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Synthesis of 1,2,3,5-Oxathiadiazole 2-Oxides from Amidoximes and Thionyl Chloride and the Mechanism of Their Thermally Induced Fragmentation and Rearrangement to Carbodiimides[1]

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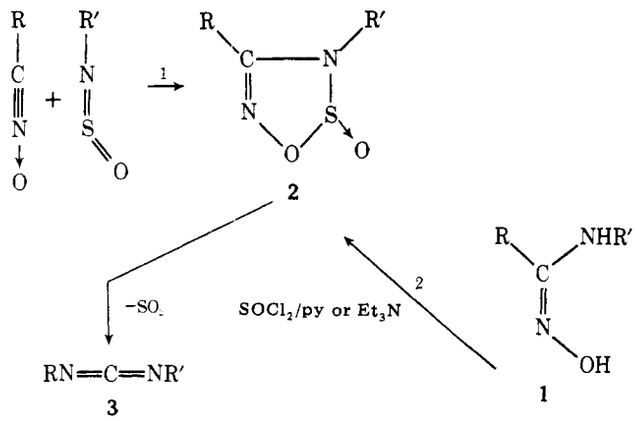
3,4-Disubstituted 1,2,3,5-oxathiadiazole 2-oxides **2** are prepared in good yields by cyclization of *N*-alkyl- and *N*-arylamidoximes **1** with thionyl chloride in the presence of triethylamine. The reaction provides a convenient route to heterocycles **2** as an alternative to the cycloaddition of *N*-sulfinylamines to nitrile oxides. 4-Aryl substituted heterocycles **2** decompose under mild thermal conditions to sulfur dioxide and carbodiimides **3**. Kinetic evidence as well as the failure to detect unstable intermediates by trapping experiments suggests that the conversion of **2** into **3** is a one-step process where the fragmentation and rearrangement occur concertedly via a single transition state.

The synthesis of 3,4-disubstituted 1,2,3,5-oxathiadiazole 2-oxides **2**, heterocycles of some interest as fungicides[3] and precursors of carbodiimides **3**, has been described by 1,3-dipolar cycloaddition of *N*-sulfinylamines to nitrile oxides[3,4] (route 1). Of the alternative entry to heterocycles **2** from amidoximes **1** and thionyl chloride in the presence of a tertiary



amine (route 2), a single example has been so far described[4b] in order to confirm the structure of the product **2** (R = *p*-$NO_2C_6H_4$, R′ = *p*-MeC_6H_4) obtained from the cycloaddition reaction.

As route 2 appeared a promising alternative to route 1, we have examined the cyclization of a number of *N*-alkyl- and *N*-arylamidoximes with thionyl chloride in order to define the scope and limitations of this reaction. We have then employed the easy thermal fragmentation of various oxathiadiazole 2-oxides for the preparation of carbodiimides and investigated the kinetics of the reaction as well as attempted trapping experiments in order to gain some insight into its mechanism.

Results and Discussion

Synthesis of Heterocycles 2. The cyclization of amidoximes **1a–r** with thionyl chloride in the presence of triethylamine occurred readily in methylene chloride below room temperature to give the corresponding 3,4-disubstituted 1,2,3,5-oxathiadiazole 2-oxides (**2a–r**) (Table I). Structural proof of new compounds was based on spectral data (IR, NMR,[5] and MS). Compounds **2a–k** and **2q** were isolated in good yields (70–90%), whereas other products were obtained in much lower yields or could not be isolated. For **2m–p** this can be explained by the observation (IR at 2140 cm^{-1}) that these compounds rearranged into the corresponding carbodiimides when the reaction mixture was allowed to warm up to room temperature. The low yield of **2l** was due to both its partial conversion to *N*-*tert*-butyl-*N*′-phenylcarbodiimide (**3g**) and to some reluctance of *N*-*tert*-butylbenzamidoxime (**1l**) to undergo the cyclization (see footnote *j* of Table I). Also **2r** was obtained in very low yield from *N*-*tert*-butyltrimethylacetamidoxime (**1r**) under the standard conditions (−15 or 0 °C, 1 h at room temperature), but its thermal stability allowed the reaction temperature to be raised to 10 °C, and the yield increased to an acceptable value (60%).

The yields were not optimized nor were the effects of changing solvent or the tertiary amine investigated in detail. However, it was observed that almost identical results were obtained when the cyclization of *N*-phenylbenzamidoxime (**1i**) was carried out in benzene solvent instead of methylene chloride and/or by using pyridine in place of Et_3N (Table I, footnote *h*).

