para to an *ortho* position are outweighed by greater decreases in the ΔH^*.

The methyl group should be expected to retard more from the *ortho* than from the *para* position because of its powerful +I effect and, because of its great steric requirements, it exhibits a large *ortho* effect: $k_6/k_4 = 0.033$ due to a greater ΔH^* and a lower ΔS^*. A similar ratio ($k_6/k_4 = 0.037$) is found when bromide is the leaving group.[14]

ortho **Effects and the Entropy of Activation.**—Besides the effects considered there are others which specially affect the entropy of activation. These are hydrogen bonding, built-in solvation, and steric hindrance to motion in the transition state and intermediate complex.

Hydrogen bonding and built-in solvation stabilize the transition state and the intermediate complex. It can be assumed that both effects are mainly associated with the *o*-nitro group which is always present; therefore they are roughly constant through the series.

It can be expected that a bulky substituent near the reaction site, despite its polar nature, will reduce the number of accessible energy levels available to the transition state relative to the initial state. This "bulk" effect will decrease ΔS^*. In all the cases studied the entropy variation ($\Delta\Delta S$, Table V) on going from the *para* to the *ortho* position is negative, when greater than experimental error.

The very low entropy for the reaction of 2-chloro-3-nitroaniline can be explained by an additional effect of electrostatic repulsion in the transition state between the hydrogen atoms of the amino group, and those on the entering nitrogen atom, which is positively charged. (Such repulsions limit the freedom of vibrational and rotational motion.) The same repulsion can exist to a smaller amount in the transition state for the reaction of 2-chloro-3-nitroanisole, but entropy decreases are outweighed by the energy increases owing to the polar effects.

In the case of methyl group an energy increase due to its powerful +I effect is added to the entropy decrease with a consequent large decrease of the rate.

Nitro and bromo groups are "bulky" substituents, and steric hindrance decreases ΔS^*. London forces[51] seem to be unimportant in this type of reaction, because of the low polarizability of the nucleophile.

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Dipolar Addition Reactions of Nitrile Oxides. II.[1] A New Synthesis of Carbodiimides

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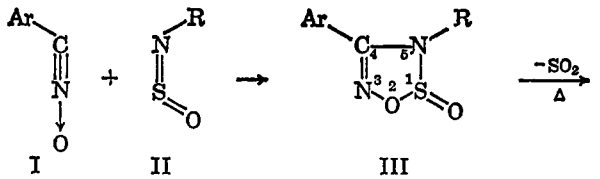
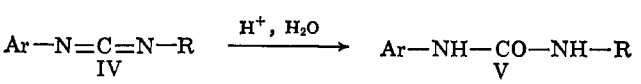
A general method for the preparation of carbodiimides by the pyrolysis of 4,5-disubstituted 1-oxo-1,2,3,5-thiaoxadiazoles is described.

The synthesis of 4,5-diphenyl-1-oxo-1,2,3,5-thiaoxadiazole (IIIa), a representative of a new heterocyclic system, and its pyrolysis to diphenylcarbodiimide (IVa) with the concomitant extrusion of sulfur dioxide were described in a recent communication.[2]

We have examined this reaction in detail to find that the pyrolysis of this novel class of compounds (III) is indeed a general one and that it constitutes a new method for the synthesis of symmetrical and unsymmetrical carbodiimides.



I II III



IV V

Va, Ar = 4-chlorophenyl; R = 4-methoxyphenyl
b, Ar = 4-chlorophenyl; R = 4-methylphenyl
c, Ar = 4-chlorophenyl; R = 4-methylbenzenesulfonyl

The 1-oxo-1,2,3,5-thiaoxadiazoles IIIa–h (Table I) are easily obtained by the dipolar cycloaddition of nitrile oxides (I) to N-sulfinyl compounds (II)[3] and they decompose readily at or just above their melting points yielding the carbodiimides IVa–h (Table II) and sulfur dioxide. This pyrolysis reaction, which is similar to those of 1,5-diaryltetrazoles VI[4] and 3,4-diaryl-Δ^2-1,2,4-oxadiazolin-5-ones VII,[5] differs from them in that, apart from sulfur dioxide, only carbodiimides are formed in this case. Pyrolysis of tetrazoles of the type VI has been reported to yield a mixture of carbodiimides and arimidazoles[4] and that of oxadiazolinones of the type VII arimidazoles[5] only.

