Dichloromaleimide Chemistry.[1] II. A Thionyl Chloride–Pyridine Method for the Conversion of Maleimides to Dichloromaleimides

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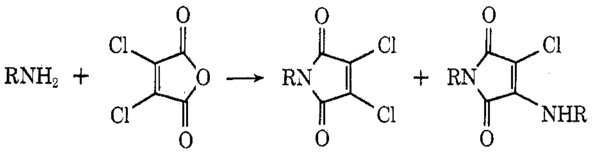
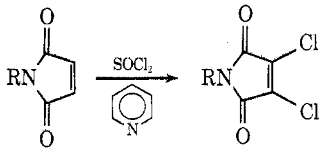
Maleimides are converted to dichloromaleimides by treatment with pyridine and thionyl chloride. The yields are high and no other products appear to be produced. Intermediates are present during the overall conversions and, by appropriate choice of conditions, these were isolated and/or identified. The mechanism of these reactions was investigated and is discussed herein.

Dichloromaleimides have been prepared by the reaction of dichloromaleic anhydride with primary amines. The yields are relatively high if care is taken to avoid the formation[2] of a secondary product, **1**.



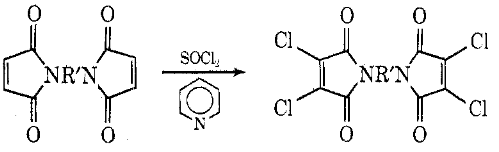
1 (1)

We have recently uncovered an alternate route to dichloromaleimides which involves treatment of maleimides with thionyl chloride and pyridine (eq 2 and 3).

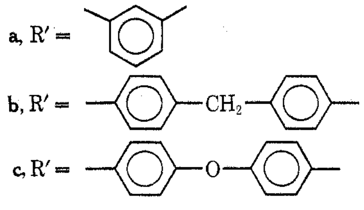


2 **3** (2)

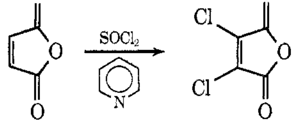
a, R = C_6H_5
b, R = CH_3
c, R = H



4 **5** (3)



Similar treatment of maleic anhydride gave dichloromaleic anhydride in very high yield. These results are summarized in Table I.



6 **7**

TABLE I
CONVERSION OF MALEIMIDES TO DICHLOROMALEIMIDES IN THIONYL CHLORIDE

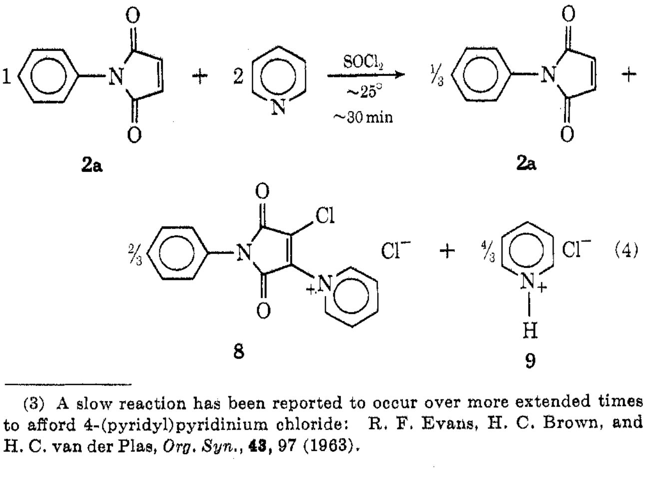
Starting material	Moles of pyridine	Product	Crude yield, % Nmr	Crude yield, % Vpc	Isolated yield, %[a]
2a	2	**3a**	100	99	76
2b	2	**3b**	87		20
2c	2	**3c**	[b]		25
4a	4	**5a**	100		50
4b	4	**5b**	100		65
4c	4	**5c**	100		60
6	2	**7**	100		80

[a] After recrystallization. [b] Not determined with certainty.

The overall course of these reactions was quite surprising since, at first glance, it appeared to be straightforward replacement of hydrogen by chlorine under conditions which are conducive to "normal ionic" reactions, that is, reactions in which hydrogen and chlorine would be expected to ionize in opposite senses. It therefore seemed appropriate to undertake an investigation of the mechanism of these conversions. In general, it was most convenient to employ *N*-phenylmaleimide (**2a**) for this purpose, but some evidence was also obtained from other maleimide systems which, in all cases, appeared to substantiate the findings from the former system.

It was established at the outset that (a) **2a** does not react with thionyl chloride alone, (b) pyridine, under *our* reaction conditions, does not react with thionyl chloride,[3] and (c) **2a** does not react with pyridine in nonpolar (methylene chloride) or polar (dimethyl sulfoxide) solvents at temperatures and concentrations where reactions occurred readily in thionyl chloride solutions.

When a solution of **2a** in thionyl chloride was treated with two equivalents of pyridine and the slightly exothermic reaction maintained at 20–30° for 30 min, the solution was found to contain $^1/_3$, $^2/_3$, and $^4/_3$ mol equiv of **2a**, **8**, and pyridine hydrochloride, **9**, respectively (eq 4). The relative amounts of these three substances



2a **2a** **8** **9**

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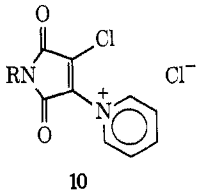
[1] Organic Chemistry in Thionyl Chloride. I.

[2] A Salmony and H. Simonis, *Ber.*, **38**, 2594 (1905).

[3] A slow reaction has been reported to occur over more extended times to afford 4-(pyridyl)pyridinium chloride: R. F. Evans, H. C. Brown, and H. C. van der Plas, *Org. Syn.*, **43**, 97 (1963).

were determined by integration of the vinyl singlet of **2a**, the α-pyridinium multiplet of **8**, and the NH singlet of **9** (see Figure 1C; downfield acidic proton peak not shown in 1C or 1D). Isolation of each was then achieved after removal of the excess thionyl chloride. Compound **8** was separated and displayed an nmr spectrum in methanol in complete agreement with the assigned structure (see Experimental Section). It was then converted to its tetrafluoroborate salt in 94% overall yield, *i.e.*, 94% of two-thirds mol equiv (the amount determined to be present by nmr). The remaining **2a** was isolated and identified by nmr and vapor-phase chromatography (vpc); the only other component detected was a trace of **3a**. Pyridine hydrochloride was also separated and identified by its nmr spectrum.

Similarly, the reactions of **2b**, **4a**, **4b**, and **4c** were carried out initially at ~25° and, in each case, nmr results indicated *ca.* $^1/_3$:$^2/_3$:$^4/_3$ relative mol equiv of unreacted olefinic groups,[4] pyridinium salt groups **10**,[4] and pyridine hydrochloride **9**, respectively. The results are summarized in Table II and indicate that three molecules of pyridine were consumed in converting each maleimide double bond to products, one giving rise to **8** (or **10**) and two others leading to **9**. Thus, since only 2 mol equiv of pyridine were present initially, only two-thirds of the maleimide double bonds reacted under these conditions.



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When the reaction of **2a** with 2 equiv of pyridine was allowed to proceed at 25° for 15.5 hr, a significant amount of further reaction was noted (see Table II and compare with the 3-hr results). At that point in time, addition of another 0.55 mol equiv of pyridine caused a reduction in the amount of **2a**, a corresponding increase in **8**, a corresponding double increase in **9**, but no appreciable change in **3a**[5] (see Table II). This result again indicates that, in the initial reaction of **2a**, three molecules of pyridine were consumed.