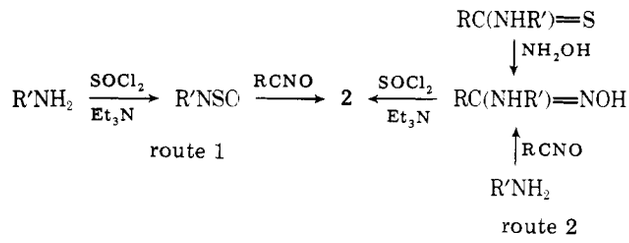
From the examples reported in Table I it appears that the cyclization of amidoximes with thionyl chloride can be conveniently employed for the synthesis of heterocycles **2** in a number of cases. This reaction offers several advantages with respect to the nitrile oxide–*N*-sulfinylamine cycloaddition (route 1), since: (i) it circumvents the preparation of *N*-sulfinylamines; (ii) it does not suffer from side reactions[4c] such as dimerization and isomerization of nitrile oxides,[6] and decomposition of *N*-sulfinylamines by moisture and air[7]; (iii) it occurs at low temperature, which is an important factor in view of the thermal instability of heterocycles **2**; (iv) it employes stable and easily available starting materials: *N*-sub-

Table I. 1,2,3,5-Oxathiadiazole 2-Oxides[a] 2 from Reaction of Amidoximes 1 and $SOCl_2$–Et_3N[b] in CH_2Cl_2

Compd 2	Registry no.	R	R′	Temp,[c] °C	Yield,[d] %	Crystn Solvent[e]	Mp,[f] °C	IR,[g] cm^{-1}
a	63105-00-0	*m*-ClPh	Ph	−10	84	Bz–PE	87–88	1360, 1210
b	63105-01-1	*p*-ClPh	Ph	−10	84	Bz–PE	87–88	1370, 1210
c	63105-02-2	*p*-CH_3Ph	Ph	−15	70	Bz–PE	93–94	1370, 1210
d	65105-03-3	*p*-CH_3OPh	Ph	−15	70	Bz–PE	91–92	1365, 1205
e	3815-53-0	Ph	*p*-CH_3OPh	−15	83	E–PE	93–94[i]	1370, 1205
f	63105-04-4	Ph	*p*-CH_3Ph	−15	82	E–PE	74–75	1365, 1205
g	63105-05-5	Ph	*p*-ClPh	−15	84	Bz–PE	82–83	1365, 1210
h	63105-06-6	Ph	*m*-ClPh	−15	85	Bz–PE	60–61	1360, 1210
i[h]	3815-50-7	Ph	Ph	−15	78	E–PE	74–75[i]	1370, 1210
j	63105-07-7	Ph	CH_3	−15	78	E–PE	58–59	1360, 1195
k	63105-08-8	CH_3	Ph	−15	80	E–PE	38–40	1370, 1205
l	63105-09-9	Ph	$(CH_3)_3C$	0	25[j]	E–PE	83–85	1370, 1205
m	63133-66-4	Mesityl	Ph	−15	*k*		*k*	1370, 1200
n	63133-67-5	Ph	Mesityl	0	24	PE	99–101	1365, 1205
o	63133-72-2	Mesityl	Mesityl	−5	*k*		*k*	1370, 1200
p	63105-10-2	2,4-$(CH_3)_2$Ph	Ph	−15	20	E–PE	64–65	1350, 1205
q	63105-11-3	2,6-Cl_2Ph	Ph	0	92	E–PE	92–93	1350, 1210
r	63105-12-4	$(CH_3)_3C$	$(CH_3)_3C$	10	60		*l*	1370, 1200

[a] Satisfactory analytical values for all new compounds (±0.3% for C, H, N, S). [b] Mole ratio amidoxime–$SOCl_2$–Et_3N 1:5:2.5. [c] Reaction temperature followed by warming to room temperature (1 h). [d] Based on the material recovered before recrystallization. [e] In acetone–carbon dioxide bath; Bz = benzene; PE = petroleum ether; E = ethyl ether. [f] Although determined in a preheated bath, the observed melting points may be lower than the actual values because of the thermal instability of the products. [g] In CCl_4–CS_2; attributable to [OS(O)N], see F. Wudl and T. B. K. Lee, *J. Am. Chem. Soc.*, **95**, 6349 (1973). [h] Obtained in 70–75% yield by using benzene solvent or benzene and $SOCl_2$–pyridine at 0 °C. [i] Reference 4a. [j] Allowed to stand at room temperature for 3 h; unreacted amidoxime was recovered. [k] Not determined because the product partly decomposed to carbodiimide at room temperature; identified by IR and TLC (silica, benzene). [l] Mass spectrum M^+ 218; oil impure of traces of carbodiimide.

stituted amidoximes can be prepared from two different routes, viz. from thioamides and hydroxylamine[8] or nitrile oxides and amines.[9] Finally it may be observed that the costs of the processes 1 and 2 are comparable, since they use the

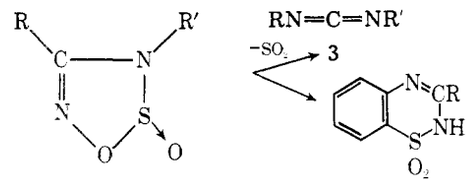


same commercial materials, although in a different succession of steps.

