the product dissolved in 500 ml. of ether and extracted with 500 ml. of 1*N* hydrochloric acid. The 3-dimethylamino-5-pentylphenol was precipitated by adding sodium bicarbonate, extracted with ether, washed with water, and distilled to yield 20 g. (50% yield), b.p. 141–145° at 0.2 mm.

Anal. Calcd. for $C_{13}H_{21}ON$: C, 75.3; H, 10.2; N, 6.76. Found: C, 74.9; H, 9.9; N, 6.5.

Attempted condensation of 3-dimethylamino-5-pentylphenol with ethyl 5-methylcyclohexanone-2-carboxylate. When a solution of 18 g. (0.1 mole) of 3-dimethylamino-5-pentylphenol, 20.2 g. (0.11 mole) of ethyl 5-methylcyclohexanone-2-carboxylate and 14 g. (0.1 mole) of anhydrous zinc chloride in 40 ml. of ethanol was refluxed for 20 hr., the starting materials were recovered unchanged. If the same ratio of reactants was heated for 7 hr. in an oil bath at 110° in the absence of a solvent, the resulting product after removal of the zinc chloride gave only starting material and a nondistillable residue.

Acknowledgment The authors are indebted to R. E. Benson, D. D. Campbell, and R. J. