Preparation and Properties of Some New N,N'-Biisoimides and Their Cyclic Isomers. Reaction of N,N'-Biisomaleimide with Dienes

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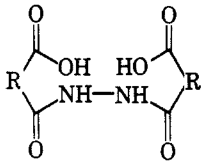
The synthesis of new N,N'-biisoimides by the dehydration of diacids derived from the reaction of cyclic anhydrides with hydrazine appears to require the presence of unsaturation between the carboxyl and amide functions. For example, dehydration of the diacid from citraconic anhydride or phthalic anhydride and hydrazine led to the corresponding N,N'-biisoimides, while attempts to prepare saturated N,N'-biisosuccinimides by by the same procedure gave N,N'-biimide isomers. N,N'-Biimide products were also obtained directly from the reaction of both dimethylmaleic anhydride or dichloromaleic anhydride and hydrazine. However, the diacid derived from dichloromaleic anhydride and phenylenediamine did give the biisoimide isomer in the presence of trifluoroacetic anhydride. Similarly, a number of other N,N'-biisoimides were obtained from dehydration of diacids derived from the reaction of diamines or dihydrazides with maleic anhydride or phthalic anhydride. Finally, the first examples of N,N'-biisosuccinimides were obtained from the Diels–Alder reaction of N,N'-biisomaleimide with dienes. A discussion of the limitations of the diacid dehydration route in terms of possible reaction intermediates, the tendency of various biisoimides to undergo acyl oxygen to nitrogen rearrangements, and the ultraviolet and infrared spectra of the new biisoimides are given.

In the preceding report[1] we described the synthesis and proof of structure for N,N'-biisomaleimide and two of its isomers. Criteria for assigning the N,N'-biisoimide structure also were discussed. These involved the use of infrared, ultraviolet, and nmr spectra and chemical reactivity. In this paper we have attempted to determine the accessibility of various analogous N,N'-biisoimides by straightforward synthetic methods. These involve the dehydration of diacids (I) derived from the reaction of substituted maleic anhydrides, phthalic anhydride, and succinic anhydrides with hydrazine. For comparative purposes, the use of diamines other than hydrazine to construct biisoimides is examined. Finally, the preparation of a number of isosuccinimide derivatives through the Diels–Alder reaction of N,N'-biisomaleimide with dienes will be shown to be a fairly general reaction.



I

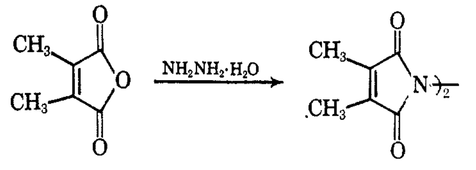
Results and Discussion

N,N'-Biisomaleimides from Substituted Maleic Anhydrides.—The previously described preparation[1] of N,N'-biisomaleimide from maleic anhydride and hydrazine involved the prior formation of the corresponding diacid I from 1 mole of hydrazine and 2 moles of maleic anhydride in acetic acid solvent. The diacid was then cyclized with a variety of dehydrating agents such as trifluoroacetic anhydride, acetyl chloride, or thionyl chloride.

In contrast, the reaction of citraconic anhydride with hydrazine in acetic acid did not give the desired diacid. Only methylmaleic hydrazide (III) was isolated. Methylmaleic hydrazide has been reported in the literature[2] but to our knowledge without adequate description or proof of structure. In our case, proof of structure followed from the elemental analysis and the infrared spectrum [λ_{CO}^{Nujol} 6.0 μ (br)]. Also, the hydrazide III was treated with acetyl chloride, giving N- or O-acetylmethylmaleic hydrazide (IV). The assignment of a pyridazinedione structure for IV rather than an imide or isoimide structure follows from the infrared, ultraviolet, and nmr spectra. Thus, the presence of three broad absorptions in the infrared spectrum at 5.66, 5.99, and 6.20 μ is consistent with the acylated pyridazinedione structure.[1] More important, the ultraviolet spectrum consists of bands with λ_{max} 213 mμ (ϵ 6200) and 290 mμ (ϵ 3070),[1] while the nmr spectrum in trifluoroacetic anhydride has three resonances at 7.35 (vinyl), 2.30 ($COCH_3$), and 2.10 ($CH_3CR{=}$) ppm in the proper area ratio.

It was subsequently found that the diacid V could be isolated by simply carrying out the reaction of citraconic anhydride with hydrazine in acetic acid–methanol. This solvent combination also was found to lead to diacids in other examples (see below) where the use of acetic acid solvent alone was unsuccessful. Dehydration of V with trifluoroacetic anhydride gave the biisoimide VI (Scheme I). This biisoimide has two sharp bands at 5.5 and 6.0 μ in the infrared and an ultraviolet spectrum with λ_{max} 312 mμ (ϵ 1.98 × 10^4) which agrees well with similar data for other isomaleimides.[1]

When dimethylmaleic anhydride was combined with hydrazine in acetic acid, the N,N'-biimide VII was obtained directly as in the case of some of the succinic anhydrides discussed below. The structure was assigned on the basis of the spectral data given in Table I.[1] The absence of significant ultraviolet absorption in the 300-mμ region rules out the pyridazinedione isomer.[1]



VII

The reaction between hydrazine and dimethylmaleic anhydride gave what appears to be a mixture of diacid and biimide when carried out under conditions used to

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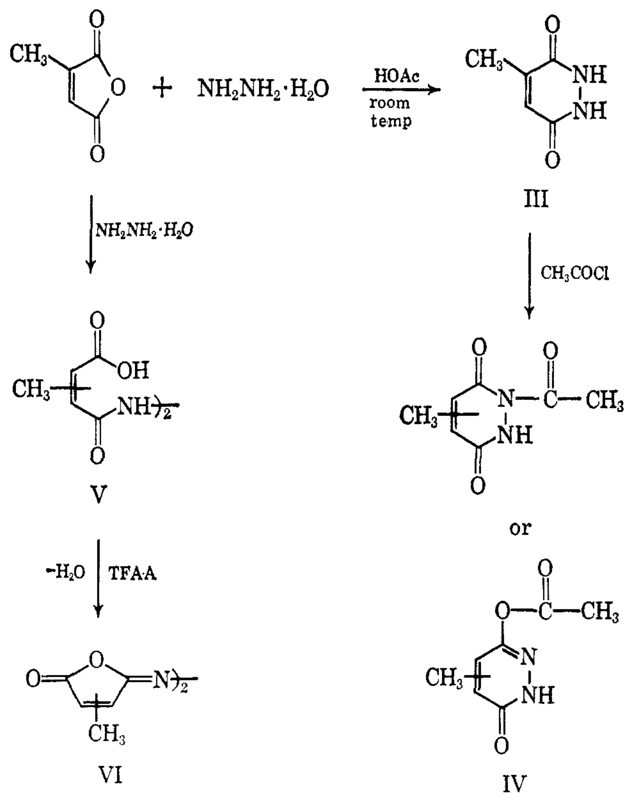
[1] E. Hedaya, R. L. Hinman, and S. Theodoropoulos, *J. Org. Chem.*, **31**, 1311 (1966).

[2] (a) D. Stefanye and W. J. Howard, *ibid.*, **19**, 115 (1954); (b) Yu. A. Baskakov and N. N. Mel'nikov, *Zh. Obshch. Khim.*, **24**, 1216 (1954).

SCHEME I



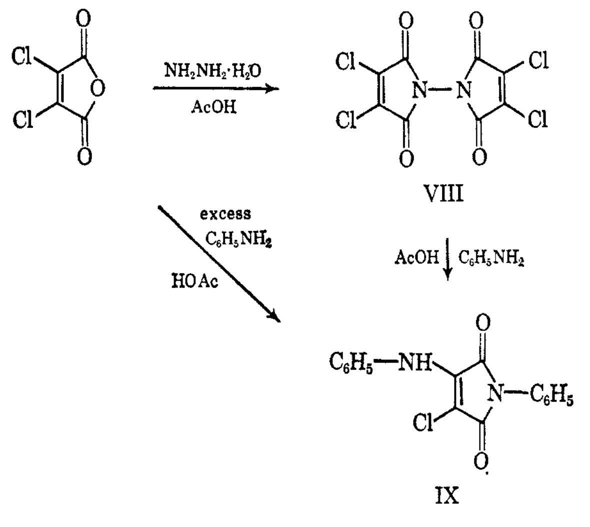
obtain the diacid from citraconic anhydride. However, dehydration of this mixture again gave the biimide.