While the mechanism of the cyclization of amidoximes with $SOCl_2/Et_3N$ is unknown, its ready occurrence is consistent with the stereochemistry recently assigned to the most stable form of *N*-monosubstituted benzamidoximes in solution[10] and solid state,[11] viz. the *Z* configuration about the C=N bond (OH cis to NHR′) and the s-trans conformation about the amidic nitrogen (H of NHR′ faces the OH group). From the results of compounds **2l** and **2r**, the reaction appears somewhat retarded when the size of the groups R and R′ are increased. This parallels the observation[10] that bulky groups R and R′ give rise to a partial conformational change on the NHR′ group; this leads to the presence of the s-cis form which constitutes evidently an unfavorable arrangement for cyclization.

Thermal Decomposition of Heterocycles 2. A. Preparation of Carbodiimides 3. 3,4-Disubstituted 1,2,3,5-oxathiadiazole 2-oxides **2** have been reported to fragment at or just above their melting points to give carbodiimides **3** and sulfur dioxide when R is an aryl group[4] and/or undergo ring enlargement to 1,2,4-benzothiadiazine 1,1-dioxides[12] (**5**) when R is an alkyl and R′ an aryl group.

Our results on the thermal fragmentation of 4-aryl-1,2,3,5-oxathiadiazole 2-oxides (**2a–j** and **2l–q**) confirm the expectations based on previous findings[4] and give details on



R = alkyl, R′ = Ph

the preparation of a number of carbodiimides **3a–k** (Table II). The carbodiimides **3** yields were satisfactory (70–80%) with the exception of *N*-methyl-*N*′-phenylcarbodiimide (**3f**), whose low yield[13] is probably due to a considerable tendency to polymerize.[14] This demonstrates that the preparative value of this reaction depends on the stability of the carbodiimide at the temperature required for the fragmentation of its precursor. Carbodiimides which partly decompose on distillation were conveniently identified after conversion to the corresponding ureas **4**. In the same way, all compounds **3** of Table II could have been employed in situ for other reactions, their impurities being some polymeric material which, however, could be easily removed by dissolving the carbodiimide in a proper solvent, such as petroleum ether, and filtration.

For most of the heterocycles **2** the pyrolysis was carried out at 100–125 °C for 10–30 min. However, the two 4-mesityl derivatives **2m** and **2o** and the 4-(2,4-dimethylphenyl) derivative **2p** converted into the corresponding carbodiimides **3h, 3i,** and **3j** already at room temperature. This prevented the isolation of **2m** and **2o** from the originating reaction mixture of amidoximes **1h** and **1i** with thionyl chloride (see previous section and footnote *k* of Table I). Evidently, other factors being equal, the ease of conversion **2** → **3** depends on the migratory aptitude of R from carbon to nitrogen,[15] which appears to be favored when R is an aryl group with electron-donating substituents and inhibited when R is an alkyl group, particularly methyl. The latter observation accounts for the failure to obtain the carbodiimide **3f** from **2k** (R = CH_3, R′ = Ph)[13] and in general for the preferential formation of benzothiadiazines **5** when R is an alkyl group.[12]

Table II. Carbodiimides[a] 3 from the Thermolysis of 1,2,3,5-Oxathiadiazole 2-Oxides 2

Compd 3	Registry no.	Precursor 2	R	R′	Time, min	Temp, °C	Yield, %	Bp (mm) or mp, °C	IR (CCl_4), cm^{-1}	Urea 4, mp, °C	Registry no.
a	63105-13-5	**a**	*m*-ClPh	Ph	20	120	70[b]	*c*	2140	185–186	2008-71-1
a		**h**	Ph	*m*-ClPh	20	110	70[b]	*c*	2140	185–186	
b	53288-64-5	**b**	*p*-ClPh	Ph	15	120	80[b]	135–138 (0.2)	2140	240 dec	1967-26-6
b		**g**	Ph	*p*-ClPh	20	100	80[b]	*c*	2140	240 dec	
c	19244-07-6	**c**	*p*-CH_3Ph	Ph	20	100	85[b]	*c*	2140	217–218	4300-33-8
c		**f**	Ph	*p*-CH_3Ph	20	120	80[b]	*c*	2140	217–218	
d	3815-60-9	**d**	*p*-CH_3OPh	Ph	10	100	80[b]	*c*	2140	193–194	3746-53-0
d		**e**	Ph	*p*-CH_3O-Ph	30	125	80[b]	*c*	2140	193–194	
e	622-16-2	**i**	Ph	Ph	30	120	75	121–122 (0.5)	2140	239–240	102-07-8
f	4172-91-2	**j**	Ph	CH_3	30	110	20[b]	*d*	2140	150–151	1007-36-9
g	2219-34-3	**l**	Ph	$(CH_3)_3C$	15	100	88[b]	73–75 (760)	2120	167–168	15054-54-3
h	60986-29-0	**m**	Mesityl	Ph		*e*	82	145–158 (0.4)[c]	2150	236–237	2904-67-8
h		**n**	Ph	Mesityl	30	105	80	*c*	2150	236–237	
i	63105-14-6	**o**	Mesityl	Mesityl		*f*	77	41–41.5 (PE)	2160	310	6095-81-4
j	63105-15-7	**p**	2,4-$(CH_3)_2$-Ph	Ph	20	55	60[f]	oil[c]	2140	219–220	13140-55-1
k	63105-16-8	**q**	2,6-Cl_2Ph	Ph	30	115	89	46–47 (PE)	2160	240–241	63105-17-9

[a] All compounds 3 and the corresponding ureas 4 gave satisfactory analytical data (±0.3% for C, H, and N). [b] Determined after conversion to the corresponding urea by acid-catalyzed hydration (see Experimental Section). [c] Partly decomposed on distillation, giving material boiling in a large range of temperature. A pure sample was obtained by column chromatography (silica, benzene, or petroleum ether–methylene chloride 2:1). [d] Not isolated in a pure state. [e] At room temperature without isolation of the oxathiadiazole *S*-oxide (see Table I, footnote *k*); yields refer to the initial amount of amidoxime. [f] Obtained in 79% yield following the conditions of footnote *e*.

The selective thermal breakdown to carbodiimides and the mild conditions required appears to be a characteristic of 3,4-diaryl-1,2,3,5-oxathiadiazole 2-oxides **2**, since structurally related five-membered heterocycles behave differently. For instance, 3,4-diaryl-1,2,4-oxadiazolin-5-ones fragment at 260 °C into carbon dioxide and benzimidazoles,[16] whereas 1,5-diaryltetrazoles give mixtures of benzimidazoles and carbodiimides by loss of nitrogen at 200 °C.[17]

If we now look at the overall process **1** → **3**, we can conclude that the key step of this conversion is the formation of the heterocycle **2**, which activates the amidoxime **1** for the dehydration and rearrangement processes. The thermodynamic stability of the departing sulfur dioxide molecule is probably the driving force of the breakdown process. Similar examples of activation of hydroxamic acid derivatives through cyclic or open-chain intermediates include the thermal conversion of benzohydroxamic acids to isocyanates through their esters (Lossen rearrangement)[18] or through 1,3,2,4-dioxathiazole 2-oxides[19] and of amidoximes to carbodiimides by benzenesulfonyl chloride through the *O*-benzenesulfonyl ester[20] or by phosphorus oxychloride through a postulated phosphazole intermediate.[21]

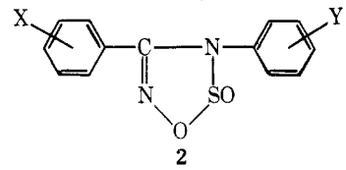
B. Mechanism of the Thermal Conversion 2 → 3. It has already been suggested[4a] that the thermolysis of heterocycles **2** to carbodiimides **3** is a concerted reaction, so that the loss of sulfur dioxide is concomitant with the migration of R from carbon to nitrogen. In order to gain further insight into the mechanism of the reaction, we have studied the kinetics of the thermal decomposition of 3,4-diaryl-1,2,3,5-oxathiadiazole 2-oxides (**2a–i**) and carried out proper experiments in order to exclude more justifiably the presence of unstable intermediates.