Further substantiation of the stoichiometry of these initial reactions was obtained when **2a** was treated with 3 mol equiv of pyridine at 25° in thionyl chloride. After 3 hr, examination of the nmr spectrum of the reaction mixture indicated that the mole ratio of **2a**:**8**:**9** was 0.02:0.98:2.00. Again, **8** was isolated from this reaction mixture and its structure was established by nmr, infrared, and mass spectrometry and by its facile hydrolysis to **11**, presumably *via* the path described in

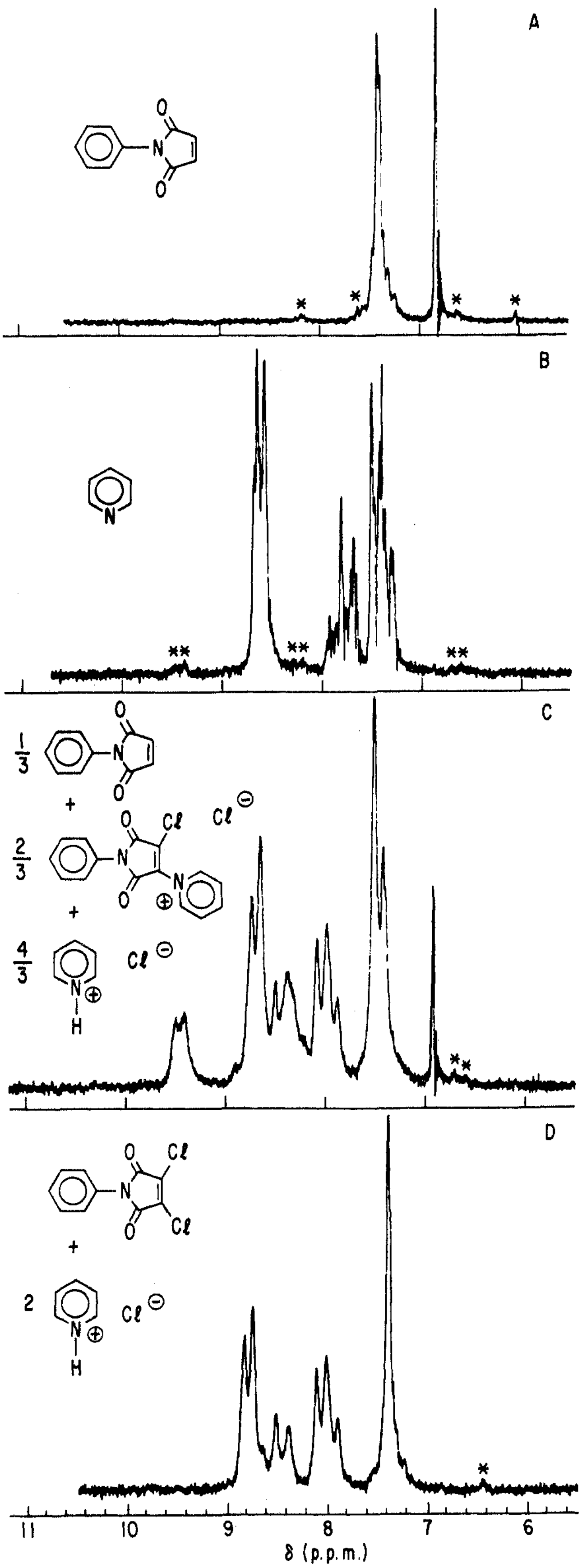

Figure 1.—Nmr spectra in thionyl chloride solution (external tetramethylsilane as reference). An asterisk denotes a spinning side band. (A) *N*-phenylmaleimide (**2a**); (B) pyridine; (C) reaction mixture after 1 hr at ambient temperatures (**2a**, **8**, and **9**); (D) reaction mixture after 1 hr at reflux (**3a** and **9** only).

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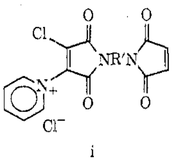
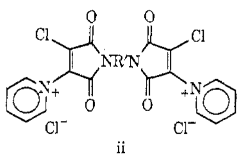
[4] For the bisimide cases (**4a–c**), mixtures of **4**, i, and ii would be expected to be present.



i



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[5] The fact that **3a** definitely did not diminish is critical to later discussions (*vide infra*).

TABLE II

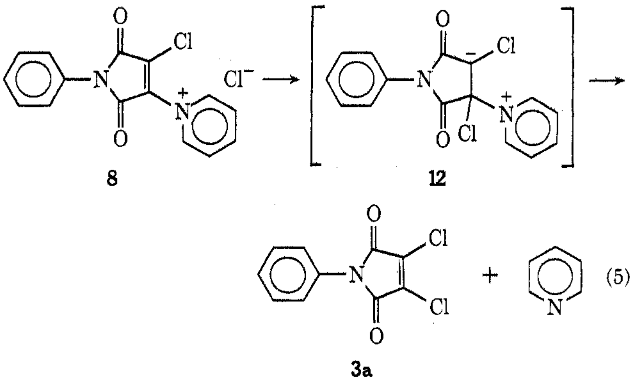
NMR RESULTS OF REACTIONS AT 25° IN THE PRESENCE OF 2 MOL EQUIV[a] OF PYRIDINE PER MALEIMIDE DOUBLE BOND

		Chemical Shift, δ^b			Relative moles of groups[c]			
Starting material	Reaction time, hr	Vinyl protons (s)	α-Pyridinium protons of **8** or **10** (m)	NH Protons of **9**[d] (s)	Vinyl	**8** or **10**	**9**	Dichlorovinyl[e]
2a	0.5	6.82	9.35–9.64	16.9	0.31	0.68	1.39	0.01
2a	2.0	6.82	9.41–9.68	17.1	0.33	0.66	1.47	0.01
2a	3.0	6.83	9.38–9.61	16.9	0.29	0.67	1.45	0.04
2b	1.0	6.62	9.18–9.43	16.8	0.35	0.65	1.37	0.00
4a	1.0	6.82	9.30–9.55	16.8	0.31	0.69	1.38	0.00
4b	16.0[f]	6.72	9.25–9.50	16.7	0.25[f]	0.64[f]	1.50[f]	0.11[f]
4c	1.0	6.75	9.32–9.52	16.9	0.30	0.70	1.42	0.00
2a	15.5	6.80	9.31–9.54	17.0	0.26	0.52	1.53	0.22
2a	18.5[g]				0.05	0.71	1.87	0.24

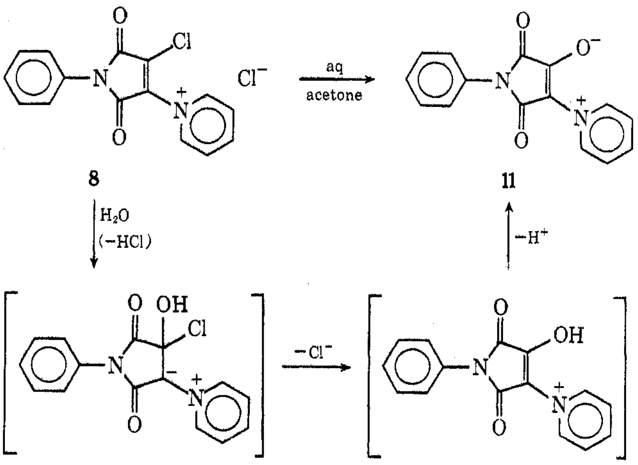
[a] Complete details in Experimental Section (NOTE: 2.1 mol equiv of pyridine were usually used since enough HCl was always present in the $SOCl_2$ to neutralize ~0.1 mol equiv.) [b] Ppm downfield from external tetramethylsilane. [c] Values may have ±4% error. [d] The very large chemical shifts observed for the NH protons of **9** are probably due to NH···Cl hydrogen bonding; see H. M. Relles, *J. Org. Chem.*, **35**, 4280 (1970). [e] α,β-Dichloromaleimide groups determined by difference (see Experimental Section). [f] Differences largely due to further reaction during this 16-hr period (*vide infra*). [g] This represents analysis of a reaction mixture which, after 15.5 hr, had an additional 0.55 mol equiv of pyridine added to it.