TABLE I

PROPERTIES OF SOME N,N'-BIIMIDES AND PYRIDAZINEDIONES

Biimide	λ_{CO}, μ	λ, mμ	$10^{-4}\epsilon$
XXII	5.75 (br)	215	0.38
		249	0.69
		256	0.71
		264	0.76
		271	0.82
XXIII	5.73 (br)	230	0.46
		239	0.36
		248	0.18
		260	0.06
XVII	5.74 (br)	215	0.11
		245	0.034
VII	5.75 (br)	223	2.70
VIII	5.60	234	2.20
	5.68	297	0.34
	5.73		
	6.22		
XVI	5.75 (br)	222	8.12
		295	0.79
XVIII	5.71	221	0.82
	5.92		
XI	5.78 (br)	209	4.63
		304	0.63
		309	0.57

SCHEME II



Another disubstituted maleic anhydride, dichloromaleic anhydride, behaved like dimethylmaleic anhydride when treated with hydrazine in acetic acid. N,N'-Tetrachlorobimaleimide (VIII) was isolated directly instead of a diacid (Scheme II). The structural assignment was based on the infrared and ultraviolet data which is not characteristic of isoimides.[1] The spectral data given in Table I could also be consistent with a pyridazinedione structure primarily because of the ultraviolet spectrum which compares favorably with other pyridazinediones discussed previously.[1] However, comparison with dichloromaleimide [λ_{max} 228 mμ (ϵ 1.09 × 10^4), 234 (1.14 × 10^4), 288 (450)] suggests that the bathochromic shift of the 215-mμ band generally observed in maleimides and the appearance of a relatively intense band at longer wavelengths is associated with the chloro substituents.

It was anticipated that because of the electron-withdrawing chlorine substituents this biimide would react readily with nucleophiles. When N,N'-tetrachlorobimaleimide was treated with excess aniline in acetic acid the enamine IX was isolated in good yield as an orange crystalline solid. The same product was obtained by treating dichloromaleic anhydride with excess aniline in acetic acid. When an equimolar amount of aniline reacted with the biimide (VIII) the same product was isolated in lower yields. It has been reported that an intermediate product, N-phenyldichloromaleimide, can be isolated from the reaction of dichloromaleic anhydride with 1 mole of aniline.[3]

An attempt was made to obtain a N,N'-biisoimide from chloromaleic anhydride by the same general procedure. However, no pure diacid, dimer, or hydrazide could be obtained when this anhydride was combined with hydrazine in acetic acid. Further treatment of the mixture obtained in this reaction with dehydrating agents such as trifluoroacetic anhydride gave only N,N'-biisomaleimide in surprisingly substantial amounts. The implication is that dechlorination occurs in the hydrazine reaction.

Preparation of N,N'-Biisophthalimide.—In an excellent study Drew and Hatt[4] earlier described the preparation and proof of structure for N,N'-biphthalimide (X) and the corresponding six-membered ring isomer XI. Their syntheses are given in Scheme III. The more recent work of Kealy,[5] who also obtained XI from the oxidation of 1,4-phthalazinedione, further supports the work of Drew and Hatt.

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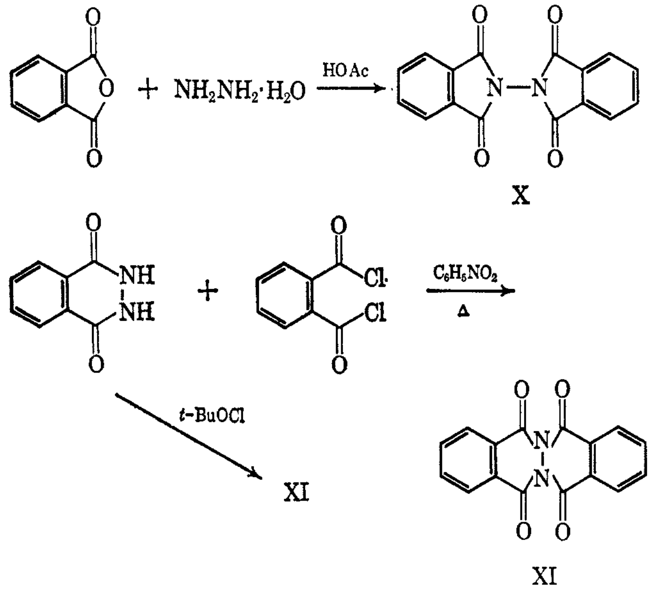
[3] E. L. Martin, C. L. Dickinson, and J. R. Rolands, *J. Org. Chem.*, **26**, 2032 (1961).

[4] H. D. K. Drew and H. H. Hatt, *J. Chem. Soc.*, 16 (1937).

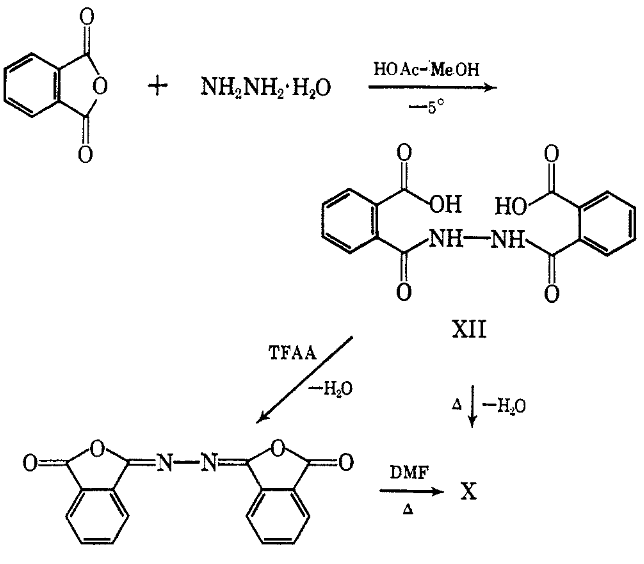
[5] T. J. Kealy, *J. Am. Chem. Soc.*, **84**, 966 (1962).

Scheme III



We have found that by carrying out the reaction of phthalic anhydride and hydrazine in a mixture of acetic acid and methanol, which are the conditions used with citraconic anhydride, one can isolate the diacid XII (Scheme IV). When XII is treated with trifluoroacetic anhydride N,N′-biisophthalimide (XIII) was obtained in high yield. Other dehydrating agents such as acetic anhydride or acetyl chloride gave mixtures of imide and isoimide. Furthermore, XII readily cyclizes thermally to give the biimide X.

Scheme IV



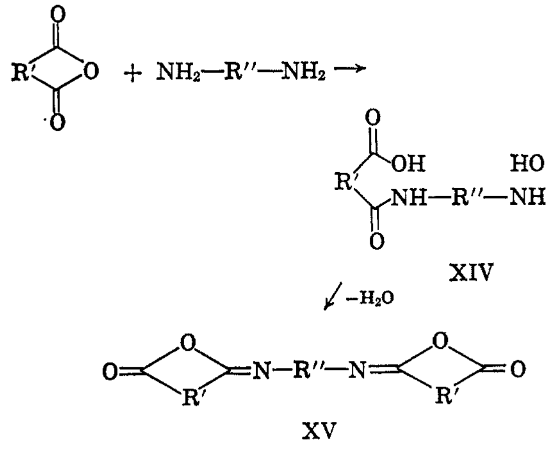
XIII

The isoimide has characteristic infrared bands at 5.6 and 6.1 μ. The ultraviolet spectrum has λ_{max} 220 mμ (ϵ 5.25 × 10^4), 323 mμ (ϵ 1.46 × 10^4). In comparison, N,N′-biphthalimide has λ_{CO} 5.75 μ (br) and λ_{max} 222 and 295 mμ (ϵ 8.12 × 10^4 and 7.92 × 10^3). The phthalazinedione absorbs in the infrared at λ 5.78 μ (br) and in the ultraviolet at λ_{max} 209, 304, and 339 mμ (ϵ 4.63 × 10^4, 6.25 × 10^3, and 5.68 × 10^3). Thus, the infrared spectrum clearly is indicative of an isoimide while the ultraviolet data is less clear-cut since all isomers absorb at long wavelength. However, the isoimide has the most intense absorption in this region.

N,N′-Biisophthalimide rearranges easily to the imide and care must be exercised in its recrystallization. For example, when the isoimide is dissolved in hot dimethylformamide (100°) and kept at that temperature for *ca.* 0.5 hr, essentially complete rearrangement to the imide occurs.

N,N′-Biisoimides Derived from Diamines and Dihydrazides.—Cotter[6] has shown that biisomaleimides can be obtained from maleic anhydride and diamines according to the general reaction given in Scheme V.