The reactions of **2a–i** were followed to at least 2 half-lives and were found to be of first-order throughout. In reactions allowed to proceed for infinite time, the values of conversion into carbodiimide varied from 80 to 95% (Table III), the lower yields being found in the slowest runs where the extent of polymerization of the carbodiimide became significant. Reactions at different initial concentrations of **2** gave reproducible first-order rate constants which exclude intermolecular processes or catalytic phenomena. The results of Table III illustrate the substituent effect on the reaction rate, which in fact appeared to be affected in opposite ways by substitution in the 3-phenyl (*N*-Ph) and 4-phenyl (*C*-Ph) ring. A plot of log k against σ^+ values[22] for substituents X in *C*-Ph fitted in a good straight line with negative slope ($\rho^+ = -1.92$, $r = 0.992$), whereas the plot against σ values[22] produced a less satisfactory correlation ($\rho = -3.04$, $r = 0.962$). The accelerating effect by electron-donating substituents X in the migrating aryl group R as well as its magnitude compare quite well to those observed in classical [1,2] shifts from carbon to nitrogen, such as in benzamides (Hofmann degradation $\rho = -2.5$),[23] in benzohydroxamic acid esters (Lossen rearrangement $\rho = -2.6$),[23] and in acetophenone oximes (Beckmann rearrangement $\rho = -1.95$, $\rho^+ = -1.70$).[23,24] On the other hand, a good correlation with a positive slope ($\rho = 0.61$, $r = 0.992$) was found to hold between log k and σ values for substituents Y in *N*-Ph, a result which points out that the reaction is retarded by electron-releasing, and accelerated by electron-withdrawing, substituents Y.

In Table IV are reported the data aiming to elucidate the effects of the solvent and temperature on the rate of decomposition of the representative compound 3,4-diphenyl derivative **2i**. The rate constant determined in four solvents of markedly different character changes little with the polarity of the solvent; the value in nitrobenzene ($\epsilon = 34.8$) was only about double that in chlorobenzene ($\epsilon = 5.62$). From the rate constants measured at different temperatures in chlorobenzene solvent the following activation parameters were calculated: $\Delta G^{\ddagger} = 27.9$ kcal mol^{-1}, $E_a = 28.1$ kcal mol^{-1}, $\Delta S^{\ddagger} = -1.4$ eu.

These kinetic results are consistent with a single-step mechanism and it is suggested that the [1,2] aryl shift[25] from carbon to the electron-deficient nitrogen[26] occurs intramolecularly in concert with the loss of sulfur dioxide in the transition state a (Scheme I). Owing to the simultaneous electron redistribution, the transition state a must possess little polarity, a characteristic which accounts for the slight dependence of the rate on the polarity of the solvent. The participation of the migrating aryl group in the transition state explains the substantial effect of substituents X on rate[27] and accounts for the low temperature of decomposition,[28] a fact

Table III. Rate Constants for the Thermal Decomposition of 3,4-Diaryl-1,2,3,5-oxathiadiazole 2-Oxides 2 in Chlorobenzene at 100 °C



2

Compd 2	X	Y	10^2 [2][a]	10^4k, s^{-1}	$t_{1/2}$, min	λ (ε),[b] cm^{-1}	Yield,[c] %
a	*m*-Cl	H	2.471	0.565		1360 (26.5)	
			4.910	0.570		1360	78
				mean 0.568	203		
b	*p*-Cl	H	2.685[d]	1.36		2140 (187.5)	81
			2.685[d]	1.36		1360 (27.8)	
			8.079	1.39		1370	
				mean 1.37	84		
c	*p*-CH_3	H	0.441	12.0		2140 (164.5)	81
			1.319	11.6		2140	
				mean 11.8	9.8		
d	*p*-CH_3O	H	0.403	83.5		2140 (158.5)	98
			1.207	82.0		2140	
				mean 82.8	1.4		
e	H	*p*-CH_3O	0.464	2.78		2140 (158.5)	82
			7.495	3.03		1365 (18.9)	97
				mean 2.91	40		
f	H	*p*-CH_3	0.446	2.94		2140 (164.5)	90
			1.324	2.88		2140	
				mean 2.91	40		
g	H	*p*-Cl	0.382	5.40		2140 (187.5)	96
			1.151	5.41		2140	
				mean 5.41	21		
h	H	*m*-Cl	5.442[d]	6.52		1360 (26.5)	
			5.442[d]	6.47		2140 (186.7)	
			16.32	6.58		1360	92
				mean 6.52	18		
i	H	H		3.61[e]	32		

[a] At room temperature. [b] Analytical wavelength, molar extinction coefficient in parentheses (1-mm NaCl cell). [c] Of carbodiimide; determined from the absorbance at 2140 cm^{-1} after 5 or 6 half-lives. [d] Single run followed at two wavelengths. [e] Extrapolated from the Arrhenius parameters (Table IV).

