[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY, THE UNIVERSITY OF CHICAGO]

# The "Isomerism" of N-Substituted Maleimides

BY WILLIAM R. RODERICK[1]

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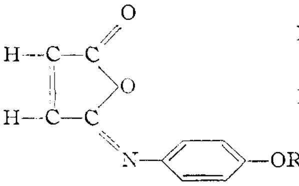
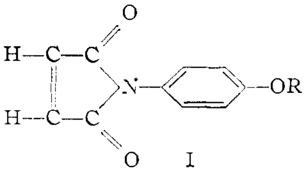
N-(*p*-Methoxyphenyl)-maleimide and N-(*p*-ethoxyphenyl)-maleimide have been prepared by dehydration of the corresponding maleamic acids with phosphorus pentoxide and with acetic anhydride, the former imide also by vigorous dehydration with acetyl chloride. These imides are both yellow, and the normal or symmetrical structure is indicated. The compounds designated in the literature as the corresponding white unsymmetrical maleimides have been shown to be $\alpha$-chloro-N-(*p*-methoxyphenyl)-succinimide and $\alpha$-chloro-N-(*p*-ethoxyphenyl)-succinimide, respectively. Both have been prepared by addition of hydrogen chloride to the respective maleimides, the former also by dehydration of the maleamic acid with acetyl chloride. Attempts to prepare N-(*p*-ethoxyphenyl)- and N-(*p*-nitrophenyl)-isomaleimides were unsuccessful.

Flett and Gardner state that the existence of the maleimides in both a symmetrical and unsymmetrical form has been shown clearly only in the case of the alkoxy-phenyl derivatives.[2] Piutti[3] prepared N-(*p*-methoxyphenyl)-maleimide and N-(*p*-ethoxyphenyl)-maleimide, each in both a yellow and a white form which he designated as having the symmetrical and unsymmetrical structures I and II, respectively. This assignment was "confirmed" by measurement of their absorption spectra in the visible region (2000–6500 Å.), in which the spectra showed the expected difference.[4]



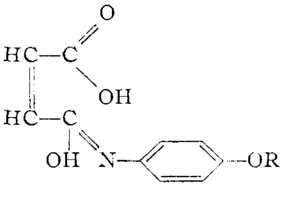
II



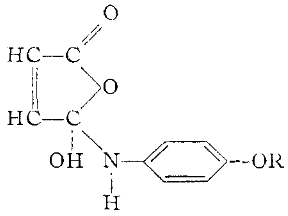
I

The yellow (symmetrical) compound was obtained by Piutti by dehydration of the maleamic acid with phosphorus pentoxide; the white compound (designated by Piutti as the unsymmetrical form) was obtained by dehydration with acetyl chloride, a method previously employed in the preparation of the isophthalimides.[5] Because of discrepancies between this reported isomerism and that obtaining in the case of the phthalimides, and also because it was anticipated that the infrared absorption spectra in the carbonyl region would probably be sufficient to enable structural assignments, it was decided to repeat Piutti's work.

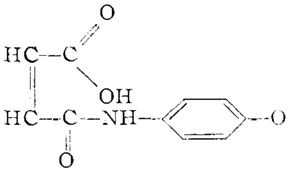
The N-(*p*-methoxyphenyl)-maleamic acid had been reported to give a violet color with ferric chloride, this being interpreted as evidence for an enolic structure IIIa or IIIb for the acid.[6] It was found that neither the crude nor recrystallized acid gives a color with ferric chloride, but that on boiling in aqueous ethanol for one minute, the acid is hydrolyzed to a certain extent, and the *p*-anisidine thus liberated is responsible for the violet color with ferric chloride. The acid may, therefore, be assumed to have the usual amic structure IV.



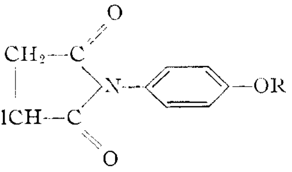
IIIa



IIIb



IV



V

Dehydration of the N-(*p*-methoxyphenyl)-maleamic acid (IV, R = $CH_3$) with phosphorus pentoxide in toluene gave a yellow compound; gentle heating of the acid with acetyl chloride in acetone gave a white compound. On strong heating of the acid with acetyl chloride, a yellow compound identical with that from the phosphorus pentoxide dehydration was obtained. However, the infrared absorption spectra, while showing some differences, were identical in the carbonyl region; since the spectra of the phthalimides and isophthalimides are significantly different in this region,[7] this identity was interpreted as evidence for the same type of imide linkage in both the yellow and white compounds.

Characterization of these compounds then revealed that the white dehydration product does not decolorize aqueous permanganate and that it contains halogen, thus indicating addition of hydrogen chloride to the double bond of the maleimide to form $\alpha$-chloro-N-(*p*-methoxyphenyl)-succinimide (V, R = $CH_3$). The literature reports a similar addition of hydrogen chloride during the preparation of maleanil by dehydration with acetyl chlo-

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(1) Standard Oil Foundation (Indiana) Fellow, 1955–1956.

(2) L. H. Flett and W. H. Gardner, "Maleic Anhydride Derivatives," John Wiley and Sons, Inc., New York, N. Y., 1952, p. 108.

(3) A. Piutti, *Atti. reale accad. Lincei, Classe sci. fis. mat. e nat.*, [5] **18**, II, 312 (1909); *C. A.*, **4**, 2451 (1910).

(4) A. Piutti and E. de'Conno, *Mem. reale accad. Lincei, Classe sci. fis. mat. e nat.*, [5] **8**, 793 (1911).

(5) (a) S. Hoogewerff and W. A. van Dorp, *Rec. trav. chim.*, **13**, 93 (1895); (b) *cf.* M. L. Sherrill, F. L. Schaeffer and E. P. Shoyer, THIS JOURNAL, **50**, 474 (1928).

(6) A. Piutti, *Atti. reale accad. Lincei, Classe sci. fis. mat. e nat.*, [5] **17**, I, 635 (1908); *C. A.*, **3**, 2939 (1909).

(7) (a) W. G. Brown and W. R. Roderick, unpublished; (*b*) private communication from L. Carpino.

ride[8] and with phosphorus oxychloride,[9] and during the preparation of various maleimides using phosphorus pentachloride and thionyl chloride.[10]

To confirm these findings, the white product was carefully hydrolyzed with dilute aqueous alkali to give a pale yellow acid, m.p. 320°, containing nitrogen and halogen. (Piutti had reported that in one instance hydrolysis of the white imide gave, on acidification, a white acid which soon turned yellow.) The N-(*p*-methoxyphenyl)-maleimide was prepared by dehydration of the maleamic acid with acetic anhydride containing potassium acetate,[11] the yellow maleimide so obtained being identical in physical properties and infrared spectrum with the compound prepared by phosphorus pentoxide and vigorous acetyl chloride dehydrations. Hydrogen chloride was added to the yellow maleimide dissolved in glacial acetic acid, yielding white $\alpha$-chloro-N-(*p*-methoxyphenyl)-succinimide, identical in physical properties and infrared spectrum with the compound obtained by gentle acetyl chloride dehydration.

Several facts offer strong evidence for the symmetrical structure (I) for the yellow maleimide and consequently also for the $\alpha$-chlorosuccinimide: (1) The infrared absorption spectra of the maleimides are similar to those of the phthalimides in possessing a broad intense band at 1700 cm.$^{-1}$ (1715 for the $\alpha$-chlorosuccinimides) with a smaller band at 1780 cm.$^{-1}$; the two carbonyl frequencies of the isophthalimides appear with approximately equal intensity and width. (2) The isophthalimides are quite unstable and easily convert to the phthalimides[5]; the maleimides are stable. (3) The isophthalimides are basic[5] (phthalimides are not), easily forming hydrochlorides; the maleimides are not basic.

Attempts were made to convert the N-(*p*-ethoxyphenyl)- and N-(*p*-nitrophenyl)-maleamic acids into the corresponding isomaleimides *via* the method of Hoogewerff and van Dorp.[5] In each instance unreacted acid was recovered. With the former a yellow compound was obtained, m.p. 160.0–160.5° (cor.), which decolorized aqueous permanganate; the infrared spectrum showed bands at 3280 and 1553 cm.$^{-1}$ (N–H) and 1605 cm.$^{-1}$ (amide C=O). These facts are consistent with the structure N,N′-bis-(*p*-ethoxyphenyl)-maleamide. From the latter attempt, two different substances were obtained with infrared spectra different from that of the imide and that expected for the isoimide; they were not further characterized. While this inability to prepare isomaleimides by the method of Hoogewerff, van Dorp and Piutti appears to indicate that they cannot be prepared by this method, in one case a different method has been successful. N-(4-Hydroxy-1-naphthyl)-isomaleimide has been reported as being obtained by dehydration of the maleamic acid with trifluoroacetic anhydride.[12]

The action of alcoholic alkali on the $\alpha$-chloro-N-(*p*-alkoxyphenyl)-succinimides to give a transient pink color has been studied briefly under the assumption that it could be more easily explained now than under the misconception that it involved an unsymmetrical maleimide. The red color is not formed on aqueous hydrolysis. Interestingly, the N-alkyl maleimides have also been reported to give a red color with alcoholic alkali, and tests made with N-ethyl-[13] and N-isobutylmaleimides confirmed this. The color differs in being a very bright red and in persisting for a much longer time (up to 24 hours in a solution of sodium ethoxide in absolute ethanol at room temperature.) Maleanil also gives a red color while N-(*p*-nitrophenyl)-maleimide gives a yellow color; the N-(*p*-alkoxyphenyl)-maleimides give no color. The explanation for these various color formations presents a problem, the further study of which has not been attempted.

The ultraviolet absorption spectra of the maleimides have been measured in isoöctane and are given in Table I.

TABLE I

| N-Substituent | λ, max, mμ | ε |
|---|---|---|
| Isobutyl | <220 | (λ = 220, 9500) |
| | 295 | 700 |
| Phenyl | <220 | (λ = 220, 19,000) |
| | 320 | 490 |
| *p*-Methoxyphenyl | 223 | 25,000 |
| | 275 | 910 |
| | 345 | 220 |
| *p*-Ethoxyphenyl | 223 | 44,800 |
| | 275 | 1380 |
| | 345 | 340 |
| *p*-Nitrophenyl | ≪220 | (λ = 220, 6900) |
| | 275 | 5780 |

**Acknowledgment.**—The helpful comments and criticism of Professor W. G. Brown are sincerely appreciated.

## Experimental

All m.p.'s reported are corrected.

**N-(*p*-Methoxyphenyl)-maleimide. A.**—A suspension of 2.0 g. (0.009 mole) of N-(*p*-methoxyphenyl)-maleamic acid[3,14] and approximately 12 g. of phosphorus pentoxide in 70 ml. of toluene was refluxed 3 hr. The hot toluene solution was decanted and evaporated, leaving 0.4 g. (20%) of orange-yellow needles. Recrystallization from ethanol gave pale yellow needles, m.p. 150–151° (lit. 148.5°,[3] 148°[10]).

**B.**—To a suspension of 3.0 g. (0.013 mole) of the maleamic acid in 27 ml. of dry acetone, 9 g. (0.12 mole) of acetyl chloride was added. The mixture was vigorously refluxed (flame heated) 30 minutes to effect complete solution and then evaporated to dryness on a hot-plate. The viscous brown residue solidified after a few hours and on reduced pressure sublimation yielded a few mg. of yellow sublimate. Recrystallization from ethanol gave long bright-yellow needles, m.p. 148.0–148.5°.

**C.**—A mixture of 2.0 g. (0.009 mole) of the maleamic acid, 3.1 g. (0.03 mole) of acetic anhydride and 0.49 g. (0.005 mole) of fused potassium acetate was heated with stirring to 80°. The clear orange solution was maintained at 80–100° for a few minutes, then cooled to room temperature and water added. The yellow crystals were filtered off, washed

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[8] (a) E. Giustiniani, *Gazz. chim. ital.*, **28**, II, 191 (1898); (b) K. von Auwers, *Ann.*, **309**, 347 (1899).