Scheme V



R′ = *cis*-C=C-, R″ = $(CH_2)_6$-).

Because of our interest in these biisoimides in general and for comparative purposes, we have prepared some biisoimides of type XV derived from anhydrides other than maleic anhydride and dihydrazides instead of diamines. These are listed in Table II. Structure proof was based on infrared, ultraviolet, and, where solubility permitted, nmr spectra.

Of particular interest is the comparative tendency of these isoimides to rearrange. In contrast to biisophthalimide (XIII) where care must be exercised, XVa and XVb could both be recrystallized from dimethylformamide. Rearrangement to imide did occur, however, when XVa was refluxed in acetic acid for 15 min. The tetrachlorobiisoimide (XVc) could be obtained and was rearranged to imide in refluxing acetic acid. Also, when the solid tetrachloro diacid XIVc stood for an extended period at room temperature, spontaneous dehydration to the biimide occurred. The isoimide XVf is an interesting example of an isomaleimide which rearranges rapidly in hot dimethylformamide to a compound which appears to be the pyridazinedione XVI on the basis of the infrared (Table I) and nmr spectra, the latter having four equivalent aromatic protons and four vinyl protons in an AB pattern.

Attempt to Obtain N,N′-Biisoimides from Succinic Anhydrides.—We previously found that, when the diacid obtained from 2 moles of succinic anhydride and 1 mole of hydrazine was treated with dehydrating agents, only the imide, N,N′-bisuccinimide,[7] was obtained. Also, the maleic anhydride adduct of furan[1]

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[6] R. J. Cotter, C. K. Sauers, and J. M. Whelan, *J. Org. Chem.*, **26**, 10 (1961).

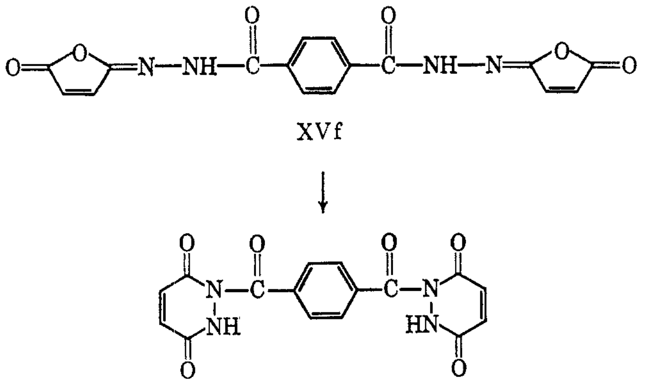
[7] E. Hedaya, R. L. Hinman, and S. Theodoropulos, *J. Am. Chem. Soc.*, **85**, 3052 (1963); E. Hedaya and S. Solomon, unpublished work.

TABLE II

SOME N,N′-BIISOIMIDES (XV) DERIVED FROM DIAMINES AND DIHYDRAZIDES

Compd	R′	R″	λ_{CO}, μ	λ_{max}, mμ	$\epsilon \times 10^{-4}$
XVa	o-C_6H_4	p-C_6H_4	5.5, 5.7	300[a]	0.83
				345	1.03
XVb	o-C_6H_4	—$(CH_2)_6$—	5.6, 5.8	213	1.78
				245 (sh)	1.30
				282	0.31
				290	0.34
				300	0.32
XVc	$\overset{\vert}{C}Cl{=}\overset{\vert}{C}Cl$	p-C_6H_4	5.6, 5.9	236	4.51
				245	4.31
				268	3.88
				343	2.20
XVd	$\overset{\vert}{C}H{=}\overset{\vert}{C}H$	$—NH\overset{O}{\overset{\Vert}{C}}NH—$	5.6, 6.0	305[b]	0.82
XVe	o-C_6H_4	$—NH\overset{O}{\overset{\Vert}{C}}NH—$	5.6, 5.8, 6.1	275 (sh)[b]	0.41
				285	0.46
				300	0.41
XVf	$\overset{\vert}{C}H{=}\overset{\vert}{C}H$	p-$(NHCO)_2C_6H_4$	5.5, 5.8	...	...

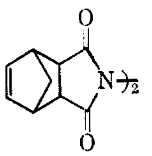
[a] Very intense absorption starts at 290 mμ with no maximum above 215 mμ. [b] Intense absorption starts at 225 mμ with no maximum above 215 mμ.



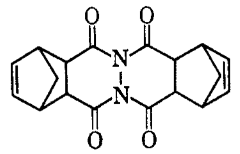
XVf

XVI

reacts with hydrazine to give the N,N′-biimide directly. Attempts to isolate a biisoimide from the maleic anhydride adduct of cyclopentadiene by the diacid dehydration route similarly failed; only the N,N′-biimide XVII was obtained. Chemical support for the structural assignment was obtained from the reaction of 1,4,6,9-tetraketopyridazo[1,2-*a*]pyridazine with cyclopentadiene which gave the six-membered ring isomer XVIII and the reaction of cyclopentadiene with N,N′-biisomaleimide which gave the isoimide isomer (see below).



XVII



XVIII

The only previous report of saturated isoimides is that of N-substituted camphorisoimides,[8] which are obtained from dehydration of the corresponding amic acids with acetyl chloride or phosphorus oxychloride. One example of this interesting series, N-methyl α-camphorisoimide, has been confirmed recently.[9] Unsuccessful attempts to obtain isoimides from saturated amic acids such as succinamic, glutaramic, and adipamic acids have been described.[9]

Synthetic Limitations for the Formation of N,N′-Biisoimides by the Diacid Dehydration Route.—The results described in the above sections can be summarized by noting that, for the cases where the diacid could be obtained, biisoimide formation in the presence of potent dehydrating agents requires the presence of unsaturation between the carboxyl and amide functions. This appears to apply to simple isoimides as well.[9] When cyclization occurs directly under the reaction conditions of the hydrazine–anhydride reaction without isolation of the diacid the N,N′-biimide product is obtained. An exception is the example of citraconic anhydride where methylmaleic hydrazide was obtained. Also, thermal dehydration or dehydration in acetic acid solvent as in the example of 1,2-bis(2-carboxybenzoyl)-hydrazine (XII) leads to a biimide product.

It is instructive to consider the limitations given above in terms of possible reactive intermediates. Two types are the most plausible and these are given in Chart I for the case of dehydration by trifluoroacetic anhydride.

It is clear that XIXb, XIXc, and XXa would give rise to isoimide products on cyclization, while XIXa and XXb would lead to imide isomers. Similar intermediates can be written for other dehydrating agents.

Strong support for the importance of intermediates XIXb and/or XIXc has been recently obtained from carboxyl O^{18} labeling experiments[10] where it was found that close to half of the label was retained in the isoimide product and the other half in the fragment derived from the dehydrating agent (CF_3COO–, in our case). If XXb were the intermediate, all of the carboxyl O^{18} label should be retained in the isoimide

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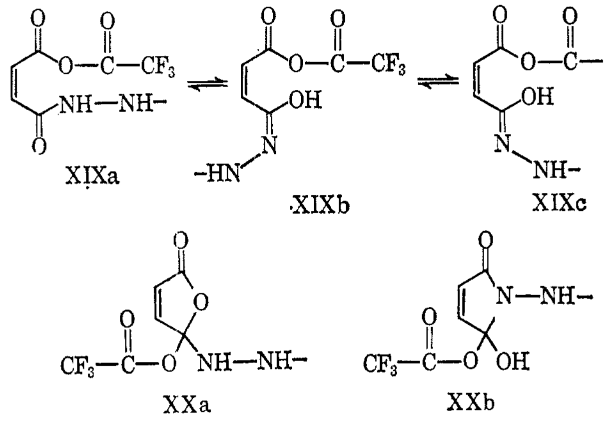
[8] S. Hoogewerff and W. A. van Dorp, *Rec. Trav. Chim.*, **12**, 15, 17 (1893); **14**, 261, 266, 269 (1895).

[9] W. R. Roderick and P. L. Bhatia, *J. Org. Chem.*, **28**, 2018 (1963).

[10] (a) R. Paul and A. S. Kende, *J. Am. Chem. Soc.*, **86**, 4162 (1964); (b) *ibid.*, **86**, 741 (1964); (c) D. V. Kashelikav and C. Ressler, *ibid.*, **86**, 2467 (1964).

Chart I

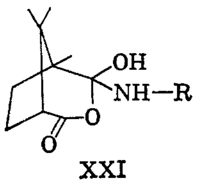

XIXa XIXb XIXc

XXa XXb

product. The labeling experiments specifically involved N-butylmaleamic acid and asparagine derivatives while dicyclohexenecarbodiimide was the dehydrating agent. In the latter case an isoimide is a presumed intermediate leading to the final nitrile.