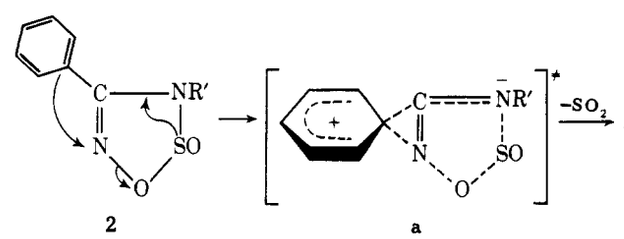
Table IV. Rate Constants[a] for the Thermal Conversion of 3,4-Diphenyl-1,2,3,5-oxathiadiazole 2-Oxide (2i) to Diphenylcarbodiimide (3e) in Various Solvents

Solvent[b]	Temp, °C	10^4k, s^{-1}	$t_{1/2}$, min	Yield,[c] %
Chlorobenzene (5.62)	70	0.134[d]	861	95
	86	0.823[d]	140	90
	90	1.28[d]	90	96
	110	9.90[d]	12	93
o-Dichlorobenzene (9.93)	86	0.966	119	92
Nitrobenzene (34.8)	86	2.21	52	92
Me_2SO (46.6)	86	6.6[e]	18	80

[a] Average of three runs with a standard error of ±2%; initial concentrations of **2i:** 0.004–0.02 M in chlorobenzene and dichlorobenzene [λ (ε), 2140 (187), 1-mm NaCl cell]; 0.009–0.04 M in nitrobenzene and Me_2SO [λ (ε), 2140 (182, 230), 0.5-mm NaCl cell]. [b] Dielectric constants in parentheses (ref 33). [c] Of carbodiimide **3e** (see footnote *c* of Table III). [d] The activation parameters calculated from these rate constants were: E_a = 28.1 ± 0.1 kcal mol^{-1}, $\Delta S^{\ddagger}$ (90 °C) = −1.4 ± 0.3 eu, $\Delta H^{\ddagger}$ (90 °C) = 27.4 ± 0.1 kcal mol^{-1}, $\Delta G^{\ddagger}$ (90 °C) = 27.9 ± 0.1 kcal mol^{-1}. [e] Inaccurate because of the slow reaction of **3e** with Me_2SO: J. G. Moffatt, *J. Org. Chem.*, **36,** 1909 (1971).

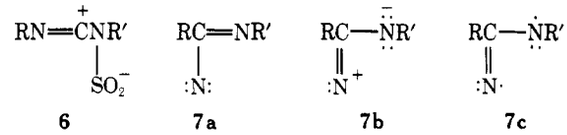
which is reflected in the moderate value of the activation energy (28 kcal mol^{-1}). Finally, the small negative entropy value (−1.4 eu), which is well comparable with those recorded for the Beckmann[24] and Curtius[29] rearrangements, is consistent with the transition state a, whereas a large positive value would be expected for the rate-limiting formation of an open-chain intermediate.[29]

Scheme I



2 a

In line with the kinetic data, trapping experiments failed to reveal the presence of open-chain intermediates. In fact, the amount of carbodiimide **3e** from the thermolysis of 3,4-diphenyl 1,2,3,5-oxathiadiazole 2-oxide (**2i**) was practically independent of the solvent employed[30] (Tables IV and V), whereas lower and/or variable yields were expected if intermediates **6** or **7** were formed, since it seems unlikely[25c,31] that



6 7a 7b 7c

they should not be at least partially trapped by any of the solvents employed. Moreover, while benzimidazoles, diagnostic for azomethine nitrene **7a,** are formed from the fragmentation of 3,4-diaryl-1,2,4-oxadiazolin-5-ones[32] and 1,5-diaryltetrazoles,[14] the presence of 2-phenylbenzimidazole was not detected by VPC of the reaction mixture from the thermolysis of **2i** in cyclohexane.

Table V. Thermal Fragmentation of 3,4-Diphenyl-1,2,3,5-Oxathiadiazole 2-Oxide (2i) in Various Solvents

Solvent	Time, h	Carbodiimide 3e, %[a]
None[b]		75
Cyclohexane	48	76
Anisole	24	81 (34)
Acetonitrile	20	79 (4)
Benzene (DMADC)[c]	24	70

[a] Number in parentheses refers to the amount of **3e** isolated as *N,N'*-diphenylurea. [b] See Table II. [c] Plus 15 molar excess with respect to **2i** of dimethyl acetylenedicarboxylate (DMADC).

In conclusion, the implication of our kinetic results and our failure to detect any unstable intermediates is that the decomposition of the heterocycles **2** to carbodiimides **3** and sulfur dioxide most probably occurs by a concerted process.

Experimental Section[33]

Reagents and Solvents. Thionyl chloride, amines, and solvents for preparative experiments were distilled or recrystallized before use. Triethylamine and pyridine were distilled twice over potassium hydroxide pellets. The petroleum ether corresponds to fraction bp 40–60 °C. Solvents for kinetic experiments were purified by proper procedures[34] and were distilled twice over anidrone just prior to use.