[9] S. Hoogewerff and W. A. van Dorp, *Rec. trav. chim.*, **17**, 197 (1898).

[10] A. E. Kretov and N. E. Kul'chitskaya, *Zhur. Obshchei Khim.*, **26**, 208 (1956).

[11] (a) N. E. Searle, U. S. Patent 2,444,536 (1948); *C. A.*, **42**, 7340 (1948); (b) H. W. Arnold and N. E. Searle, U. S. Patent 2,462,835 (1949); *C. A.*, **43**, 4421 (1949).

[12] K. C. Tsou, R. J. Barrnett and A. M. Seligman, THIS JOURNAL, **77**, 4613 (1955).

[13] D. H. Marrian, *J. Chem. Soc.*, 1515 (1949).

[14] C. D. Hurd, A. S. Roe and J. W. Williams, *J. Org. Chem.*, **2**, 314 (1937).

with aqueous sodium bicarbonate and water. Recrystallization from ethanol gave 0.9 g. (50%) of yellow plates. Part was decolorized with Norite, giving lighter yellow, long needles, m.p. 149–150°.

**α-Chloro-N-(*p*-methoxyphenyl)-succinimide. A.**—To a suspension of 2.0 g. (0.009 mole) of the maleamic acid in 18 ml. of dry acetone, 5.5 g. (0.07 mole) of acetyl chloride was added. The mixture was refluxed gently on a steam-bath for 30 minutes to effect complete solution, after which the condenser was removed and heating continued while a stream of air was directed into the flask. The tan-yellow residue was washed with a few ml. of cold ethanol, and the off-white residue recrystallized from ethanol twice, giving 0.5 g. (30%) of fine, colorless needles, m.p. 144–145.5° (lit. 145–146°,[8] 142–143°[10]).

*Anal.*[15] Calcd. for $C_{11}H_{10}O_3NCl$: C, 55.12; H, 4.21; Cl, 14.80. Found: C, 55.26; H, 4.04; Cl, 14.62.

**B.**—A solution of 53 mg. of N-(*p*-methoxyphenyl)-maleimide in 2 ml. of glacial acetic acid was cooled in an ice-bath while moist hydrogen chloride, obtained by heating concentrated hydrochloric acid, was bubbled in for about 15 minutes. The solution then was warmed slowly to 80° in a water-bath. On pouring into water, a white precipitate formed and was filtered off, washed with aqueous sodium bicarbonate and with water. Recrystallization from ethanol gave 25 mg. (40%) of colorless needles, m.p. 145–147°, not depressed on mixing with the compound prepared with acetyl chloride in A.

**Other Maleimides and Chlorosuccinimides.**—The experimental procedures were similar to those described for the N-(*p*-methoxyphenyl) derivatives.

| Compound | Yield, % | Color | M.p., °C. Obsd. | Lit. |
|---|---|---|---|---|
| N-(*p*-Ethoxyphenyl)-maleimide | 75 | Yellow | 133.5–134.5 | 134–135[3,16] |
| N-Phenylmaleimide | 46 | Yellow | 89.5–90 | 90–91[11] |
| N-(*p*-Nitrophenyl)-maleimide | 58 | Off-white | 162–165 | 167–168[11] |
| α-Chloro-N-(*p*-ethoxyphenyl)-succinimide | .. | Colorless | 125–127 | 127,[8] 125[10] |

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[15] For the α-chlorosuccinimides, Piutti reported molecular weights larger than calculated for maleimides. Moreover, because low values of 56% C were obtained in several analyses of the α-chloro-N-(*p*-ethoxyphenyl)-succinimide (*i.e.*, low assuming a maleimide structure), he hydrogenated it to the succinimide (apparently the α-chlorine is easily hydrogenolyzed) for which a correct analysis was obtained.

[16] Searle (reference 11) has reported a m.p. of 75° which could not be reproduced.