The intermediates XIXd and c of course would be much less stable compared with XIXa when the olefinic double bond is saturated and one can rationalize the failure of saturated diacids of type I to give isoimides on this basis. In contrast, saturation of the double bond in XXa would not lead to any appreciable destabilization compared with XXb, and consequently this model does not appear to be valid for our examples.

It is conceivable, however, that the dehydration of N-substituted camphoramic[9] acids, giving isoimides such as N-methyl-α-camphorisoimide, might involve a reactive intermediate such as XXb. In this case one must postulate that the acid itself has a structure such as XXI of appreciable stability. The driving force for such a strong intramolecular interaction would be the relief of methyl–methyl steric strain in the free acid. On the basis of this hypothesis it should be possible to design other saturated amic acids or diacids I which would similarly cyclize to isoimides with the appropriate dehydrating agent.

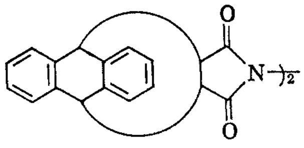

XXI

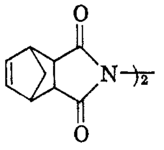
It must be emphasized that, even if reactive intermediates such as XIXb and c predominate in dehydrative cyclizations of unsaturated diacids of type I or maleamic and phthalamic acid derivatives, this does not imply that the free acids are also predominantly enolized. Thermal dehydrations, dehydrations in acetic acid solvent, or cyclizations under the conditions of the hydrazine–anhydride reaction can be understood on this basis since they all lead to imide formation. The partitioning of 1,2-bis(2-carboxybenzoyl)hydrazine (XII) between isoimide and imide with dehydrating agents other than trifluoroacetic anhydride may similarly depend upon the relative stability of XIXa, b, and c when derived from these other dehydrating agents. Alternatively, N,N'-biimide formation may result from the fast rearrangement of the isoimide isomer under the reaction conditions.[6,9,11] This pathway was recently ruled out for an isophthalimide derivative.[11]

In conclusion, it would seem possible to obtain tetrasubstituted N,N'-biisomaleimides provided that one could isolate the required diacid precursor. For example, the diacid derived from dichloromaleic anhydride and *p*-phenylenediamine was isolable and gave the corresponding N,N'-biisoimide in the presence of trifluoroacetic anhydride.

N,N'-Biisomaleimide as a Dienophile. Synthesis of Substituted N,N'-Biisosuccinimides.—A route to some examples of biisosuccinimides other than the unsuccessful diacid dehydration method would appear to be the Diels–Alder reaction of N,N'-biisomaleimide with dienes. We have found that N,N'-biisomaleimide does react with a variety of dienes including 2,3-dimethylbutadiene, cyclohexadiene, cyclopentadiene, anthracene, and phellandrene. These reactions were carried out in a heterogeneous system by combining N,N'-biisomaleimide with the diene in an appropriate solvent. As the reaction progressed the originally heterogeneous, yellow reaction mixture became homogeneous and colorless. The product was then obtained by straightforward methods. The properties of the adduct and the reaction conditions are listed in Table III. A characteristic feature of the spectral data is the presence of bands at *ca.* 5.6 and 6.0 μ in the infrared spectrum, which is characteristic of isoimides.[1]

In some solvents or when the reaction is prolonged, rearrangement to imide occurs. Thus, when the anthracene reaction is carried out in dimethylformamide at 110° for 48 hr, the imide XXII is obtained. Also, when 1,3-cyclohexadiene was refluxed with N,N'-biisomaleimide in nitromethane for 48 hr instead of 3 hr, only the rearranged imide XXIII is obtained. The properties of some of these imides are listed in Table I. It was subsequently found that the adduct isoimides themselves rearrange to imides under similar reaction conditions. For example, both the anthracene and cyclohexadiene adducts rearranged to imide after 48 hr in hot dimethylformamide and 48 hr in refluxing nitromethane, respectively. In contrast, the cyclopentadiene adduct was recovered unchanged after refluxing in nitromethane for 28 hr and underwent about 20% rearrangement after 48 hr. The rearrangements of isoimides are discussed in more detail below.


XXII


XXIII

The reactions of N,N'-biisomaleimide with dienes appear to be general on the basis of the data in Table III. It is of interest to compare qualitatively the reactivity of N,N'-biisomaleimide with that of maleic anhydride. While one must reflux the reaction mixture to obtain products from N,N'-biisomaleimide and cyclopentadiene, the same reaction with maleic anhydride occurs readily at room temperature or below.[12] Also, maleic anhydride will react with hexachlorocyclo-

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[11] W. R. Roderick, *J. Org. Chem.*, **29**, 745 (1964).

[12] M. C. Kloetzel, *Org. Reactions*, **4**, 1 (1948).

TABLE III

REACTION OF N,N′-BIISOMALEIMIDE WITH DIENES

Diene	Solvent	Reaction time, hr	Biisoimide yield, %	λ_{CO}, μ	λ,[a] mμ	$10^{-4}\epsilon$
Cyclopentadiene	Refluxing C_6H_6	3	66–75	5.6, 6.1	224	1.33
					230[b]	1.28
					238[b]	0.92
					247[b]	0.44
Cyclohexadiene	Refluxing C_6H_6	~240	85	5.5, 5.9	222	1.68
					230[b]	1.50
					237[b]	1.20
					248[b]	0.55
	Refluxing CH_3NO_2	2.5	60	...	...	...
1,4-Butadiene	Refluxing CH_3NO_2	3	45	5.5, 5.6, 6.0	278	1.74
	Refluxing C_6H_6	72	47	...	...	...
Anthracene	Refluxing dioxane	24	50	5.6, 6.1	225	2.95
					233[b]	2.60
					242[b]	1.9
					252[b]	0.9
					264[b]	0.33
					271	0.32

[a] Maxima unless noted. [b] Inflection.

TABLE IV

SOME REARRANGEMENTS OF N-SUBSTITUTED CYCLIC ISOIMIDES TO IMIDES

Isoimide	Solvent	Catalyst	Conditions	Ref
N-Phenylisomaleimide	Ac_2O	NaOAc	90°, 1 hr	*a*
N-Phenylisomaleimide	C_6H_6	2 equiv of Et_3N or ACOH	Reflux	*a*
N-(*p*-Chlorophenyl)isophthalimide	Ac_2O	...	65°, 20 hr	*b*
N-(*p*-Chlorophenyl)isophthalimide	Ac_2O	NaOAc	65°, 10 min	*b*
N-(*p*-Methoxyphenyl)isomaleimide	Ac_2O	NaOAc	100°, 30 min	*c*
N-Methoxyisophthalimide	CH_3NO_2	HBr	~25°, overnight	*d*
N-Phenylisophthalimide	C_6H_5Cl	...	250°, $t_{1/2}$ 24 hr	*e*

[a] See ref 6. [b] See ref 9. [c] A. E. Kretov, N. E. Kyl'Chitskaya, and A. J. Mal'nev, *Zh. Obshch. Khim.*, **31**, 2415 (1961). [d] L. A. Carpino, *J. Am. Chem. Soc.*, **79**, 98 (1957). [e] See ref. 18.

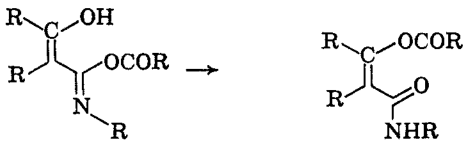
pentadiene or hexachlorobutadiene,[13] but N,N′-biisomaleimide will not. This reduced reactivity may be a result of structural differences or even of the insolubility of the isoimide.

The faster Diels–Alder reactions of N,N′-biisomaleimide in nitromethane compared to benzene must primarily be due to the higher reflux temperature of nitromethane compared to benzene and secondarily to increased solubility of the dieneophile. The rate of Diels–Alder reactions is only moderately enhanced in polar solvents.[14]

Although the products from the Diels–Alder reaction with cyclopentadiene or cyclohexadiene are most certainly mixtures containing ratios of *endo–exo* isomers which may vary with reaction solvent,[15] no attempt has been made to separate isomers or to determine their stereochemistry. It is probable, however, that under our reaction conditions there is a high proportion of *endo* isomers in accordance with the Alder rule.