Amidoximes. These compounds were prepared by addition of amines to nitrile oxides. Details on the preparation of amidoximes **1b, 1f, 1t, 1i, 1j, 1m, 1n,** and **1q** have already been reported.[10] For the other compounds the reaction mixtures (CCl_4, 5 molar excess of amine) were allowed to stand at room temperature for 24–36 h. The excess of amine and by-products deriving from self-reaction of the nitrile oxide was removed by chromatography (silica), eluent benzene; the amidoxime was then recovered almost pure by elution with benzene–ethyl ether (9:1 or 9:2). After recrystallization from benzene–petroleum ether, unless not otherwise noted, all compounds gave satisfactory analytical data and IR spectra (CCl_4–C_2Cl_4–CS_2), showing the characteristic bands at 3600 (OH), 3400 (NH), ~3300 br (OH), and 1630 cm^{-1} (C=N): **1a** (R = *m*-ClPh, R' = Ph), mp 131–132 °C; **1c** (R = *p*-CH_3Ph, R' = Ph), mp 124–125 °C; **1d** (R = *p*-CH_3OPh, R' = Ph), mp 121–122 °C; **1e** (R = Ph, R' = *p*-CH_3OPh), mp 160–162 °C; **1h** (R = Ph, R' = *m*-ClPh), mp 129–130 °C (from ethanol); **1k** (R = CH_3, R' = Ph), mp 117–118 °C (from benzene); **1l** [R = Ph, R' = $(CH_3)_3C$], mp 129–130 °C (from methanol); **1o** (R = R' = mesityl), mp 198–200 °C; **1p** [R = 2,4-$(CH_3)_2$Ph, R' = Ph], mp 163–164 °C; **1r** [R = R' = $(CH_3)_3C$], mp 134–135 °C (from ethanol).

1,2,3,5-Oxathiadiazole 2-Oxides 2. The cyclizations were carried out in a four-neck 1-L flask equipped with a stirrer, a thermometer, an addition funnel, and a gas outlet tube protected with a $CaCl_2$ valve. The solution of the amidoxime **1** (18–30 mmol) and 2.5 molar excess of triethylamine in 250–300 mL of methylene chloride was cooled at the required temperature (Table I) in the reaction flask. To this mixture was added with efficient stirring over a 15-min period a 5 molar excess of thionyl chloride in 20 mL of methylene chloride. The mixture was allowed to warm to room temperature (1 h) and then 250 mL of a 10% solution of $NaHCO_3$ in water was added with vigorous stirring and cooling. The heterogeneous mixture was stirred for an additional 30-min period and then allowed to stand until the two phases were well separated. The organic phase was washed with cold water and dried over $CaSO_4$. Evaporation of the solvent under reduced pressure at room temperature gave an oil which solidified on treating with petroleum ether and cooling in an acetone–carbon dioxide bath. In the case of compounds **2m, 2o,** and **2p** the oil residue showed the presence of a considerable amount of carbodiimide (IR absorption at 2140 cm^{-1}). Details of the experimental conditions and properties of compounds **2** are given in Table I.

Thermolysis of 1,2,3,5-Oxathiadiazole 2-Oxides 2 to Carbodiimides 3. A. Preparative Scale. A 25-mL thick wall vial was charged with 2.0 g of **2** and connected to a vacuum system. When the vacuum was regulated at 100–120 mmHg, the vial was carefully placed in a preheated oil bath. This produced an almost instant melting of the solid material and an intense gas evolution, which ceased within a few minutes. Heating under slight vacuum was continued for an additional period (Table II). After cooling the vial to room temperature, proper tests (TLC and IR) on the oil residue showed the total disappearance of **2** (absence of the 1360–1370-cm^{-1} band) and the formation of **3** (IR absorption at 2140–2160 cm^{-1}). All carbodiimides **3** were identified after conversion to the corresponding ureas **4** by heating the oil residue on a steam bath (1 h) with 25 mL of 20% HCl. The N,N'-disubstituted ureas **4,** which simply crystallized on cooling, exhibited the expected IR (Nujol) bands [3300 (NH) and 1650 cm^{-1} (CONH)] and gave satisfactory analytical data. Comparisons with authentic samples were also made.

B. Trapping Experiments. Solutions of 3,4-diphenyl 1,2,3,5-oxathiadiazole 2-oxide (**2i**) (1.5–2.0 g) in the selected solvent (40 mL) were refluxed with exclusion of the moisture till the total disappearance on TLC. The solvent was evaporated under reduced pressure and the residue was chromatographed (silica, benzene) to give the carbodiimide **3e** and then the corresponding urea (eluent, benzene–ethyl ether 1:1) (Table V).