Scheme I.[6] Compound **11** was isolated and identified through its infrared and mass spectra.

When the reaction of **2a** with 1 mol equiv of pyridine and excess thionyl chloride was carried out in methylene chloride at 25° for 15 hr, there was obtained only a mixture of **2a**, **9**, and **3a** in the ratio of 0.5:1.0:0.5, respectively. It was thus apparent that either (a) **8** was not an intermediate in this case, or (b) it had been present and was converted to **3a** and pyridine by the mechanism shown in eq 5. Clearly, if this latter alternative had prevailed, the regenerated pyridine was then available to cause additional conversion of **2a** to **3a** *via* **8** and **12**. It is perhaps not unreasonable to expect that methylene chloride, being considerably less polar than thionyl chloride, would induce stronger ion-pair formation, thereby increasing the localized concentrations of the reactant ions and increasing the rate of conversion of **8** to **3a**.[7]

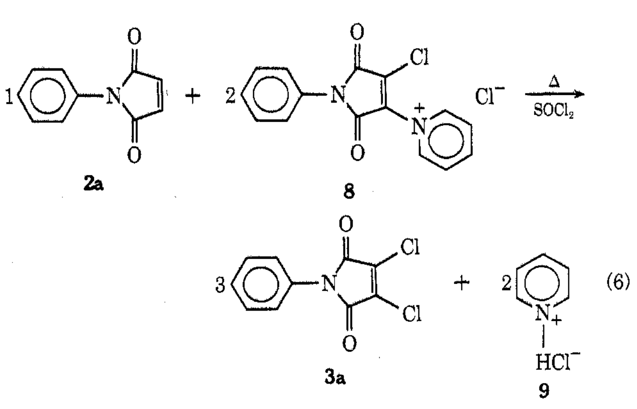


SCHEME I



On heating the reaction mixtures initially obtained from **2a**, **2b**, **4a**, **4b**, or **4c** (in which 2 mol equiv of pyridine in thionyl chloride solution was used) at reflux for short periods, it was observed by nmr that the resulting solutions contained only **3a**, **3b**, **5a**, **5b** or **5c**, respectively, along with 2 mol equiv of **9** per mol equiv of maleimide group. Each of the dichloromaleimide products was then isolated in good yield (see Table I).

It was also found that by refluxing 1 mol of **2a** with 2 mol of previously isolated **8** in thionyl chloride, a 3:2 mixture of **3a** and **9**, respectively (eq 6), was obtained.



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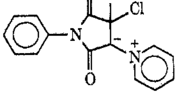
(6) For the presentation of a strictly analogous methanolysis in a series of 12 similar compounds, see M. J. Karten, S. L. Shapiro, E. S. Isaacs, and L. Freedman, *J. Org. Chem.*, **30**, 2657 (1965).

(7) Viewed in the extreme, perhaps an excellent way for chloride ion to become solvated in such a poorly solvating medium is by forming **12** (or possibly iii, which, of course, would not lead to products).



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These results argue strongly that **8** was converted thermally to **3a** (*via* **12**) and that the pyridine thus generated caused more **2a** to react to give more **3a** (*via* **8** and **12**). These observations also account for the fact that one maleimide group only requires two pyridine molecules to be converted to a dichloromaleimide group in the *overall* reaction sequence; this is summarized in Scheme II.

SCHEME II

2a (1 mol) + pyridine (2 mol)

$\Big\downarrow \text{SOCl}_2, 25°$

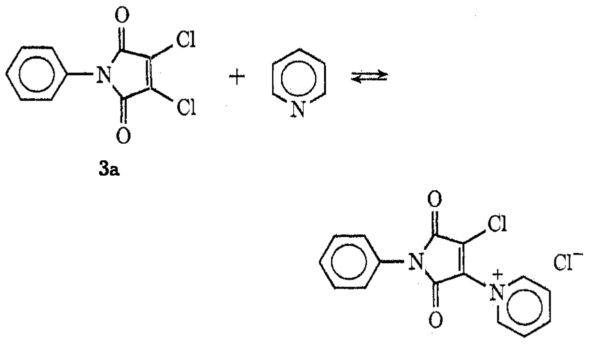
products of eq 4

$\Big\downarrow \text{SOCl}_2, \Delta$

3a (1 mol) + **9** (2 mol)

Having established the stoichiometry of both the facile ambient- and reflux-temperature reactions and a probable mechanism to explain the latter, it was of interest to attempt to learn something about the mechanism of the former.

Control experiments (see Experimental Section) indicated that **3a** was not a precursor for **8** *during the reaction* because (a) the ambient-temperature reaction leading from **2a** to **8** was much faster than pyridine was found capable of reacting with **3a** to give **8** under the same reaction conditions, and (b) pyridine was found to be *unable to completely convert* **3a** to **8** under the reaction conditions (while *initially none* of **3a** was observed during the conversion of **2a** to **8**). This fact (b) is in agreement with the equilibrium shown in eq 7 ($K \cong 3$). Interestingly, extended periods in the ambient-temperature reaction (equation 4) did lead to the formation of some **3a** (see Table II, **2a** at 15.5 hr and also note that the **4b** reaction after 16 hr showed evidence for dichloromaleimide groups), a fact also in agreement with the equilibrium (eq 7) being approached more slowly from the right than from the left. By heating the reaction mixture, equilibration became more rapid, pyridine was regenerated, and it then reacted further with **2a**. Ultimately, all of the pyridine was neutralized by the HCl produced and was then no longer able to take part in the equilibration. Hence, only **3a** and **9** remained after the heating period.



3a

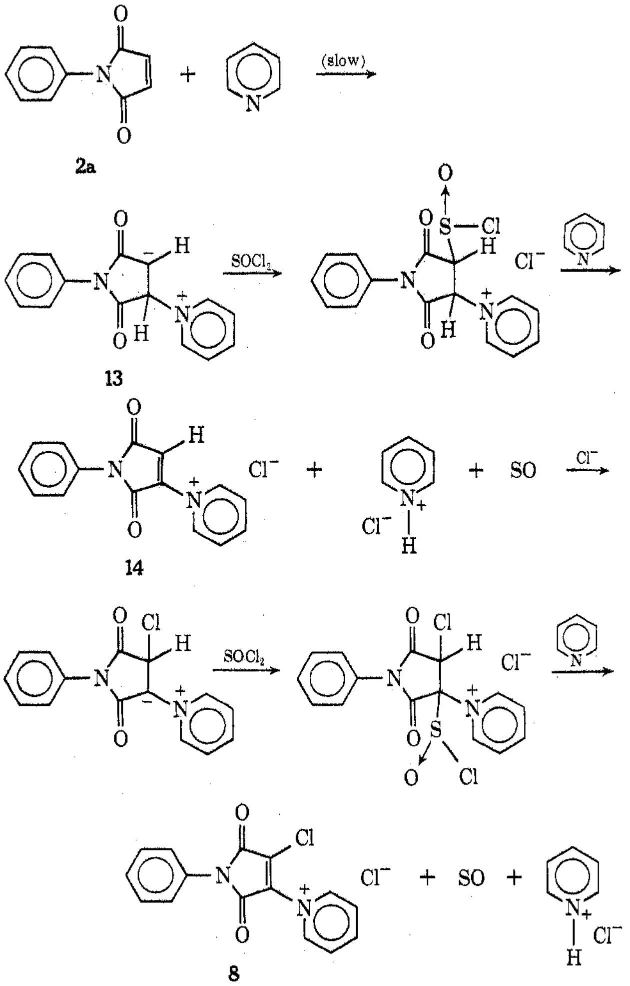
8

(7)

No other intermediates were ever observed during the reactions using vpc or nmr techniques, although any reasonable mechanism requires that they be invoked. Presumably, if they were present, they were consumed much faster than they were produced.