Rearrangement of Isoimides.—One general feature of N-substituted isoimides is their rearrangement to imides, and numerous examples can be found in the literature. Some of these acyl oxygen to nitrogen rearrangements are summarized in Table IV. Besides the rearrangement of cyclic isoimides, there are also examples of rearrangements of open-chain isoimides to imides where the isoimide is postulated as a nonisolable intermediate. These include the reaction of carboxylic acids with ketenimines[16] and the reaction of imido chlorides[17] with salts of carboxylic acids.

Very recently, Curtin and Miller[18] succeeded in isolating a series of acyclic isoimides from reaction of N-(2,4-dinitrophenyl)benzimidoyl chloride with *para*-substituted silver benzoates and studied their rearrangement to imides. A particularly interesting example of a rearrangement is the isoimide XXVI postulated in the



XXVI

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(13) S. H. Herzfield, R. E. Lidou, and H. Bluestone, U. S. Patent 2,606,910 (1952).

(14) E. S. Gould, "Mechanism and Structure in Organic Chemistry," Henry Holt and Co., Inc., New York, N. Y., 1959, p 537.

(15) J. A. Berson, Z. Hamlet, and W. A. Mueller, *J. Am. Chem. Soc.*, **84**, 297 (1962).

(16) C. L. Stevens and M. E. Munk, *ibid.*, **80**, 4065 (1958).

(17) F. Cramer and R. Baer, *Ber.*, **93**, 1231 (1960).

(18) D. Y. Curtin and L. L. Miller, *Tetrahedron Letters*, **No. 23**, 1869 (1965).

reaction of isoxazolium cations with bases,[19] where an acyl oxygen to oxygen rearrangement apparently occurs rather than an acyl oxygen to nitrogen rearrangement.

Despite the fundamental aspects of this rearrangement a systematic mechanistic investigation has not been carried out except for the work of Curtin and Miller.[18] However, the data in Table IV do show that the rearrangement of cyclic isoimides is base and possibly acid catalyzed, as one might anticipate.

We are not yet in a position to make detailed statements on the nature of this rearrangement with regard to either N-substituted isoimides or N,N'-biisoimides. However, from the examples of rearrangements summarized in Table V some qualitative generalizations can be made.

TABLE V

SOME REARRANGEMENTS OF N,N'-BIISOMIDES[a]

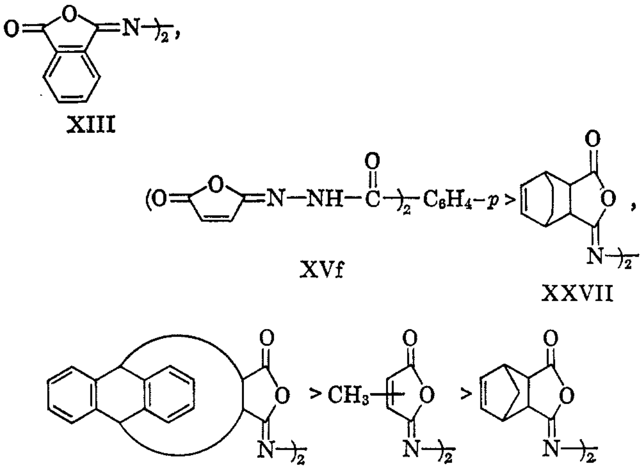
Biisoimide	Solvent	Conditions	% rearrangement
XXIX	CH_3NO_2	Reflux, 48 hr	20[b]
XXVII	CH_3NO_2	Reflux, 48 hr	100
XXVIII	DMF	Reflux, 48 hr	100
XXVIII	Dioxane	Reflux, 48 hr	0
VI	CH_3NO_2	Reflux, 68 hr	70[b]
XIII	DMF	~100°, 10 min	100
XVa	AcOH	Reflux, 15 min	100
XVc	AcOH	Reflux, 15 min	100
XVf	DMF	~100°, 10 min	100[c]

[a] Products are N,N'-biimides unless indicated. Indicated yields are qualitative. [b] Very roughly estimated from the infrared spectrum of the product. [c] Product is a pyridazinedione.

The rate of rearrangement first of all is dependent on the nature of the solvent. For example, the anthracene adduct of N,N'-biisomaleimide (XXVIII) is stable in refluxing benzene or dioxane but rearranges to imide in hot dimethylformamide. The rate of rearrangement is dependent on structure since biisophthalimide (XIII) rearranges rapidly and completely to imide in hot dimethylformamide, whereas the various diene adducts of N,N-biisomaleimide are considerably more stable in dimethylformamide. Also, XVa, which is the biisophthalimide derived from phenylenediamine, can be crystallized from dimethylformamide without noticeable rearrangement. However, when XVa is refluxed in acetic acid for 15 min, complete rearrangement to imide occurs. In this same series, XVf shows a remarkable tendency to rearrange, since on attempted recrystallization from dimethylformamide a rearranged product was isolated which is a pyridazinedione. Finally, the cyclopentadiene adduct XXIX and the dimethyl derivative of biisomaleimide (VI) appear to be more stable than the cyclohexadiene adduct or anthracene adduct.

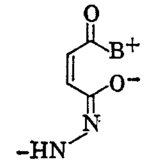
A very rough scale of rearrangement tendency can be generated from these observations and is given in Chart II.

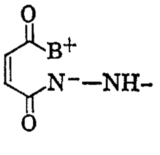
CHART II



It is important that the tendency to rearrange does not parallel the tendency to form isoimides from dehydration of the appropriate diacids. Thus even though XXVII–XXIX cannot be obtained *via* a diacid dehydration route, the tendency to rearrange is less than that of N,N'-biisophthalimide which can be prepared directly. This indicates that the tendency to rearrange must reflect thermodynamic stability while the dehydration route reflects kinetic control. In general, the isoimide cycle is thermodynamically less stable than the imide cycle, since the former generally rearranges to the latter. Furthermore, rearrangements of pyridazinediones to imides can also occur as demonstrated by the rearrangement of perhydro-1,4,6,9-tetraketopyridazo[1,2-*a*]pyridazine to N,N'-bisuccinimide.[7] In some cases, such as N-acetylaminoisomaleimide[1] and XVf, the pyridazinedione ring, however, may be more stable than the imide. The stability of the pyridazinedione in these cases is probably related to the ability of N-monosubstituted pyridazinediones such as XVf to enolize. Evidence for such enolization has been obtained.[20]

The mechanism for the rearrangement must involve the attack of a nucleophilic site of the solvent or another molecule of isoimide at the activated carbonyl, giving charged intermediates of the type XXX and XXXI. The rate of rearrangement can thus depend on the reactivity of the isoimide carbonyl, the relative stability of the imide or pyridazinedione isomer, and/or the relative rates of cyclization of the intermediates XXX and XXXI. A more quantitative study is obviously necessary before one can understand how these various factors lead to the qualitative order of rearrangement rate given above, or the order for any series of examples.


XXX


XXXI

The lack of isolation of acyclic isoimides most likely is a consequence of the availability of an intramolecular, four-center rearrangement path shown below.[16,18] The cyclic isoimides discussed above cannot undergo rearrangement *via* this path with any facility.

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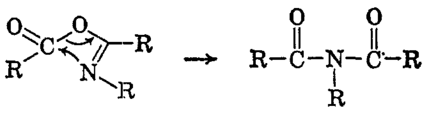
(19) R. B. Woodward and R. A. Olofson, *J. Am. Chem. Soc.*, **83**, 1007 (1961).

(20) (a) A. R. Katrisky and A. J. Waring, *J. Chem. Soc.*, 1523 (1964); (b) O. Ohashi, M. Mashima, and M. Kubo, *Can. J. Chem.*, **42**, 970 (1964); (c) D. M. Miller, *ibid.*, **33**, 1806 (1955).



Infrared and Ultraviolet Spectra as Criteria for Structure Determination.—In the previous report[1] a set of criteria for distinguishing between biisoimides and their isomers involving infrared and ultraviolet spectra and chemical reactivity was discussed. In this report we have described a number of new biisoimides and it is interesting to see how the criteria based on absorption spectra must be modified, if at all.

Our previous statement concerning the distinctive and unambiguous infrared carbonyl absorption of isoimides compared to its isomers is further substantiated. All of the new biisoimides, whether they involve saturated or unsaturated isoimide rings, have twin absorptions at around 5.6 and 6.0 μ, respectively. In comparison, the isomeric imides or pyridazinediones have the usual broad carbonyl absorptions with maximum centered near 5.75 μ. However, one cannot distinguish pyridazinedione and imide isomers as the data in Table I show for N,N′-biphthalimide (X) and its six-membered ring isomer XI, or the cyclopentadiene adduct of bimaleimide (XVII) and its six-membered ring isomer XVIII.