C. Kinetic Measurements. The reactions were initiated by adding a weighed amount (0.02–0.2 g) of the selected compound **2** in a small thin-wall vial to the preheated solvent (20–50 mL) which was contained in a kinetic flask placed in a thermostatted oil bath. Aliquots were removed at intervals and quenched by cooling in liquid nitrogen. The kinetics were followed spectroscopically by monitoring the carbodiimide at 2140 cm^{-1} or the unreacted oxathiadiazole 2-oxide at 1360 cm^{-1} or both compounds. In the first case, in order to have measurable absorbance values (1- or 0.5-mm NaCl cells), the aliquots were diluted with the same solvent employed for the reaction. In the second case, the solvent of the aliquots was removed under vacuum at room temperature and the residue dissolved in carbon tetrachloride for the IR measurements. Normally, 10–15 readings were taken for a given reaction, which was followed to at least 2 half-lives. First-order rate constants were calculated from linear plots of ln C_t vs. time (C_t, concentration of **2**) or more simply of ln A_t at 1360 cm^{-1} vs. time. For reactions followed through the 2140-cm^{-1} band, the C_t values were calculated from $(C_0 - x)$, where C_0 was the initial concentration of **2** and x the concentrations of the carbodiimide calculated from the measured absorbances by the Lambert–Beer law. Control experiments showed: (i) the stability of the carbodiimide for at least 2 half-lives of a given reaction; (ii) the occurrence of the Lambert–Beer law at the analytical wavelengths in the range of concentrations employed.

The activation parameters were calculated by standard method:[35] E_a from the linear plot of ln k vs. $1/T$ (Table IV), $\Delta S^{\ddagger}$ from log A (13.0 s^{-1} at 90 °C), $\Delta H^{\ddagger}$ from the approximation $\Delta H^{\ddagger} = (E_a - RT)$, and $\Delta G^{\ddagger}$ from $\Delta H^{\ddagger} - T\Delta S^{\ddagger}$.

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Registry No.—**1a,** 63163-64-4; **1b,** 28051-07-2; **1c,** 57984-77-7; **1d,** 60404-64-0; **1e,** 52395-23-0; **1f,** 36954-50-4; **1g,** 57767-05-2; **1h,** 63133-68-6; **1i,** 3488-57-1; **1j,** 28267-98-3; **1k,** 5661-30-3; **1l,** 20002-26-0; **1m,** 3023-19-6; **1n,** 36954-51-5; **1o,** 16031-60-0; **1p,** 63133-69-7; **1q,** 63133-70-0; **1r,** 63133-71-1; $SOCl_2$, 7719-09-7; H_2NR' (R' = Ph), 62-53-3; H_2NR' (R' = *p*CH_3OPh), 104-94-9; H_2NR' (R' = *m*-ClPh), 108-42-9; H_2NR' (R' = *t*-Bu), 75-64-9; H_2NR' (R' = mesityl), 88-05-1; O=N≡CR (R = *m*-ClPh), 13820-15-0; O=N≡CR (R = *p*CH_3Ph), 13820-14-9; O=N≡CR (R = *p*-CH_3OPh), 15500-73-9; O=N≡CR (R = Ph), 873-67-6; O=N≡CR (R = CH_3), 7063-95-8; O=N≡CR (R = mesityl), 2904-57-6; O=N≡CR [R = 2,4-$(CH_3)_2$Ph], 63105-18-0; O=N≡CR (R = *t*-Bu), 27143-81-3.

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Condensation of Aldehydes with Methylimidazo[1,2-*a*]pyridines

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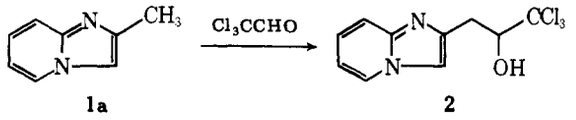
The reactions of various methylimidazo[1,2-*a*]pyridines (**1**) with acetaldehyde and chloral follow the usual course of electrophilic substitution at the 3 position, contrary to an earlier report of condensation at a methyl group. Initially formed adducts **6a–c** and **8** give secondary products, **5a–c**, **7a–c**, and **9**. Unusual IR, UV, and ^1H NMR spectral properties of the dichloro ketone **9** and the aldehyde **12**, which was formed by treating the chloral adduct **8** with strong base, are discussed.

The reported reaction[1] of the methyl group in 2-methylimidazo[1,2-*a*]pyridine (**1a**) with chloral to give the condensation product **2** must proceed via the anion **3**. Facile formation of such an anion, however, is incompatible with our finding that 7-methylimidazo[1,2-*a*]pyridine, which is expected to give a more stable anion (see **4**), does not readily give such an anion as shown by its failure to be oxidized to the aldehyde by selenium dioxide.[2] Further, reactions of imidazo[1,2-*a*]pyridine with other electrophilic reagents[3] generally occur at position 3. The reactivity of the methyl group in compound **1**, and concomitant correctness of structure **2**, therefore become questionable. The condensation of acetaldehyde with various methylimidazo[1,2-*a*]pyridines as



1a **2**