The pyrolytic formation of carbodiimides from compounds of the type III was ascribed[2] to the migration of the group initially at the 4 position to an electron-deficient nitrogen arising from the release of sulfur di-

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(3) G. Kresze, A. Maschke, R. Albrecht, K. Bederke, H. P. Patzschke, H. Smalla, and A. Trede, *ibid.*, **74**, 135 (1962).
(4) P. A. S. Smith and E. Leon, *J. Am. Chem. Soc.*, **80**, 4647 (1958).
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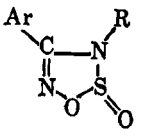
TABLE I



III

Compd.	Ar	R	M.p., °C.	Recrystn. solvent	Formula	Calcd., % C	H	N	Found, % C	H	N
a	Phenyl[a]	Phenyl[a]	72–73	Benzene–*n*-hexane	$C_{13}H_{10}N_2O_2S$	60.45	3.90	12.41	60.60	3.83	12.16
b	4-Chlorophenyl	4-Nitrophenyl	112–113 dec.	Ethyl acetate–*n*-hexane	$C_{13}H_8ClN_3O_4S$	46.23	2.39	12.45	46.67	2.70	12.60
c	4-Chlorophenyl	4-Chlorophenyl	124–126 dec.	Methanol	$C_{13}H_8Cl_2N_2O_2S$	47.73	2.46	8.57	47.51	2.50	8.89
d	Phenyl	4-Methoxyphenyl	91–93°	Methanol	$C_{14}H_{12}N_2O_3S$	58.33	4.20	9.72	58.48	4.60	9.69
e	3,4-Dichlorophenyl	4-Nitrophenyl	150–151 dec.	Benzene–*n*-hexane	$C_{13}H_7Cl_2N_3O_4S$	41.96	1.90	11.29	42.01	1.95	11.25
f	4-Chlorophenyl	4-Methylbenzenesulfonyl	89–90 dec.	Benzene–*n*-hexane	$C_{14}H_{11}ClN_2O_4S_2$	45.36	2.99	7.56	46.46	3.24	7.97
g	4-Chlorophenyl	4-Methoxyphenyl	123–125	Methanol	$C_{14}H_{11}ClN_2O_3S$	52.10	3.44	8.68	52.18	3.20	8.88
h	4-Chlorophenyl	4-Methylphenyl	119–121	Methanol	$C_{14}H_{11}ClN_2O_2S$	54.82	3.62	9.14	55.10	3.82	9.00

[a] See ref. 2.

TABLE II

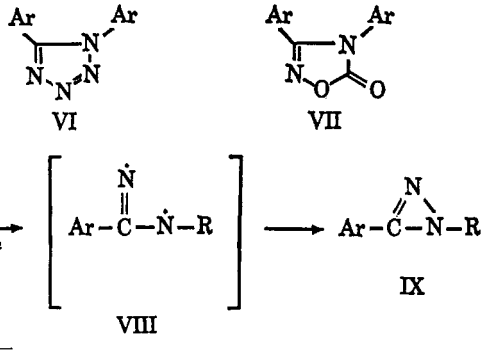
Ar—N=C=N—R

IV

Compd.	Ar	R	B.p. (mm.) or m.p., °C.	Recrystn. solvent	Formula	Calcd., % C	H	N	Found, % C	H	N
a	Phenyl[a]	Phenyl[a]	106–107 (0.1)[b]		$C_{13}H_{10}N_2$	80.38	5.19	14.42	80.39	5.47	14.19
b	4-Chlorophenyl	4-Nitrophenyl	96–98	Benzene–*n*-hexane	$C_{13}H_8ClN_3O_2$	57.05	2.95	15.35	56.76	3.36	15.76
c	4-Chlorophenyl	4-Chlorophenyl	52–53[c]	*n*-Hexane	$C_{13}H_8Cl_2N_2$	59.34	3.06	10.65	59.12	2.87	10.29
d	Phenyl	4-Methoxyphenyl	165–170 (1–2)		$C_{14}H_{12}N_2O$	74.99	5.38	...	75.48	5.48	...
e	3,4-Dichlorophenyl	4-Nitrophenyl	114–116	Benzene–*n*-hexane	$C_{13}H_7Cl_2N_3O_2$	50.67	2.29	13.64	50.76	2.25	13.81
f	4-Chlorophenyl	4-Methylbenzenesulfonyl	59–61	*n*-Hexane	$C_{14}H_{11}ClN_2O_2S$	54.82	3.59	9.14	54.65	3.85	9.33
g[d]	4-Chlorophenyl	4-Methoxyphenyl	*e*								
h[d]	4-Chlorophenyl	4-Methylphenyl	*e*								