In order to discuss the ultraviolet data it is convenient to consider the saturated isoimides derived from the Diels–Alder reactions, the isoimides derived from diamines, and the isoimides derived from hydrazine or substituted hydrazines separately. In the first category the most conspicuous feature is the much more intense absorption found in the isoimides compared to imides or pyridazinediones, even though there is no significant long wavelength absorption because of the absence of extensive conjugation. The nature of the absorption for the imide isomers is that anticipated since N,N′-bisuccinimide has similar relatively low-intensity absorption.[7] It is of interest to compare these isoimides with aliphatic azines. Cyclohexanone azine has an absorption maximum at 240 mμ (ε 2.5 × 10^3); absorption at lower wavelengths was not reported.[21] The azine derived from butyraldehyde also absorbs strongly at 240 mμ and has bands at 206 and 208 mμ (ε 1.30 × 10^4 and 1.15 × 10^4). The maxima at higher wavelengths compare favorably with both the cyclopentadiene and cyclohexadiene adducts of N,N′-biisomaleimide (first two entries of Table III). The substantial shift toward higher wavelength observed for the dimethylbutadiene adduct suggests that the position of the absorption maximum for the saturated isoimide chromophore is strongly dependent on the nature of the ring.

The two new biisoimides derived from hydrazine, N,N′-biisomethylmaleimide (VI) and N,N′-biisophthalimide (XIII), both have ultraviolet spectra consistent with isoimide structure, although in the latter case the distinction between isomers is less clean-cut, since isomeric structures also have long wavelength absorption. The single intense absorption at 312 mμ (ε 1.98 × 10^4) for VI is very close to that of N,N′-biisomaleimide, 297 mμ (ε 1.8 × 10^4). The appearance of a single band at long wavelengths is also characteristic of azines derived from conjugated aldehydes as previously mentioned.[1] Similarly, benzalazine absorbs[22] at 300 mμ (ε 3.60 × 10^4) and 308 mμ (ε 3.50 × 10^4) which is near the position of the long wavelength band of N,N′-biisophthalimide (XIII), 323 mμ (ε 1.46 × 10^4).

The biisoimides derived from dihydrazides (XVd, etc.) have absorption similar to that of the biisoimides derived from hydrazine since there is intense absorption at around 300 mμ along with absorption due to other chromophores in the molecule. The absorption at 300 mμ is similar to that observed for N-acetylaminoisomaleimide.[1] The absorption at high wavelength could be due to the free electron pair on the nitrogen adjacent to the isoimide nitrogen.

The biisoimides derived from diamines (XVa–c) have long wavelength absorption characteristic of the biisoimide chromophore and chromophores due to other functionalities in the molecule. An interesting comparison is that between the biisophthalimide derived from phenylenediamine (XVa) and hexamethylenediamine (XVb). In the first, the isoimide rings are conjugated with one another through the benzene ring while in the latter the two isoimide rings are insulated from each other. There is correspondingly much more intense long wavelength absorption for XVa than for XVb. Also, XVa has a maximum at higher wavelengths. This long wavelength absorption furthermore appears in the other biisoimide derived from phenylenediamine, XVc.

Experimental Section

All infrared spectra were obtained on a Beckman IR-5A instrument in potassium bromide pellets of Nujol mulls. Ultraviolet spectra were recorded on a Beckman DK-2 spectrophotometer. Solvents were Spectrograde acetonitrile, dioxane, or 95% ethanol. Nmr spectra were obtained on a Varian A-60 instrument and data are expressed in parts per million relative to tetramethylsilane. All melting points are uncorrected.

Reaction of Citraconic Anhydride with Hydrazine in Acetic Acid. Preparation of Methylmaleic Hydrazide (III).—Citraconic anhydride (2.24 g, 0.02 mole) was added to 15 ml of glacial acetic acid and cooled with an ice bath. Hydrazine hydrate (99%, 0.5 g, 0.01 mole) was added dropwise with stirring over a period of 15 min. After completion of the addition the mixture was allowed to come to room temperature and left standing overnight. The reaction mixture was diluted with 10 ml of methanol and the white precipitate was filtered and washed with methanol and ether: yield 1.5 g (59%), mp 278–280°.

Anal. Calcd for $C_5H_6N_2O_2$: C, 47.61; H, 4.49; N, 22.21. Found: C, 47.60; H, 4.86; N, 21.99.

An acetyl derivative was prepared by refluxing 1 g of the hydrazide in excess acetic anhydride for 1 hr. The residue obtained after removal of the solvent *in vacuo* was recrystallized from dioxane, giving the acetyl derivative, mp 174–176°, in nearly quantitative yield.

Anal. Calcd for $C_7H_8N_2O_3$: C, 49.99; H, 4.79; N, 16.65. Found: C, 49.95; H, 4.72; N, 16.32.

Reaction of Citraconic Anhydride with Hydrazine in Methanol–Acetic Acid. Preparation of the Diacid V.—Citraconic anhydride (11.2 g, 0.10 mole) was dissolved in 80 ml of methanol and 50 ml of glacial acetic acid. The solution was cooled with an ice-methanol bath, and 2.5 g (0.05 mole) of 99% hydrazine hydrate dissolved in 20 ml of methanol was added dropwise over a period of 30 min with stirring. The reaction mixture was then allowed to warm to room temperature and stirring continued for 2 hr. The yellow precipitate was filtered and washed thoroughly with ether, giving 9.4 g (73%) of the diacid, mp 155° (resolidifies and melts again at 233–235°).

Anal. Calcd for $C_5H_6NO_3$: C, 46.87; H, 4.72; N, 10.93. Found: C, 47.04; H, 4.80; N, 11.01.

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[21] P. Grammaticakis, *Bull. Soc. Chim. France*, 973 (1948).

[22] H. C. Barany, E. A. Braude, and M. Pianka, *J. Chem. Soc.*, 1898 (1949).

Preparation of Dimethyl-N,N′-biisomaleimide (VI).—The diacid V (4.0 g, 1.6 mmoles) was stirred at room temperature in 30 ml of trifluoroacetic anhydride overnight. Ether was added to precipitate the yellow product completely. After recrystallization from dioxane (benzene can also be used), 2.3 g (67%) of the isoimide was obtained: mp 189–190°.

Anal. Calcd for $C_5H_4NO_2$: C, 54.54; H, 3.66; N, 12.72. Found: C, 54.58; H, 3.45; N, 12.79.

Reaction of Dimethylmaleic Anhydride with Hydrazine. Preparation of Tetramethylbimaleimide (VII).—Dimethylmaleic anhydride (3.0 g, 0.0234 mole) was dissolved in 20 ml of glacial acetic acid and cooled with an ice bath. Hydrazine hydrate (99%, 0.6 g, 0.012 mole) in 3 ml of glacial acetic acid was added dropwise with stirring. The reaction mixture was then stirred at room temperature for 3 hr. The precipitate was filtered off and washed with ether, giving 2.0 g (65%) of product, mp 235°. This could be recrystallized from dioxane, giving material with mp 237–238°.

Anal. Calcd for $C_6H_6NO_2$: C, 58.05; H, 4.87; N, 11.28. Found: C, 58.10; H, 4.72; N, 11.39.

The same product was isolated in a similar reaction when methanol was used as a solvent at room temperature.

Reaction of Dichloromaleic Anhydride with Hydrazine. Preparation of Tetrachlorobimaleimide (VIII).—Dichloromaleic anhydride (17.3 g, 0.1 mole) was dissolved in 100 ml of glacial acetic acid and cooled with an ice bath. A solution of 99% hydrazine hydrate (2.5 g, 0.05 mole) in 50 ml of glacial acetic acid was added dropwise with stirring. The reaction mixture was then stirred 3 hr at room temperature. The yellow product (8.0 g, 50%) was filtered off and washed, mp 268–270°. Recrystallization from dioxane gave material with mp 270–272°.

Anal. Calcd for $C_4Cl_2NO_2$: C, 29.10; N, 8.48; Cl, 43.01. Found: C, 28.95; N, 8.64; Cl, 42.79.

Reaction of Tetrachlorobimaleimide and Dichloromaleic Anhydride with Aniline. Preparation of N-Phenyl(1-anilino-2-chloro)maleimide (IX).—A mixture of 0.80 g (0.0085 mole) of tetrachlorobimaleimide and 0.93 g (0.01 mole) of aniline in glacial acetic acid was refluxed for 2 min and cooled. Water was added and the orange-yellow product was filtered off and dried: yield 0.9 g (66%), mp 187–189°. The material could be recrystallized from acetic acid.