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[CONTRIBUTION FROM ROHM AND HAAS CO., REDSTONE ARSENAL RESEARCH DIVISION]

# The Reaction of Dinitrogen Tetroxide with Acetylenes[1]

BY JEREMIAH P. FREEMAN AND WILLIAM D. EMMONS

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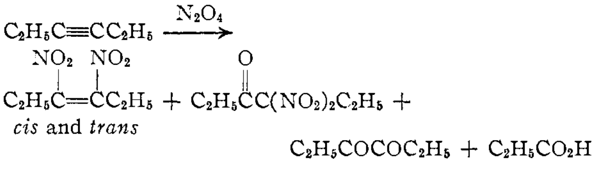
The addition of dinitrogen tetroxide to dialkylacetylenes has been effected; the products isolated were the corresponding *cis*- and *trans*-dinitroölefins, an α-diketone and an α,α-dinitroketone. The stereochemistry of the dinitroölefins and possible mechanisms for these reactions are discussed.

Although much is known about the reaction of dinitrogen tetroxide with olefinic compounds,[2] relatively little study has been made of its reaction with acetylenes. Most of the work on acetylenes has been done with tolane[3–5] where the products have been identified as the *cis*- and *trans*-dinitrostilbenes and 5-nitro-2-phenylisatogen. Wieland also has reported addition to phenylacetylene and phenylpropiolic acid, but the structures of these rather unstable products were not proven rigorously.[4] Very recently the reaction of dinitrogen tetroxide with 2-butyne was reported.[6] Only one compound was isolated and it was assigned the *trans*-2,3-dinitro-2-butene structure on rather tenuous grounds. As this work has a direct bearing on that reported herein, it will be considered later.

In general it was found that the product mixtures from these reactions were rather unstable and frequently decomposed during the fractional distillations required to purify them. As the 3-hexyne reaction mixture proved to be relatively more stable than that from other acetylenes, most of the work was carried out with this compound. It was found that the reaction is much more complex than a simple addition to produce dinitroolefins, and the instability of the mixtures is apparently due to the formation of minor reactive products. In all, five components of the mixture obtained from dinitrogen tetroxide and 3-hexyne were identified; these included propionic acid (6%), dipropionyl (16%), *cis*- and *trans*-3,4-dinitro-3-hexene (4.5 and 31%, respectively) and 4,4-dinitro-3-hexanone (I) (8%). The structure of the dinitroketone, one of a rare group of compounds,[7] was established by degradation evidence and infrared analysis. Upon treatment with methanolic potassium hydroxide, the ketone was cleaved to produce potassium 1-nitro-2-propylnitronate and presumably potassium propionate. When the ketone was heated with aniline, it was cleaved to N-phenylpropionamide and the aniline salt of dinitropropane (not isolated). The infrared spectrum of the dinitroketone had a strong band at



$$C_2H_5C{\equiv}CC_2H_5 \xrightarrow{N_2O_4} \underset{cis\text{ and }trans}{C_2H_5\overset{NO_2}{\overset{|}{C}}{=}\overset{NO_2}{\overset{|}{C}}C_2H_5} + C_2H_5\overset{O}{\overset{\|}{C}}C(NO_2)_2C_2H_5 + C_2H_5COCOC_2H_5 + C_2H_5CO_2H$$

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[1] This research was carried out under Army Ordnance Contract W-01-021-ORD-334.

[2] (a) N. Levy and J. D. Rose, *Quart. Revs.*, **1**, 358 (1948); (b) H. Shechter and F. Conrad, THIS JOURNAL, **75**, 5610 (1953).

[3] J. Schmidt, *Ber.*, **34**, 619 (1901).

[4] H. Wieland and E. Blumlich, *Ann.*, **424**, 100 (1921).

[5] K. N. Campbell, J. Shavel, Jr., and B. K. Campbell, THIS JOURNAL, **75**, 2400 (1953).

[6] H. H. Schlubach and W. Rott, *Ann.*, **594**, 59 (1955).

[7] Dinitroketones of this type have previously been reported by M. Fileti and G. Ponzio [*J. prakt. Chem.*, **55**, 186 (1897)]. They obtained two of these compounds by the action of nitric acid on ethyl isopropyl and ethyl isobutyl ketones. Hydrolysis provided dinitroethane establishing the position of the nitro groups on the methylene group of the ethyl radical. We are indebted to the referee for pointing out this reference.