[a] See ref. 2. [b] S. Hünig, H. Lehmann, and G. Grimmer [*Ann.*, **579**, 77 (1953)] reported b.p. 163–165° (11 mm.). [c] Hunig, *et al.*,[b] gave m.p. 54°. [d] Identified by infrared spectrum and conversion to the corresponding urea by acid-catalyzed hydration (*cf.* Experimental Section). [e] Decomposed on distillation, being a high-boiling liquid.

oxide. If this reaction follows a free-radical pathway, it is reasonable to assume that the diradical intermediate VIII (which is likely to be formed momentarily) might, before rearrangement, couple to yield the interesting three-membered heterocyclic system IX (which would be isomeric to the known diazirines[6]), particularly because the reaction proceeds at much lower temperatures than are usually involved in most pyrolysis reactions. Careful examination of the products, however, showed that IX was not one of them. Neither was it possible (if an ionic mechanism is attributed to this reaction) to trap the intermediate dipole, before rearrangement, with highly reactive dipolaraphiles as in the case of diphenylnitrilimine which is obtained by the pyrolysis of 2,5-diphenyltetrazole.[7] These facts serve to confirm the earlier postulation[2] that the loss of the elements of sulfur dioxide and the formation of carbodiimides by the rearrangement of the resulting fragment proceed through a single concerted step.



VI VII

III $\xrightarrow[-SO_2]{\Delta}$ [Ar–C(=N·)–N·–R] ⟶ Ar–C(=N–R)

VIII IX

The carbodiimides IVa–h were isolated in nearly quantitative yields and identified by their typically intense absorption in the 4.5–5.0-μ region of the infrared and analyses and, in some cases, by conversion to the

(6) E. Schmitz, *Angew. Chem. Intern. Ed. Engl.*, **3**, 333 (1964).

(7) R. Huisgen, M. Seidel, G. Wallbillich, and H. Knupfer, *Tetrahedron*, **17**, 3 (1962).

corresponding urea Va–c (*cf.* Experimental Section) by acid-catalyzed hydration. Compound IIIf gave, on pyrolysis, the N-sulfonylcarbodiimide IVf, a class of compounds until recently not described in literature,[8] and this (IVf) in turn yielded the N-sulfonylurea Vc (*cf.* Experimental Section) on hydration.

Experimental Section[9]

4,5-Diphenyl-1-oxo-1,2,3,5-thiaoxadiazole (IIIa).—A solution of benzhydroxamoyl chloride (7.8 g., 0.05 mole) in ether (250 ml.) was extracted with a cold 4% aqueous solution of sodium hydroxide (50 g., equivalent to 0.05 mole of NaOH) in a separatory funnel and the ether layer containing benzonitrile oxide was then removed, washed with a small quantity of water, dried over anhydrous calcium chloride for about 2 min., and treated with N-sulfinylaniline[3] (7.0 g., 0.05 mole) with agitation. A vigorous exothermic reaction developed almost immediately at the end of which the clear reaction mixture was set aside for about 2 hr. at room temperature. Removal of the solvent under diminished pressure afforded an oily product which was treated with a small quantity of methanol and left in the refrigerator overnight. The solid that had separated was filtered, washed with a little ice-cold methanol, air-dried, and recrystallized from a mixture of benzene and *n*-hexane, m.p. 72–73°, yield 8.5 g.

With the exception of IIIf, all the compounds listed in Table I were prepared by an essentially similar procedure.

4-(4-Chlorophenyl)-5-(4-methylbenzenesulfonyl)-1-oxo-1,2,3,-5-thiaoxadiazole (IIIf).—Anhydrous triethylamine (5.1 g., 0.05 mole) was added in one portion to an ice-cooled and well-stirred solution of 4-chlorobenzhydroxamoyl chloride (9.5 g., 0.05 mole) in absolute ether (250 ml.) and, after a few minutes, the precipitate of triethylamine hydrochloride was filtered rapidly and washed with a small quantity of absolute ether. The combined filtrates were stirred and, with the exclusion of moisture, treated immediately with N-sulfinyl-4-methylbenzenesulfonamide[3] (10.9 g., 0.05 mole) added in one lot. The reaction mixture, protected from moisture, was then set aside for about 2 hr. at room temperature, filtered to remove a small quantity of precipitate, and stripped of solvent under diminished pressure. The residue was recrystallized from *n*-hexane, m.p. 89–90° dec., yield 8.5 g.