Anal. Calcd for $C_{16}H_{12}ClN_2O_2$: C, 64.10; H, 4.03; Cl, 11.84; N, 9.34. Found: C, 64.25; H, 3.80; Cl, 11.82; N, 10.14.

The same product could be obtained in 78% yield by refluxing a mixture of dichloromaleic anhydride and a 1.5-molar excess of aniline in glacial acetic acid for 10 min.

Preparation of 1,2-Bis(2-carboxybenzoyl)hydrazine (XII).—Hydrazine hydrate (99%, 2.5 g, 0.05 mole) in 10 ml of methanol was added to a solution of 14.8 g (0.1 mole) of phthalic anhydride in 75 ml of acetic acid and 50 ml of methanol cooled with an ice–methanol bath. After stirring with cooling for 1 hr, ether was added and the white solid was filtered off. This was washed with ether to give 16.4 g (100%) of the diacid, mp 245° dec (softens and melts at 280–310°).

Anal. Calcd for $C_8H_6NO_3$: C, 58.53; H, 3.68; N, 8.53. Found: C, 58.56; H, 3.78; N, 8.32.

Cyclization of this diacid to N,N′-biphthalimide[5] occurs on melting or in hot acetic acid.

Preparation of N,N′-Biisophthalimide (XIII).—1,2-Bis(2-carboxybenzoyl)hydrazine (2 g, 0.006 mole) was refluxed in 25 ml of trifluoroacetic anhydride overnight. The mixture was cooled and the trifluoroacetic anhydride was distilled *in vacuo*. After washing with methanol and careful recrystallization from dimethylformamide, 1.5 g (86%) of pale yellow material was obtained: mp 260°. Prolonged heating at around 100° in dimethylformamide (0.5 hr) led to essentially complete rearrangement to N,N′-biphthalimide.

Anal. Calcd for $C_8H_4NO_2$: C, 65.75; H, 2.80; N, 9.60. Found: C, 65.62; H, 2.79; N, 9.40.

When dehydration was attempted in refluxing acetyl chloride (2 hr), refluxing acetyl chloride–ether (5 hr), refluxing thionyl chloride, or acetic anhydride, mixtures of the biimide and biisoimide isomers were obtained.

Reaction of Phthalic Anhydride with *p*-Phenylenediamine. Preparation of XVa.—*p*-Phenylenediamine (1 g, 0.01 mole) was added in three portions over a period of 15 min to a solution of 2.96 g (0.02 mole) of phthalic anhydride in 30 ml of acetic acid at room temperature. The mixture was stirred for 3 hr, and then ether was added to precipitate the product completely. This was filtered and washed with ether, yielding 3.5 g (85%) of diacid, mp >350°.

Anal. Calcd for $C_{11}H_{18}NO_3$: C, 65.37; H, 3.99; N, 6.93. Found: C, 65.41; H, 4.29; N, 6.97.

The above diacid (1.0 g, 25 mmoles) was stirred in excess trifluoroacetic anhydride overnight. Ether was added and the precipitate was filtered off, yielding 0.92 g (100%) of the isoimide product, mp 286°. After recrystallization from dimethyl sulfoxide or dimethylformamide, material having mp 301–303° was obtained.

Anal. Calcd for $C_{11}H_6NO_2$: C, 71.73; H, 3.28; N, 7.60. Found: C, 71.98; H, 3.35; N, 7.83.

The same biisoimide could be prepared by using dicyclohexylcarbodiimide as a dehydrating agent. A mixture of 5.0 g (0.0125 mole) of the diacid and 6.0 g (0.0297 mole) of dicyclohexylcarbodiimide was refluxed with stirring in 75 ml of methylal for a few minutes. The mixture was cooled and ether was added to precipitate the crude product completely. This was filtered off and washed in ether. The crude product was triturated with hot dimethylformamide, filtered, and finally washed with ether, yielding 4.5 g (98%) of the biisoimide, mp 301–303°.

The isoimide was rearranged to the N,N′-biimide isomer, mp 335–340°, when refluxed in glacial acetic acid for 15 min. The structural assignment was based on the loss of characteristic isoimide bands at 5.6 and 5.9 μ and the appearance of a characteristic imide band at 5.8 μ.

Reaction of Phthalic Anhydride withHex amethylenediamine. Preparation of XVb.—A mixture of 3.0 g (0.02 mole) of phthalic anhydride and 1.16 g (0.01 mole) of hexamethylenediamine in 30 ml of acetic acid was stirred overnight at room temperature. After filtration and washing with ether, 3.0 g of the diacid was obtained: mp 185°.

Anal. Calcd for $C_{11}H_{12}NO_3$: C, 64.06; H, 5.86; N, 6.79. Found: C, 64.29; H, 5.71; N, 6.57.

Dehydration of the diacid was accomplished by stirring 1.0 g in 5 ml of trifluoroacetic anhydride at room temperature for 5 hr. Excess trifluoroacetic anhydride was removed *in vacuo*. The residue was crystallized from ether, yielding 0.78 g of the white biisoimide, mp 115°.

Anal. Calcd for $C_{11}H_{10}NO_2$: C, 70.19; H, 5.35; N, 7.44. Found: C, 69.56; H, 5.40; N, 7.47.

Reaction of Dichloromaleic Anhydride with *p*-Phenylenediamine. Preparation of XVc.—*p*-Phenylenediamine (1.08 g, 0.01 mole) was added dropwise with stirring at −10° to a solution of 3.4 g (0.02 mole) of dichloromaleic anhydride in 20 ml of 1:1 glacial acetic acid–dimethoxyethane. The mixture was stirred at this temperature for 3 hr. Hexane (50–60 ml) was added and the precipitate was collected and washed with more hexane. The yield was essentially quantitative, mp >350°.

The above diacid (1.0 g, 2.4 mmoles) was stirred in 5 ml of trifluoroacetic anhydride for 2 min. Ether was added and the precipitate was collected and washed with more ether. The filtrate was evaporated and the residue was again washed with ether, yielding 0.65 g (67%) of combined product, mp 235–237°. Purification was effected by warming the product in hot dioxane and filtration of any insolubles, after cooling to room temperature. The dioxane was removed *in vacuo;* the precipitate was filtered and washed with ether, yielding a yellow compound, mp 238–240°.

Anal. Calcd for $C_7H_2Cl_2NO_2$: C, 41.41; H, 0.99; N, 6.9. Found: C, 41.72; H, 1.05; N, 7.15.

When the above isoimide was refluxed in glacial acetic acid for 15 min, rearrangment to the white biimide occurred: mp >350°. The same biimide could be obtained by letting the solid diacid stand at room temperature for 15 days or by heating the diacid to 80° *in vacuo*.

Anal. Calcd for $C_7H_2Cl_2NO_2$: C, 41.41; H, 0.99; N, 6.90. Found: C, 41.46; H, 1.07; N, 7.08.

Reaction of Maleic Anhydride with Carbohydrazide. Preparation of XVd.—Carbohydrazide (1.8 g, 0.02 mole) was added with stirring to a solution of 4.0 g (0.04 mole) of maleic anhydride in 50 ml of glacial acetic acid which was cooled with an ice bath. The mixture was stirred for 30 min with cooling and then at room temperature for 3 hr. The diacid product (5.5 g, 95%) was filtered off and washed with methanol and ether: mp 187–189°.

The above diacid (1.0 g, 0.0035 mole) was refluxed in 5 ml of trifluoroacetic anhydride with stirring for 5 hr. The solvent was removed *in vacuo* and the residue was washed with acetone and ether, yielding 0.7 g (80%) of product. The biisoimide could be recrystallized from dimethylformamide with complete recovery yielding material with mp 233–235°.

Anal. Calcd for $C_9H_6N_4O_5$: C, 43.20; H, 2.41; N, 22.39. Found: C, 43.34; H, 2.70; N, 22.09.

Reaction of Phthalic Anhydride with Carbohydrazide. Preparation of XVe.—Carbohydrazide (4.5 g, 0.05 mole) was added in small portions to a solution of 14.8 g (0.1 mole) of phthalic anhydride in 300 ml of glacial acetic acid over a period of 1 hr. The mixture was stirred an additional 3 hr. The white product (19.3 g, *ca.* 100%) was filtered off and washed with ether: mp 388–390°.

The above diacid (2.0 g) was stirred in excess trifluoroacetic anhydride overnight. Ether was added and the precipitate was washed with ether. This was recrystallized from dimethylformamide, yielding 1.45 g (80%) of white biisoimide, mp 275–277°.