One mechanism which is consistent with observations on the formation of **8** from **2a** is depicted below (Scheme III). This should apply equally well to the other maleimides examined.

SCHEME III



2a

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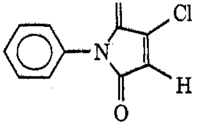
14

8

We favor this mechanism over other mechanisms in which **15** might be invoked as an intermediate. In view of the sluggishness of attack of pyridine on **3a**, one would predict a rate of attack of pyridine on **15** to be at least slow enough to allow **15** to be observed in the system when all of the pyridine had been consumed. However, *none was observed.* On the other hand, **14** (Scheme III) should be much more reactive than **2a**, **15**, or **3a** toward a nucleophile (Cl⁻) and, indeed, might not be expected to be observed. The formation of sulfur monoxide has been observed or



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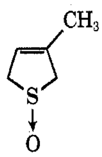
invoked in several previous instances.[3,8,9] However, our efforts to trap this very unstable molecule with isoprene[10] were completely unsuccessful since the isoprene reacted rapidly with **2a** under the usual reaction conditions (thionyl chloride solution), or slightly modified reaction conditions (methylene chloride solution), to give the expected Diels–Alder adduct along with other unidentified products;[11] none of **16** was produced, however.



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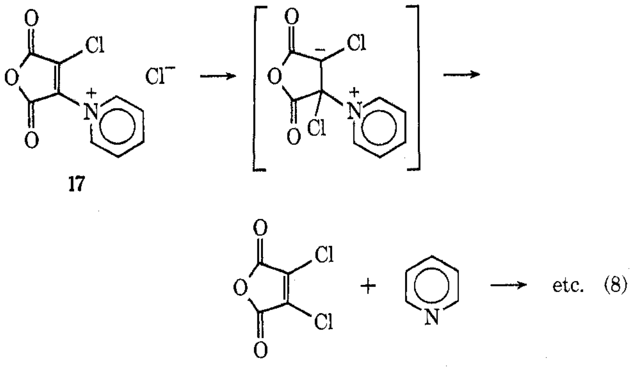
Some nmr evidence was obtained for the intermediacy of **17** in the conversion of **6** to **7**; **17** was much more reactive than **8** (or **10**) and underwent facile conversion to products (eq 8) at ambient temperatures.



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7

In light of the above discussion, it is possible that the reported conversion[12] of acetylenedicarboxylic acid to **7** could occur by (1) HCl addition to the triple bond, (2) ring closure to monochloromaleic anhydride, and (3) reaction with pyridine–thionyl chloride to give **7** *via* **17**.

Experimental Section

Nmr spectra were recorded with a Varian Associates T-60 spectrometer (abbreviations: m = multiplet, s = single peak, d = doublet). Infrared spectra were taken (KBr pellets) on a Perkin-Elmer 521 grating infrared spectrophotometer.

Mass spectra were recorded on a C. E. C. 21-104 analytical mass spectrometer. Vapor-phase chromatographic (vpc) analyses were done with a silicone rubber (SE-30) column. Melting points were taken with a Mel-Temp apparatus and are uncorrected.

The pyridine used was Eastman "Karl Fischer" reagent grade; the thionyl chloride was obtained from Matheson Coleman and Bell. The maleimides (**2a** and **4a–c**) were prepared from the appropriate amines and maleic anhydride by a standard literature technique;[13] **2b** and **2c** were obtained from the Aldrich Chemical Co.

Conversion of *N*-Phenylmaleimide (2a) to *N*-Phenyldichloromaleimide (3a) Using 2 Equiv of Pyridine in Thionyl Chloride. A. Synthetic Procedure.—To a solution of 1.73 g (0.0100 mol) of **2a** in 20 ml of thionyl chloride was added 1.66 g (0.0210 mol) of pyridine while the system stirred in a cold-water bath. Stirring was continued at ~20° for 15 min and then the slightly turbid solution was heated for 1 hr at reflux.

All of the excess thionyl chloride was then removed *in vacuo* and the residue was taken up in 100 ml of chloroform. The chloroform solution was extracted with dilute HCl (to remove the pyridine hydrochloride), dried, filtered, and freed of solvent giving 2.78 g of a solid residue which, by quantitative vapor phase chromatography (vpc), was found to contain 2.40 g (0.0099 mol) of **3a** (99% yield).

The crude product was recrystallized from chloroform to give 1.85 g of **3a** (76% isolated yield), mp 204–205° (lit.[14] mp 203°). The infrared spectrum of this material was exactly the same as that for **3a** obtained from aniline and dichloromaleic anhydride[11] and from the methylene chloride–thionyl chloride reaction described herein. The mass spectrum of **3a** showed the expected two-chlorine molecular-ion cluster at *m/e* 241–245.

B. Procedures for Mechanistic Information.—(1) To a solution of 1.73 g (0.0100 mol) of **2a** in 20 ml of thionyl chloride was added 1.58 g (0.0200 mol) of pyridine while stirring in a water bath to maintain the system at *ca.* 25°. Samples of the homogeneous solution were removed at various times and the progress of the reaction was monitored by nmr spectroscopy. The results are listed in Table II in the discussion section. The amount of **2a** was determined from the integral of vinyl proton peak at δ 6.82. The amount of **8** was determined from the integral of the α-pyridinium proton multiplet between δ 9.35–9.64. The amount of **3a** was determined from the *N*-phenyl integral after subtracting out that required by **2a** and **8**. The amount of **9** was determined from the integral of the NH singlet at δ 16.9. The α, β, and γ protons of **9** and the β and γ protons of the pyridinium ring of **8** were found as overlapping multiplets between δ 7.72 and 8.97. The experimental error was ±4%.

After the system had remained at 25° for 15.5 hr, an additional 0.0055 mol of pyridine was added and further reaction which occurred was determined (nmr) after 3 hr (see Table II).

(2) Exactly 1.73 g (0.01 mol) of **2a** was dissolved in 20 ml of thionyl chloride. The solution was stirred in a water bath at 20–25° in dry air and 1.66 g (0.0210 mol) of pyridine was added at once. After 2 hr, the nmr spectrum of a sample was obtained (see Table II) and the sample was then returned to the reaction mixture.

All of the excess thionyl chloride was then removed *in vacuo* at ~25° during 45 min. Addition of 100 ml of chloroform to the residue caused complete solution followed rapidly by the precipitation of a solid. Filtration gave (after vacuum drying) 2.45 g of slightly impure **8** which showed the expected nmr spectrum in CH_3OH: *N*-phenyl, s, δ 7.24, 5 H; β-pyridinium, m, δ 7.97–8.33, 2 H; γ-pyridinium, m, δ 8.53–8.93, 1 H; α-pyridinium, m, δ 8.93–9.18, 2 H. While this spectrum was being recorded, no changes were detected, but, after 13 hr, it had changed appreciably.[6]

A solution of 2.00 g of this salt (**8**) in 25 ml of methanol was prepared and filtered to remove ~0.01 g of insoluble material. After 3 min, this clear yellow solution was added to a solution of 1.10 g (0.01 mol) of sodium tetrafluoroborate in 40 ml of methanol. A large amount of solid separated quickly. After another 7 min, this solid was filtered, washed with some methanol, and vacuum dried for 8 hr at 60°. The resulting pale yellow solid, mp ~240° dec, was the tetrafluoroborate salt of **8** (obtained 1.86 g of **8** BF_4 from 2.00 g of impure **8** Cl; this would correspond to 2.28 g, 0.0062 mol, of **8** BF_4 from 2.45 g of impure **8** Cl, or 94% yield, based on nmr analysis of the mixture just before work-up). This material displayed an infrared spectrum (carbonyl at 1730 cm^{-1}, etc.) which was identical with that of **8** Cl (*vide infra*) except for the presence of an additional band at 1050 cm^{-1} due to the tetrafluoroborate anion.

Due to its nonvolatility, a sample of **8** BF_4 had to be heated to ~230° in an attempt to obtain a mass spectrum. At this temperature, the spectrum showed the following (*m/e*, relative intensities, and probable rationale given): 79, 100.0, pyridine$^+$; 119, 57.2, $(C_6H_5N{=}C{=}O)^+$; 225, 27.2, *N*-phenylchlorofluoromaleimide$^+$ (arising *via* a decomposition; appropriate

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[8] L. F. Fieser and Y. Okumura, *J. Org. Chem.*, **27**, 2247 (1962).

[9] (a) Y. Okumura, *ibid.*, **28**, 1075 (1963); (b) G. Büchi and G. Lukas, *J. Amer. Chem. Soc.*, **86**, 5654 (1964); (c) R. M. Dodson and R. F. Sauers, *Chem. Commun.*, 1189 (1967); (d) R. M. Dodson, and J. P. Nelson, *ibid.*, 1159 (1969); (e) Y. L. Chow, J. N. S. Tam, J. E. Blier, and H. H. Szmant, *ibid.*, 1604 (1970), and references cited therein.

[10] D. Lemal (private communication) and others,[9c–e] have been able to trap SO with dienes and trienes as cyclic sulfoxides.

[11] H. M. Relles, unpublished results.

[12] R. N. McDonald and R. A. Krueger, *J. Org. Chem.*, **28**, 2542 (1963).

[13] M. K. Hargreaves, J. G. Pritchard, and H. R. Dave, *Chem. Rev.*, **70**, 439 (1970).

[14] R. Anschütz and C. Beavis, *Justus Liebigs Ann. Chem.*, **263**, 159 (1891).

one-chlorine cluster); 241, 33.6, *N*-phenyldichloromaleimide$^+$ (arising *via* a decomposition; appropriate two-chlorine cluster); 162, 17.9, $C_6H_5N^+{\equiv}CC{\equiv}CCl$[15] (appropriate one-chlorine cluster); and 146, 13.6, $C_6H_5N^+{\equiv}CC{\equiv}CF$.

Anal. Calcd for $C_{15}H_{10}BClF_4N_2O_2$: C, 48.3; H, 2.7; N, 7.5; Found: C, 47.9; H, 2.8; N, 7.6.

All of the solvent was evaporated from the initial chloroform filtrate. The solid residue was taken up in 10 ml of deuteriochloroform and analyzed by nmr. This analysis indicated that pyridine hydrochloride (**9**) and *N*-phenylmaleimide (**2a**) were present in a molar ratio of 0.0151:0.0034, in agreement with the nmr evidence before work-up. The $CDCl_3$ solution, after extraction with D_2O/DCl, showed (nmr) that only the *N*-phenylmaleimide (**2a**) remained; all of the pyridine hydrochloride (**9**) was now present (nmr) in the D_2O phase. Further analysis of the $CDCl_3$ phase by vpc (6-ft 10% SE-30 column, 160°) showed that it contained only two volatile materials, *N*-phenylmaleimide (**2a**) and *N*-phenyldichloromaleimide (**3a**) in the molar ratio of 30:1 (again in agreement with the nmr spectrum before work-up).

(3) A solution of 1.73 g (0.01 mol) of **2a** in 20 ml of thionyl chloride was stirred at ~25° and 1.66 g (0.0210 mol) of pyridine was added at once. The reaction caused the solution temperature to increase to 45° during 6 min and then drop back slowly to 26° during the next 47 min. After a total of 60 min since the pyridine was added, the nmr spectrum of a sample showed that the mixture contained 0.0034 mol of **2a**, 0.0065 mol of **8**, 0.0001 mol of **3a**, and 0.0147 mol of **9** (spectral data the same as given in expt 1 above).

The nmr sample was returned and the homogeneous system was then heated at reflux for 1 hr. On cooling back to ~25°, much solid platelets crystallized out. The addition of 20 ml of methylene chloride or deuteriochloroform at this point caused all of the solid to redissolve. The nmr spectrum of this solution now showed (a) none of **2a**, (b) none of **8**, (c) 0.0100 mol of **3a** (aryl, m, centered at δ 7.55), (d) 0.0204 mol of **9** (NH, s, δ 17.7; α protons, m, δ 8.92–9.17; γ protons, m, δ 8.52–8.92; β protons, m, δ 7.98–8.39), and no other materials.

Conversion of *N*-Phenylmaleimide (2a) to *N*-Phenyldichloromaleimide (3a) Using 1 Equiv of Pyridine and Excess Thionyl Chloride in Methylene Chloride.—A solution of 17.30 g (0.100 mol) of *N*-phenylmaleimide, 100 ml of methylene chloride, and 20.0 ml of thionyl chloride was stirred at room temperature while 7.90 g (0.100 mol) of pyridine in 100 ml of methylene chloride was added slowly during 12 min. During 1 hr the temperature of the solution rose to *ca.* 31° and then slowly began to fall back to room temperature. A small amount of solid separated. After the system had been stirred for 15 hr, the nmr spectrum of a sample was consistent with a mixture of ~0.1 mol of **9** (β protons m, δ 7.85–8.17, 2 H; γ protons m, δ 8.32–8.68, 1 H; α protons m, δ 8.77–8.99, 2 H; NH s, δ 17.8, 1 H), *ca.* 0.05 mol of **3a** (aromatic part of the multiplet, δ 7.18–7.68, centered at δ 7.42), and ~0.05 mol of **2a** (aromatic part of the multiplet centered at δ 7.42, olefinic s, 6.87, 1 H).

HCl (100 ml, 1 *N*) was then added (CAUTION!) to destroy the excess thionyl chloride and the layers were separated. The methylene chloride layer was extracted with another 100 ml of 1 *N* HCl, then with 100 ml of H_2O, dried, and freed of solvent *in vacuo* to give a yellow solid. This solid was found by vpc (6 ft 10% SE-30 column, 200°) to contain nearly equal amounts of **2a** and **3a** (and *no other* volatile products). Fractional crystallization from chloroform afforded 7.25 g of **3a** (30%, isolated yield), mp 201–202° (lit.[14] mp 203°). The mass spectrum showed a molecular-ion cluster with the expected relative intensities at *m/e* 241, 243, 245. The nmr spectrum showed only aryl protons; the ir spectrum showed a strong double carbonyl absorption (1718 and 1732 cm^{-1}).

Anal. Calcd for $C_{10}H_5Cl_2NO_2$: C, 49.62; H, 2.08; N, 5.79. Found: C, 49.7; H, 1.99; N, 5.96.

Reaction of 2a with 3 Equiv of Pyridine in Thionyl Chloride. Deliberate Synthesis of 8 from 2a.—A solution of 1.73 g (0.0100 mol) of **2a** was dissolved in 20 ml of thionyl chloride and 2.45 g (0.0310 mol) of pyridine was added during 2 min while the temperature of the system was maintained at ~25° with external cooling. After the system had been stirred at this temperature for 3 hr, a sample was removed and found (by nmr) to contain only 0.0002 mol of **2a** (vinyl, s, δ 6.80), 0.0098 mol of **8** (α-pyridinium protons m, δ 9.39–9.65), and 0.0200 mol of pyridine hydrochloride (NH, s, δ 16.8).

All of the excess thionyl chloride was then removed *in vacuo* at 30–35° during 1 hr. Chloroform (100 ml) was added to dissolve the residue; much solid then deposited rapidly from this solution. This solid was filtered, washed with a little chloroform, and air dried to give 3.44 g of **8**; melting point with decomposition begins at 125°. Elemental analysis indicated this material contained 1 mol of HCl.

Anal. for **8** HCl: Calcd for $C_{15}H_{11}Cl_3N_2O_2$: C, 50.35; H, 3.08; N, 7.83; Cl, 29.8. Found: C, 50.1; H, 2.9; N, 7.7; Cl, 29.6.

The nmr spectrum of this material could be recorded in acetone-d_6–D_2O solution before any significant amount had been converted to **11** (*vide infra*). It shows *N*-phenyl (m, δ 6.85–7.36), 5 H), β-pyridinium (m, δ 8.00–8.43, 2 H), γ-pyridinium (m, δ 8.43–8.89, 1 H), and α-pyridinium protons (m, δ 8.89–9.24, 2 H) in accord with the assigned structure of **8**. (After 5 min changes in all of these nmr multiplets began to appear; after 30 min much solid had separated from the solution.) The infrared spectrum showed a strong, sharp carbonyl absorption at 1730 cm^{-1}. The mass spectrum had a weak molecular ion at *m/e* 285 corresponding to the cation portion of the salt **8** and other prominent peaks at 241 (91, two-chlorine cluster, **3a**$^+$), 79 (100, pyridine$^+$), and 36 (25, one-chlorine cluster, HCl) resulting from decomposition in the heated source.

Exactly 0.100 g of the above sample of **8** was dissolved in 2 ml of 70% aqueous acetone. After a short time, solid began to precipitate. After this system was kept at 25° overnight, the solid was filtered, washed with some water, and dried *in vacuo* at 40° to give 0.040 g of **11**, mp 266–268°. This material showed absorptions in the infrared spectrum at 1755 (m), 1705 (s), and 1655 (vs) cm^{-1} [lit.[7] a series of 12 compounds of this type showed corresponding bands at *ca.* 1754 (m), 1695 (s), and 1640 (vs) cm^{-1}]. Its mass spectrum was in complete accord with structure **11**: *m/e* 266 (81, molecular ion), 238 [34, (M − CO)$^+$], 194 [36, (M − CO − CO_2)$^+$], 119 (100, $C_6H_5N{=}C{=}O^+$), 91 (99, $C_6H_5N^+$), and 79 (94, pyridine$^+$).

Reaction of 2a with 2 Equiv of 8 in Thionyl Chloride.—A sample of **8** (*vide supra*), 1.64 g (0.0051 mol), and 0.43 g (0.0025 mol) of **2a** were refluxed with 15 ml of thionyl chloride for 4 hr. The nmr spectrum of a sample of the resulting solution (homogeneous above ~40°, much solid precipitates at 25°) showed the presence of 0.0002 mol of **2a** (vinyl, s, δ 6.80), 0.0074 mol of **3a** (aryl, m, δ 7.17–7.65 with main peak at δ 7.40), and 0.0050 mol of **9** (NH, s, δ 17.1, 1 H; β protons, m, δ 7.78–8.12, 2 H; γ protons, m, δ 8.32–8.65, 1 H; α protons, m, δ 8.65–8.88, 2 H).

All of the excess thionyl chloride was removed *in vacuo* and the residue was taken up in 150 ml of chloroform, extracted with 1 *N* HCl to remove the pyridine hydrochloride, dried, and freed of solvent *in vacuo*. Vpc showed that much **3a** was present. The crude product, 1.71 g, was triturated with a little methanol to remove residual **2a**. This treatment gave 1.61 g (0.0068 mol, 90% yield) of **3a**, mp 203.5–205° (lit.[14] mp 203°), the infrared spectrum of which was superimposable on that of an authentic sample of **3a**.

Reaction of 3a with 1 Equiv of Pyridine in Thionyl Chloride.—A solution of 2.42 g (0.0100 mol) of **3a** was stirred at 25° with 20 ml of thionyl chloride (most soluble) and 0.87 g (0.0110 mol) of pyridine was added (homogeneous solution after ~0.5 hr). Samples were taken at various times and analyzed for the amounts of **8**, **3a**, and pyridine by nmr spectroscopy. The α-pyridinium proton multiplet of **8** was characteristically downfield (δ 9.14–9.42) from all the rest of the absorptions (δ 7.07–8.73) so that a careful integration was possible. The results are listed in Table III.

TABLE III

Reaction time, hr	Moles[a] of **8**	Moles[b] of **3a**	Moles[b] of pyridine
0		0.0100	0.0110
1.5	0.0044	0.0056	0.0066
3.5	0.0065	0.0035	0.0045
7	0.0076	0.0024	0.0034
17.5	0.0073	0.0027	0.0037

[a] Determined from integral of α-pyridinium multiplet at δ 9.14–9.42. [b] Determined by difference.

Reaction of 3a with 1 Equiv of Pyridine in Thionyl Chloride in the Presence of 2 Equiv of Pyridine Hydrochloride.—A thionyl chloride solution containing 0.0100 mol of **3a** (most soluble) and

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[15] H. M. Relles and R. W. Schluenz, *J. Org. Chem.*, **37**, 1742 (1972).

0.0200 mol of pyridine hydrochloride was prepared by allowing 1.73 g (0.0100 mol) of **2a** to react with 1.58 g (0.0200 mol) of pyridine in 20 ml of thionyl chloride for 15 min at 25° and then for 1 hr at 80°.

On cooling back to 25°, 0.79 g (0.0100 mol) of pyridine was added, the system was stirred continuously (homogeneous after *ca.* 0.5 hr), and samples were taken at various times and analyzed by nmr spectroscpy for **8**, **3a**, pyridine, and **9**. The results are listed in Table IV.

TABLE IV

Reaction time,[a] hr	Moles[b] of **8**	Moles[c] of **3a**	Moles[c] of pyridine	Moles[d] of pyridine HCl
0		0.0100	0.0100	0.0200
0.5	0.0030	0.0070	0.0070	0.0200
1.5	0.0039	0.0061	0.0061	0.0200
13	0.0060	0.0031	0.0031	0.0200

[a] Since second portion of pyridine was added. [b] Determined from integral of α-pyridinium proton multiplet (δ 9.40–9.67). [c] Determined by difference. [d] Determined from NH integral (δ 17.2).

Competitive Reactions of 2a and 3a with 2 Equiv of Pyridine in Thionyl Chloride.—Exactly 1.73 g (0.0100 mol) of **2a** and 1.21 g (0.0050 mol) of **3a** were dissolved (completely soluble) in 20 ml of thionyl chloride. Then, 1.60 g (0.0202 mol) of pyridine was added and stirring was maintained at 25°. Samples were removed at various times and analyzed by nmr. The results are listed in Table V.

TABLE V

Reaction time, hr	Moles[a] of **2a**	Moles[b] of **8**	Moles[c] of **3a**	Moles[d] of pyridine HCl
0	0.0100		0.0050	
0.75	0.0040	0.0069	0.0041	0.0125
1.5	0.0038	0.0071	0.0041	0.0126

[a] Determined from vinyl integral. [b] Determined from integral of α-pyridinium multiplet. [c] Determined by difference. [d] Determined from NH integral.

Conversion of *m*-Phenylenediaminebismaleimide (4a) to *m*-Phenylenediaminebisdichloromaleimide (5a).—A solution of 1.34 g (0.0050 mol) of **4a** in 20 ml of thionyl chloride was stirred in a cold-water bath as 1.66 g (0.0210 mol) of pyridine was added. This system was stirred at 20–25° for 1 hr, its nmr spectrum was recorded (see Table II), and it was then refluxed for 1 hr and cooled. The nmr spectrum of a sample showed that 0.0050 mol of **5a** (aryl, m, δ 7.20–7.47) and 0.0210 mol of **9** (NH, s, δ 16.7, 1 H; β protons, m, δ 7.74–8.09, 2 H; γ protons, m, δ 8.23–8.57, 1 H; α protons, m, δ 8.57–8.82, 2 H) were the only materials present. Removal of the excess thionyl chloride followed by a chloroform–water work-up and recrystallization from benzene–cyclohexane gave 1.01 g (50% isolated yield) of **5a**, mp 172.5–174°. The infrared spectrum of this material was superimposable on that of a sample of **5a** which was prepared from *m*-phenylenediamine and 2 mol of dichloromaleic anhydride in acetic acid; both showed strong carbonyl absorption at 1729 cm^{-1}. (This latter sample of **5a** had mp 172.5–173.1°.) The mass spectrum of **5a**, in accord with the assigned structure, showed a four-chlorine cluster for the molecular ion at *m/e* 404–412.

Anal. Calcd for $C_{14}H_4Cl_4N_2O_4$: C, 41.41; H, 0.99. Found: C, 41.4; H, 1.1.

Conversion of 4,4′-Diaminodiphenylmethanebismaleimide (4b) to 4,4′-Diaminodiphenylmethanebisdichloromaleimide (5b).—Exactly 1.66 g (0.0210 mol) of pyridine was added to a solution of 1.79 g (0.0050 mol) of **4b** in 20 ml of thionyl chloride with cooling in a cold-water bath. The resulting solution was stirred at 25° for 16 hr; the nmr spectrum is summarized in Table II. After refluxing for 1 hr, the nmr spectrum indicated the presence of 0.0050 mol of **5b** (aryl, broad singlet, δ 7.18, 8 H; methylene, s, δ 3.87, 2 H) and 0.0210 mol of **9** (same data as given above in preparation of **5a**). After the excess thionyl chloride was removed *in vacuo*, the solid residue was triturated with methanol and then recrystallized from chloroform–methanol. The isolated yield of **5b** was 1.61 g (65%), mp 225–226°. The infrared spectrum of this material was superimposable on that of a sample of **5b** prepared from 4,4′-diaminodiphenylmethane and 2 mol of dichloromaleic anhydride in acetic acid, both showing strong carbonyl absorption at 1734 cm^{-1}. (This latter sample of **5b** had mp 226–227.5°). The mass spectrum of **5b** showed the expected four-chlorine molecular-ion cluster at *m/e* 494–502.

Anal. Calcd for $C_{21}H_{10}Cl_4N_2O_4$: C, 50.84; H, 2.03; N, 5.65; Cl, 28.59. Found: C, 51.03; H, 2.10; N, 5.62; Cl, 28.7.

Conversion of 4,4′-Diaminodiphenyl Ether Bismaleimide (4c) to 4,4′-Diaminodiphenyl Ether Bisdichloromaleimide (5c).—This was carried out as described for **4b** to **5b** above. The nmr data after 1 hr of reaction are summarized in Table II. After recrystallization, there was obtained a 60% yield of **5c**, mp 260–261.5°. The infrared spectrum of this material was identical with that of **5c** obtained from 4,4′-diaminodiphenyl ether and dichloromaleic anhydride; both showed strong carbonyl absorption at 1733 cm^{-1}. (The latter sample of **5c** had mp 260.5–261.5°.) The mass spectrum of **5c** showed the expected four-chlorine molecular-ion cluster at *m/e* 496–504.

Anal. Calcd for $C_{20}H_8Cl_4N_2O_5$: C, 48.2; H, 1.6; N, 5.6; Cl, 28.5. Found: C, 48.5; H, 1.6; N, 5.9; Cl, 28.7.

Conversion of *N*-Methylmaleimide (2b) to *N*-Methyldichloromaleimide (3b).—A solution of 1.11 g (0.0100 mol) of **2b** in 20 ml of thionyl chloride was stirred in a cold-water bath and 1.66 g (0.0210 mol) of pyridine was added. The system was stirred at ~25° for 1 hr. Its nmr spectrum is partially summarized in Table II. In addition it contains the following: **10**, N-CH$_3$, s, δ 3.05; **2b**, N-CH$_3$, s, δ 2.62. The solution was refluxed for 1 hr and its nmr spectrum then indicated the presence of 0.0087 mol of **3b** (N-CH$_3$, s, δ 2.95) and 0.0185 mol of **9** (same data as given above in the preparation of **5a**). Some impurities were apparent in the N-CH$_3$ region. Removal *in vacuo* of all of the excess thionyl chloride and trituration of the residue with 50% aqueous ethanol gave 0.79 g of **3b**. This was subsequently recrystallized from 50% aqueous ethanol to give 0.36 g (20% isolated yield) of **3b**, mp 81.5–82.5° (lit.[16] mp 85°). In accord with the structure of **3b**, its infrared spectrum contained a very strong carbonyl band at 1720 cm^{-1} (lit.[17] 1720 cm^{-1}), a medium intensity band at 1792 cm^{-1} (lit.[17] 1793 cm^{-1}), and a C=C band at 1621 cm^{-1} (lit.[17] 1620 cm^{-1}). The mass spectrum, as expected, showed a molecular-ion cluster at *m/e* 179 (intensity 100.0), 181 (63.5), and 183 (12.0).

Conversion of Maleimide (2c) to Dichloromaleimide (3c).—While a solution of 1.94 g (0.0200 mol) of **2c** in 40 ml of thionyl chloride was stirred in a cold-water bath, 3.24 g (0.0410 mol) of pyridine was added. Stirring was continued at *ca.* 20° for 15 min and then at reflux for 1 hr. The nmr spectrum of the resulting system showed that **9** (NH, very broad peak, δ 16.6; α, β, and γ protons same as reported above in preparation of **5a**) and probably **3c** (NH, broad peak, δ 11.0) were present in the molar ratio of 0.0410:0.0131, respectively. No peak remained for the vinyl protons of **2c** (see control expt F).

