cases of compounds **1**, **3** and **4**.

1. Infrared Spectra.

As compared to β-lactams, the carbonyl band of 1,2-oxazetidin-3-ones **1** is registered at slightly higher frequencies. The majority of derivatives **1** listed in Schemes 1 and 2 absorb in the range 1770-1785 cm^{-1} [7,9,10a,11,12, 15-17]. Still close to these values are the data of **1Al** (1790 cm^{-1} [11d]), **1Be** (1764 cm^{-1} [16]) and **1Bi** (1760 cm^{-1} [17]) whereas compound **1Aw** showed 1747 cm^{-1} [8]. The absorption of derivative **1Bk** [18] has not been reported.

The C=N bond of most 1,2-oxazetidin-3-imines **3** tabulated in Scheme 4 aborbs at 1704-1715 cm^{-1} [22,23a,c, 24,25]. Similar results have been found for **3f** (1700 cm^{-1} [24]) and **3r** (1725 cm^{-1} [25]). The fluorine-containing member **3u** (Scheme 6), however, showed 1740 cm^{-1} [34]. As expected, the C=N absorption of the isomeric 1,2-oxazetidin-4-imines **4** is shifted to higher frequencies. Save **4i** [38] and **4k** [39] (Scheme 9) which absorb at 1735 and 1730 cm^{-1}, respectively, compounds **4b-h,l** exhibit the imino band in the range 1740-1758 cm^{-1} [36-39]. Only in the case of **4a** (Scheme 8) this band appears far outside at 1815 cm^{-1} [28].

2. Nuclear Magnetic Resonance Spectra.

The ^1H nmr spectral data have been reported for nearly all compounds **1** listed in Schemes 1 and 2 [8,9,10a,11,12, 16,17]. Data are also available for several derivatives **3** (Scheme 4) [24,25] and **4** (Scheme 9) [36a,37-39]. Regarding ^{13}C nmr spectroscopy of **1** [17], **3** [24,25] and **4** [39], less copious material is at hand. Table I summarizes the most prominent features. These include high field shift of both 3-H in **4** (with respect to 4-H in **1** and **3**) and C-3 in **4** (compared to C-4 in **1** and **3**). In the ^{19}F nmr spectrum of **3u** (Scheme 6), the $C(CF_3)_3$ group was found at δ −12.1 relative to external trifluoroacetic acid [34].

Table I

NMR Shift Values (δ) of Oxazetidine-attached Hydrogen and Oxazetidine Carbon for **1**,**3** and **4** [a]

Compound	4-H or 3-H	C-3/C-4	Reference
1Av	6.30		[11c]
1Aw	5.21		[8]
1Bh	4.78	168.9 / 97.2	[17]
1Bi	5.10	163.5 / 99.1	[17]
3b	–	156.3 / [b]	[24]
3f	–	156.9 / [b]	[24]
3k	–	160.9 / [b]	[24]
3l	–	161.9 / 95.5	[24]
3m	5.18	162.7 / 93.9	[25]
3q	5.18	162.8 / 93.3	[25]
3r	4.73	159.6 / 96.1	[25]
4b	3.68		[36a]
4g	3.83		[38]
4i	4.07		[37]
4k	4.11	76.0/160.4	[39]

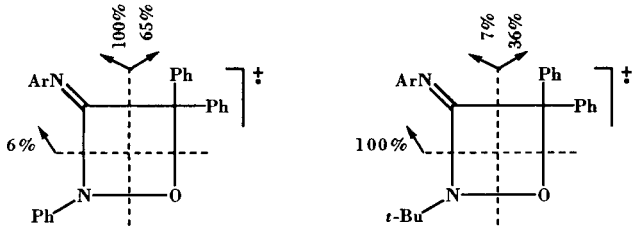
[a] Determined in deuteriochloroform except for **1Aw** (perdeuterated dimethyl sulfoxide). [b] Signal not observed.

3. Mass Spectra.

Molecular ions were observed in the EI mass spectra of all compounds **1**, **3** and **4** studied, *viz.* **1Aa(Ba)** and **1Ab** [7], **1Bh,i** [17], **3b,k** [24], **3m,n,p,r** [25], **4a** [28], **4g** [38], **4i** [37] and **4k** [39]. Major fragmentation paths constitute

[2 + 2] cycloreversion into both possible directions, *i.e.* into the compound couples: (i) nitroso component **10**/ketene **11** and isocyanate **38**/carbonyl compound **39** for **1**; (ii) **10**/ketenimine **18** and **39**/carbodiimide **46** for **3**; (iii) **10**/**18** and **38**/azomethine **12** for **4**. In some cases, preference for one direction has been reported. For example, the 2-alkyl derivative **1Bh** (Scheme 2) fragments favorably into **10** and **11** while with the 2-phenyl analog **1Bi** reversion into **38** and **39** predominates [17]. The same dependence on the 2-substituent is reflected by the cleavage properties found in the spectra of **3b** and **3k** (Scheme 24) [24]. For the closely related compounds **1Aa(Ba)** and

Scheme 24



3b **3k**

Ar = 4-MeC_6H_4

(relative abundances of [2+2] cycloreversion fragments)

1Ab the occurrence of both ring fissions has been quoted indiscriminately; yet, a ready distinction is given by either elimination of an NMe fragment from **1Ab** or loss of carbon monoxide from **1Aa(Ba)** [7].

A noteworthy feature in the behavior of ionized compounds **3** and **4** is the absence of any isocyanide extrusion (*via* [1 + 3] cycloreversion). This contrasts with the fragmentation of the related 1,2-diazetidin-3-imine structure [50].

Concluding Remarks.

From continuous work during the past two decades, the title oxazetidines have emerged as a heterocyclic class of considerable attraction. But despite much progress, achieved in particular with compounds **1** and **3**, further efforts are required in the field of synthesis and reactivity studies; certain ring substitution patterns have not been exemplified, and quite a number of preparative procedures are of either unknown or limited scope. A major aim may be exploration of the synthetic potentials of α-(hydroxyamino) acid derivatives [51] and metallated ketenimines [52]. A project of a different kind - announced some years ago [45] - includes investigation of biological properties of compounds **1**.

REFERENCES AND NOTES

[1a] No treatise in: The Chemistry of Heterocyclic Compounds, A. Weissberger and E. C. Taylor, eds, Wiley-Interscience, New York, 1983-1985, Vol **42**, Parts 1-3 (Small Ring Heterocycles, A. Hassner, ed); [b] treated *passim* in: J. W. Timberlake and E. S. Elder in Comprehensive Heterocyclic Chemistry, A. R. Katritzky and C. W. Rees, eds, Pergamon Press, Oxford, 1984, Vol **7**, p 449.

[2] L. L. Muller and J. Hamer, 1,2-Cycloaddition Reactions, Interscience Publishers, New York, 1967, p 257.

[3] H. Staudinger and S. Jelagin, *Ber.*, **44**, 365 (1911).

[4] *E.g.*, R. W. Hoffmann, U. Bressel, J. Gehlhaus and H. Häuser, *Chem. Ber.*, **104**, 873 (1971), and ref cited therein; J. E. Baldwin, A. K. Bhatnagar, S. C. Choi and T. J. Shortridge, *J. Am. Chem. Soc.*, **93**, 4082 (1971); G. Pifferi and P. Consonni, *J. Heterocyclic Chem.*, **9**, 159 (1972); see also: O. Tsuge and A. Torii, *Bull. Chem. Soc. Japan*, **45**, 3187 (1972); V. Papageorgiou and S. Zlatanos, *Chim. Chron.*, **19**, 125 (1990).

[5] C. K. Ingold and S. D. Weaver, *J. Chem. Soc.*, **125**, 1456 (1924).

[6] C. E. Griffin, N. F. Hepfinger and B. L. Shapiro, *Tetrahedron*, **21**, 2735 (1965), and refs cited therein.

[7] T. Sheradsky, U. Reichman and M. Frankel, *J. Org. Chem.*, **33**, 3619 (1968).

[8] A. Ya. Tikhonov, L. B. Volodarskii and N. V. Belova, *Khim. Geterotsikl. Soedin.*, 115 (1984); *Chem. Abstr.*, **100**, 209745z (1984).

[9] T. Lauterbach, Dissertation, Technische Universität, Braunschweig, Germany, 1985.

[10a] T. Lauterbach and D. Geffken, *Z. Naturforsch., Teil B*, **41**, 1186 (1986); [b] T. Lauterbach and D. Geffken, *Chem.-Ztg.*, **110**, 459 (1986).

[11a] D. Geffken, *Chem.-Ztg.*, **106**, 442 (1982); [b] D. Geffken, *Liebigs Ann. Chem.*, 894 (1984); [c] D. Geffken, *Chem.-Ztg.*, **108**, 293 (1984); [d] T. Lauterbach and D. Geffken, *Liebigs Ann. Chem.*, 1478 (1986).

[12] A. Burchardt and D. Geffken, *Arch. Pharm. (Weinheim)*, **323**, 967 (1990).

[13] J. Nally, N. H. R. Ordsmith and G. Procter, *Tetrahedron Letters*, **26**, 4107 (1985).

[14] D. Geffken, Habilitationsschrift, Technische Universität, Braunschweig, Germany, 1981.

[15] G. Kresze and A. Trede, *Tetrahedron*, **19**, 133 (1963).

[16] R. C. Kerber and M. C. Cann, *J. Org. Chem.*, **39**, 2552 (1974).

[17] D. Moderhack and K. Stolz, *Chem.-Ztg.*, **114**, 5 (1990).

[18] S. P. Makarov, V. A. Shpanskii, V. A. Ginsburg, A. I. Shchekotikhin, A. S. Filatov, L. L. Martynova, I. V. Pavlovskaya, A. F. Golovaneva and A. Ya. Yakubovich, *Dokl. Akad. Nauk SSSR*, **142**, 596 (1962); *Chem. Abstr.*, **57**, 4528a (1962).

[19] A. Padwa and L. Hamilton, *J. Org. Chem.*, **31**, 1995 (1966).

[20a] Y. Hata and M. Watanabe, *J. Am. Chem. Soc.*, **101**, 1323 (1979) [the *C*-phenyl analog of **15** reacted in like manner]; [b] H. Quast and H. Leybach, *Chem. Ber.*, **124**, 2105 (1991).

[21a] Y. Ito, T. Matsuura and H. Kondo, *J. Am. Chem. Soc.*, **101**, 7105 (1979); [b] W. Adam, O. De Lucchi, H. Quast, R. Recktenwald and F. Yany, *Angew. Chem., Int. Ed. Engl.*, **18**, 788 (1979); [c] Y. Ito, H. Yokoya, K. Kyono, S. Yamamura, Y. Yamada and T. Matsuura, *J. Chem. Soc., Chem. Commun.*, 898 (1980).

[22] G. R. Krow, *Angew. Chem., Int. Ed. Engl.*, **10**, 435 (1971).

[23a] M. W. Barker and J. T. Gill, *J. Heterocyclic Chem.*, **7**, 1203 (1970); [b] M. W. Barker, L. L. Combs and J. T. Gill, *J. Heterocyclic Chem.*, **9**, 77 (1972); [c] M. W. Barker and C. J. Wierengo, *J. Heterocyclic Chem.*, **11**, 633 (1974).

[24] K. Stolz, Dissertation, Technische Universität, Braunschweig, Germany, 1986.

[25] D. Moderhack and K. Stolz, *Chem. Ber.*, **119**, 3411 (1986).

[26] R. W. Freerksen, S. J. Selikson, R. R. Wroble, K. S. Kyler and D. S. Watt, *J. Org. Chem.*, **48**, 4087 (1983).

[27] L. L. Combs, M. W. Barker and J. K. Young, *Spectrosc. Letters*, **5**, 179 (1972); see also: S. I. Perumal, *Indian J. Chem., Sect. B*, **23**, 293 (1984).

[28] R. E. Banks, R. N. Haszeldine and D. R. Taylor, *J. Chem. Soc.*,

5602 (1965).

[29] N. P. Gambaryan, *Usp. Khim.*, **45**, 1251 (1976); *Chem. Abstr.*, **85**, 158789d (1976).

[30] D. Moderhack and K. Stolz, *J. Org. Chem.*, **51**, 732 (1986).

[31] D. Moderhack and K. Stolz, unpublished results.

[32] D. Moderhack and K. Stolz, *Chem.-Ztg.*, **111**, 372 (1987).

[33] *Cf.* D. Moderhack, *Synthesis*, 1083 (1985).

[34] D. P. Del'tsova, N. P. Gambaryan and É. P. Lur'e, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1788 (1979); *Chem. Abstr.*, **92**, 6475e (1980).

[35a] D. H. Coy, R. N. Haszeldine, M. J. Newlands and A. E. Tipping, *J. Chem. Soc., Chem. Commun.*, 456 (1970); [b] R. K. Howe, *J. Org. Chem.*, **33**, 2848 (1968).

[36a] D. Moderhack and M. Lorke, *J. Chem. Soc., Chem. Commun.*, 831 (1977); [b] D. Moderhack and M. Lorke, *Chem.-Ztg.*, **103**, 268 (1979).

[37] M. Lorke, Dissertation, Technische Universität, Braunschweig, Germany, 1979.

[38] D. Moderhack and M. Lorke, *Angew. Chem., Int. Ed. Engl.*, **19**, 45 (1980).

[39] D. Moderhack, M. Lorke and D. Schomburg, *Liebigs Ann. Chem.*, 1685 (1984).

[40] B. Zeeh, *Synthesis*, 37 (1969).

[41] A. Padwa and K. F. Koehler, *J. Chem. Soc., Chem. Commun.*, 789 (1986).

[42] F. D. Greene and J. F. Pazos, *J. Org. Chem.*, **34**, 2269 (1969).

[43] R. Kreher, A. Bauer and H. Hennige, *Z. Naturforsch., Teil B*, **29**, 231 (1974).

[44] H. Sterk, G. Uray and E. Ziegler, *Monatsh. Chem.*, **103**, 615 (1972).

[45] A. Burchardt, Dissertation, Universität Bonn, Germany, 1989.

[46] *E.g.*, E. C. Taylor, R. J. Clemens, H. M. L. Davies and N. F. Haley, *J. Am. Chem. Soc.*, **103**, 7659 (1981); G. Lawton, C. J. Moody and C. J. Pearson, *J. Chem. Soc., Chem. Commun.*, 754 (1984).

[47] D. Moderhack, *Liebigs Ann. Chem.*, 359 (1973).

[48] Amide structure incorrectly reviewed in ref [1b], p 460.

[49] W. D. Emmons, *J. Am. Chem. Soc.*, **79**, 5739 (1957).

[50] J. A. Deyrup, *Tetrahedron Letters*, 2191 (1971).

[51] H. C. J. Ottenheijm and J. D. M. Herscheid, *Chem. Rev.*, **86**, 697 (1986).

[52] U. Schöllkopf and I. Hoppe, *Liebigs Ann. Chem.*, 1655 (1974).