Anal. Calcd for $C_{17}H_{10}N_4O_5$: C, 58.28; H, 2.78; 15.99. Found: C, 58.28; H, 2.81; N, 16.13.

Reaction of Terphthalhydrazide with Maleic Anhydride. Preparation of XVf.—The reaction of maleic anhydride with terphthalhydrazide was carried out by the same procedure as the reaction with carbohydrazide. The diacid was obtained in essentially quantitative yield: mp 235–237°. The cyclization was also carried out in excess refluxing trifluoroacetic anhydride over a period of 2 hr. Removal of dehydrating agent *in vacuo* gave a yellow residue which after washing with methanol gave the product in 80% yield: mp >350°.

Upon recrystallization in dimethylformamide a rearranged product was obtained, mp >350°. This was identified as the pyridazinedione XVI on the basis of the infrared and nmr spectra (see text).

Anal. Calcd for $C_8H_5N_2O_3$: C, 54.24; H, 2.84; N, 15.81. Found: C, 54.05; H, 3.15; N, 15.65.

Reaction of N,N'-Biisomaleimide with 1,3-Cyclohexadiene.—Biisomaleimide (0.96 g, 0.005 mole) and 1,3-cyclohexadiene (1.5 g) was refluxed with stirring in 20 ml of nitromethane for 2.5 hr. The solvent was removed *in vacuo* and the residue was recrystallized from dioxane to give 1.01 g (57%) of the adduct, mp 270–275°. A second recrystallization from dioxane gave material with mp 278–280°.

The product had characteristic bands in the infrared spectrum at 5.5 and 5.9 μ; $\lambda_{max}^{dioxane}$ 222 mμ (ϵ 1.68 × 10^4). The nmr spectrum (deuteriochloroform) showed three broad absorptions at 1.6, 3.4, and 6.5 ppm in an approximate area ratio of 2:2:1.

The same product was obtained when the reactants were refluxed in benzene for 10 days in 85% yield.

Anal. Calcd for $C_{10}H_{10}NO_2$: C, 68.16; H, 5.72; N, 7.95. Found: C, 68.42; H, 6.01; N, 7.92.

A rearranged adduct was obtained when the reaction mixture in nitromethane was allowed to reflux for 48 hr instead of 2.5 hr. This product, which has an infrared spectrum characteristic of imides, was obtained in *ca.* 60% yield: mp 335–340°.

Anal. Calcd for $C_{10}H_{10}NO_2$: C, 68.16; H, 5.72; N, 7.95. Found: C, 68.19; H, 6.04; N, 8.17.

Reaction of N,N'-Biisomaleimide with 2,3-Dimethylbutadiene.—N,N'-Biisomaleimide (0.96 g, 0.005 mole) and a 50% excess of 2,3-dimethylbutadiene were refluxed with stirring in 20 ml of nitromethane for 3 hr. The solvent was removed *in vacuo*, and the residue was recrystallized from benzene to give the crystalline adduct, mp 202°, yield 0.8 g (45%).

The same product was isolated in refluxing benzene after 3 days in 47% yield.

The adduct has characteristic infrared bands at 5.5, 5.6, and 6.0 μ; $\lambda_{max}^{dioxane}$ 278 mμ (ϵ 1.7 × 10^4).

Anal. Calcd for $C_{10}H_{12}NO_2$: C, 67.48; H, 6.52; N, 7.92. Found: C, 67.39; H, 6.78; N, 7.86.

Reaction of N,N'-Biisomaleimide with Cyclopentadiene.—A mixture of 2 g (0.0104 mole) of biisomaleimide and 3 g (0.045 mole) of freshly distilled cyclopentadiene in 20 ml of dry benzene was refluxed until the yellow color disappeared (*ca.* 2 hr). The solution was cooled and ether was added to precipitate the solid product completely. This was washed with ether and recrystallized from dioxane to give a white crystalline solid, mp 225–227° (75%).

The product had characteristic bands in the infrared spectrum at 5.6 and 6.1 μ; $\lambda_{max}^{dioxane}$ 224 mμ (ϵ 1.33 × 10^4). The nmr spectrum in $CDCl_3$ consisted of broad resonances at 6.3, 3.5, and 1.7 ppm in an area ratio of 2:4:2, respectively. The product wae also readily soluble in 15% sodium hydroxide, but was insolubls in water.

Anal. Calcd for $C_9H_8NO_2$: C, 66.65; H, 4.97; N, 8.63. Found: C, 66.49; H, 5.20; N, 8.32.

Reaction of N,N'-Biisomaleimide with Anthracene.—Biisomaleimide (0.5 g, 0.0026 mole) and anthracene (1 g, 0.0055 mole) were slowly refluxed in 20 ml of dioxane overnight. A white solid was filtered off after cooling and washed successively with dimethylformamide and ether: mp 336–338°, yield 0.7 g (50%).

The infrared spectrum had bands at 5.6 and 6.1 μ characteristic of the isoimide ring. The ultraviolet spectrum had $\lambda_{max}^{dioxane}$ 225 mμ (ϵ 2.95 × 10^4).

Anal. Calcd for $C_{18}H_{12}NO_2$: C, 78.81; H, 4.41; N, 5.10. Found: C, 78.67; H, 4.83; N, 5.27.

When the reaction was carried out in dimethylformamide for 48 hr at 100°, a rearranged imide product instead was obtained on the basis of its characteristic absorption in the infrared spectrum. The yield was 80%, mp 368–370°.

Anal. Calcd for $C_{18}H_{12}NO_2$: C, 78.81; H, 4.41; N, 5.10. Found: C, 78.76; H, 4.37; N, 4.98.

Reaction of N,N'-Biisomaleimide with Phellandrene.—N,N'-Biisomaleimide (0.9 g, 0.005 mole) and 1.5 g of phellandrene (*p*-methan-1,5-diene) were refluxed with stirring in 15 ml of nitromethane for 1 hr. The reaction mixture was cooled and the unreacted biisomaleimide was filtered off. The solvent was removed *in vacuo*. The material had characteristic infrared bands at 5.5 and 6.0 μ. However, unreacted and/or polymerized diene was present in the mixture on the basis of the nmr spectrum.

Rearrangement of Anthracene Adduct of N,N'-Biisomaleimide to Imide.—The anthracene adduct (0.5 g) was heated in 10 ml of dimethylformamide at 100–110° for 48 hr with stirring. Ether was added after cooling, and the precipitate was filtered and washed with ether. A quantitative yield of imide isomer, mp 368–370°, was obtained.

Rearrangement of the 1,3-Cyclohexadiene and Cyclopentadiene Adduct of N,N'-Biisomaleimide.—The cyclohexadiene adduct (0.5 g) was refluxed in 10 ml of nitromethane for 48 hr. The solvent was removed *in vacuo* and the residue was washed with methanol, giving 0.45 g of the imide isomer, mp 335°. In a similar experiment the cyclopentadiene adduct of N,N'-biisomaleimide was refluxed in nitromethane for 48 hr. The infrared spectrum of the product indicated only about 20% rearrangement.

Preparation of the Diels–Alder Adduct XVIII.—Excess freshly distilled cyclopentadiene was added to 0.3 g of 1,4,6,9-tetraketopyridazo[1,2-*a*]pyridazine in 10 ml of acetone. The mixture was refluxed for 30 min. The original yellow solution became colorless after 10 min and a white precipitate appeared. This was separated and washed with ether, yielding 0.35 g of adduct (70%), mp 194–196°.

Anal. Calcd for $C_9H_8NO_2$: C, 66.65; H, 4.97; N, 8.63. Found: C, 66.69; H, 4.73; N, 8.78.

Preparation of XVII. Reaction of Bicyclo[2.2.1]-5-heptene-2,3-dicarboxylic Anhydride with Hydrazine.—Bicyclo[2.2.1]-5-heptene-2,3-dicarboxylic anhydride (1.64 g, 0.01 mole) in 10 ml of glacial acetic acid was mixed with 0.25 g (0.005 mole) of hydrazine hydrate. The mixture was stirred at room temperature for 30 min and then refluxed for 10 min to give a homogeneous solution. After cooling and removal of the solvent *in vacuo*, a residue was obtained which was washed with methanol, giving 1.1 g (68%) of crude product. After recrystallization from dimethylformamide, material with mp 283–285° was obtained.

Anal. Calcd for $C_9H_8NO_2$: C, 66.65; H, 4.97; N, 8.63. Found: C, 66.82; H, 4.96; N, 8.57.

A diacid (mp 183–186°) could be isolated from the reaction mixture if the reaction temperature was maintained below 15°. However, dehydration of the diacid with a number of agents gave the N,N'-biimide.