All of the excess thionyl chloride was removed *in vacuo* and, following the subsequent chloroform–water work-up and a chloroform recrystallization, 0.81 g (25% isolated yield) of **3c** was obtained, mp 174–175.5° (lit.[18] mp 174–175°). The infrared spectrum of this product showed very strong bands for N—H at 3215 cm^{-1} and for C=O at 1735 cm^{-1} (lit.[17] 1738 cm^{-1}), a medium intensity C=O band at 1784 cm^{-1} (lit.[17] 1785 cm^{-1}), and a C=C band at 1610 cm^{-1} (lit.[17] 1610 cm^{-1}). As expected for the structure of **3c**, the mass spectrum contained a molecular-ion cluster at *m/e* 165 (intensity 100.0), 167 (62.1), and 169 (12.1)

Conversion of Maleic Anhydride (6) to Dichloromaleic Anhydride (7).—A solution of 9.81 g (0.100 mol) of maleic anhydride in 100 ml of thionyl chloride ($SOCl_2$) was stirred in an ice bath in dry air while 16.22 g (0.205 mol) of pyridine was added dropwise during 12 min. Nmr evidence was obtained for the presence of **17** (α-pyridinium protons, m, δ 9.48–9.72) in spectra recorded *rapidly* at 25–35°. After only 30 min, all of **17** had been destroyed and only **7** and **9** were present. Following the addition, the system was heated to ~75° during 10 min and then cooled. The thionyl chloride was removed *in vacuo* and the solid residue triturated with benzene and filtered. Removal of solvent from the benzene filtrate gave 16.48 g (99% yield) of slightly impure dichloromaleic anhydride (mp 111–116°).

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[16] H. Scharf, F. Korte, H. Seidler, and R. Dittmar, *Ber.*, **98**, 764 (1965).

[17] H. Schmelzer, E. Degener, and H. Holtschmidt, *Tetrahedron Lett.*, 2801 (1967).

[18] V. I. Shevchenko and V. P. Kukhar, *Zh. Obshch. Khim.*, **36**, 735 (1966).

The product was sublimed and then Soxhlet extracted with hexane to give 13.34 g (80%) of pure dichloromaleic anhydride, mp 118–120° (lit.[19] 119°). It was further identified unequivocally by mass spectrometry: molecular-ion two-chlorine cluster at m/e 166–170 and appropriate peaks and chlorine clusters for $M - CO_2$, $M - CO_2 - CO$, $M - CO_2 - Cl$, C_2Cl, C_3O, CCl, and C_2.

Control Experiments. A.—No reaction could be detected (nmr) between **2a** (1.73 g) (vinyl, s, δ 6.83, 2 H; aromatic, m, centered at δ 7.40, 5 H) and thionyl chloride (4 ml) in methylene chloride (20 ml) during 16 hr at 25°.

B.—No reaction could be detected by nmr spectroscopy between **2a** (1.73 g) (vinyl, s, δ 6.75, 2 H; aromatic, m, centered at δ 7.33, 5 H) and thionyl chloride (20 ml) (homogeneous solution) during 19 hr at 25° or 3 hr at reflux (~80°).

C.—No reaction could be detected (nmr) between pyridine (0.87 g) (β protons, m, δ 7.27–7.62, 2 H; γ protons, m, δ 7.62–8.06, 1 H; α protons, m, δ 8.55–8.80, 2 H) and thionyl chloride (20 ml) during 17.5 hr at 25°.[3]

D.—No reaction could be detected (nmr) between pyridine (0.79 g) (α protons, m, δ 8.17–8.44, 2 H) and **2a** (1.73 g) (vinyl, s, δ 6.90, 2 H) in anhydrous dimethyl sulfoxide (20 ml) during 17 hr at 25°.

E.—No reaction could be detected (nmr) between thionyl chloride and **2b**, **4a**, **4b**, **4c**, or **6** during several hours at 25–35°.

F.—The nmr spectrum of **2c** in thionyl chloride (vinyl, d, J = 1.2 Hz, 2 H, coupling with NH; NH, very broad peak, δ 7.90, 1 H) remained unchanged during several hours at 25–35°.

Registry No.—**3a**, 3876-05-9; **5a**, 35740-25-1; **5b**, 35740-26-2; **5c**, 19544-45-7; **8**, 35725-75-8; **8** BF_4, 35740-74-0; **11**, 35740-28-4; $SOCl_2$, 7719-09-7; pyridine, 110-86-1.

Acknowledgments.—The author wishes to thank J. V. Crivello for generous gifts of **4a**, **4b**, and **4c** and Professor D. M. Lemal for copies of infrared and nmr spectra of **16**.

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Dichloromaleimide Chemistry. III. The Reaction of *N*-Aryldichloromaleimide with Phenols. The Preparation and Mass Spectral Rearrangements of *N*-Aryl-3-aryloxy-4-chloromaleimides and *N*-Aryl-3,4-bis(aryloxy)maleimides

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N-Aryldichloromaleimides have been found to react with substituted phenols under basic conditions to give aryloxychloro and/or bisaryloxy substituted maleimides, depending on the base/solvent system employed. A hindered phenol (2,6-dimethylphenol) was observed to undergo some carbon alkylation in its reaction with *N*-phenyldichloromaleimide. The mechanisms of these reactions (and some side reactions) are discussed, as are the ^{13}C nmr and mass spectra of many of the products.

A few examples of the displacement of chloride by nucleophiles in *N*-substituted dichloromaleimides have appeared in the literature in recent years. In the reaction with primary amines,[1] displacement of one chlorine occurred together with transimidation. In all other cases, a chlorine was displaced by a group ($-CN$,[2] $-SO_2R$,[2] $-SR$,[3] and $-NR_3{}^+$[4]) which subsequently facilitated the displacement of the second chlorine, presumably through its ability to stabilize an α-carbanionic center.[5] The reactions of phenols with N-substituted dichloromaleimides have not been reported previously.[6] In this paper we discuss these reactions in detail as well as the mass spectra of the products produced therein.

Results and Discussion

When *N*-aryldichloromaleimides **1a–h** were treated with phenols in the presence of base, a facile reaction ensued which led first to *N*-aryl-3-aryloxy-4-chloromaleimides (**2**) and then to *N*-aryl-3,4-bis(aryloxy)maleimides (**3**). In certain base/solvent systems this condensation could be carried out to give only **2** with total exclusion of further reaction. For example, when a methylene chloride solution of *N*-phenyl-3,4-dichloromaleimide **1d** (1 mol), 4-methylphenol (4 mol), and triethylamine (3 mol) was stirred at *ca.* 25° for 2 hr, the only product formed in >99% yield was *N*-phenyl-3-(4-methylphenoxy)-4-chloromaleimide **2dj**; no detectable amount of *N*-phenyl-3,4-bis(4-methylphenoxy)maleimide **3dj** was formed. Similarly, a 1:1 mixture of **1d** and 4-methylphenol in methylene chloride in the presence of an excess of potassium carbonate gave only **2dj**.

Most of the *N*-aryl-3-aryloxy-4-chloromaleimides (**2**) (see the first column of Table II) were prepared under similar reaction conditions (see Experimental Section) and were not contaminated with any other products. A few (**2bk**, **2dp**, **2gj**, and **2hp**) were prepared using K_2CO_3 or Na_2CO_3 in *N,N*-dimethylformamide (DMF); side reactions (*vide infra*) were minimized by appropriately limiting the reaction times in these

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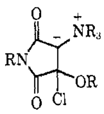
[3] (a) K. Fickentscher, *Tetrahedron Lett.*, 4273 (1969); (b) P. Dimroth and F. Reicheneder, *Angew. Chem., Int. Ed. Engl.*, **8**, 751 (1969).

[4] M. J. Karten, S. L. Shapiro, E. S. Isaacs, and L. Freedman, *J. Org. Chem.*, **30**, 2657 (1965).

[5] For example, a probable structure for one intermediate in the reactions of Karten, *et al.*,[4] is i.



i

[6] Brief mention, with no experimental details, was made[2] of a reaction which takes place between phenols, *N*-phenyldichloromaleimide, and presumably sodium cyanide.