General Procedure for the Preparation of the Carbodiimides IVa–h (Table II).—The pyrolyses of the 1-oxo-1,2,3,5-thiaoxadiazoles IIIa–h were carried out in a temperature-controlled and electrically heated oil bath. The compounds were taken in small pear-shaped distillation flasks with standard joints and, with the exclusion of moisture and under a slow stream of dry nitrogen, heated to their melting points at which temperature most of these decomposed, spontaneously splitting off sulfur dioxide. In some cases, the temperature had to be raised to a little beyond the melting points until vigorous evolution of sulfur dioxide set in. The temperature was maintained steady until the decomposition was complete and the oily product was then cooled to room temperature. Some of the carbodiimides solidified and were recrystallized from suitable solvents, and the others were distilled under vacuum and obtained as liquids (Table II). All of these compounds exhibited intense absorption in the 4.5–5.0-μ region of the infrared which is characteristic of carbodiimides.

The ureas mentioned below were obtained by treating the corresponding carbodiimides with 2 *N* hydrochloric acid.

N-(4-Chlorophenyl)-N′-(4-methoxyphenyl)urea (Va) was recrystallized from ethanol, m.p. 265–267°. The melting point on admixture with an authentic specimen (prepared by treating 4-methoxyaniline with 4-chlorophenylisocyanate) was undepressed.

N-(4-Chlorophenyl)-N′-(4-methylphenyl)urea (Vb) was recrystallized from ethanol, m.p. 298–300°.

Anal. Calcd. for $C_{14}H_{13}ClN_2O$: C, 64.49; H, 5.02; N, 10.75. Found: C, 64.82; H, 5.24; N, 10.81.

N-(4-Chlorophenyl)-N′-(4-methylbenzenesulfonyl)urea (Vc) was recrystallized from a mixture of benzene and *n*-hexane, m.p. 170–172°.

Anal. Calcd. for $C_{14}H_{13}ClN_2O_3S$: C, 51.78; H, 4.03; N, 8.63. Found: C, 51.82; H, 4.29; N, 8.52.

Acknowledgment.—The authors would like to thank Professor T. R. Govindachari for his interest in this work and Dr. S. Selvavinayakam and his staff for elemental analyses and spectra.

(8) H. Ulrich and A. A. R. Sayigh, *Angew. Chem. Intern. Ed. Engl.*, **3**, 639 (1964); R. Neidlein and E. Heukelbach, *Tetrahedron Letters*, 149 (1965).

(9) Melting points are uncorrected.

Observations on the Cyclization of a Substituted α-Formamidoamidine to Aminoimidazolecarboxamide Derivatives[1]

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The cyclization of α-formamido-N-benzylguanylacetamide (I) could be influenced by reaction conditions to yield either a ring benzyl- (II) or benzylaminoimidazole (III) as the major product. These were converted to 9-benzyl- and 3-benzylhypoxanthine, respectively.

The discovery of aminoimidazolecarboxamide derivatives as intermediates in the biosynthesis of purines[2] prompted the development of new syntheses for aminoimidazoles. Among these was the cyclization of α-formamidoamidines which provided a useful route,[3] one which was subsequently shown[4] to be the natural ring-closing step. In chemical work directed toward the possible application of this cyclization toward the synthesis of imidazole nucleosides and nucleotides, it was of interest to determine to what extent ring closure could be influenced to take place to an N-alkylamidine nitrogen since this would lead to substitution on the imidazole ring in the position characteristic of the natural derivatives as in II. The alternative product would, of course, be the alkylaminoimidazole (III).

In the work described a benzyl group served as a model substituent. The monosubstituted amidine (I, R = C_7H_7) was synthesized from cyanoacetamide by treatment of the imino ethyl ether with 1 equiv. of benzylamine; N-benzylguanylacetamide thus produced yielded the formamido derivative (I) on coupling with benzenediazonium chloride and reductive formylation. It was characterized as the formate salt.

(1) Support of the U. S. Public Health Service (through CA-05294 and GM-1240) is gratefully acknowledged.

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(3) E. Shaw and D. W. Woolley, *J. Biol. Chem.*, **181**, 89 (1949).

(4) D. A. Goldthwait, R. A. Peabody, and G. R. Greenberg, *J. Am. Chem. Soc.*, **76**, 5258 (1954); *cf.* review by J. M. Buchanan and S. C. Hartman, *Advan. Enzymol.*, **21**, 199 (1959).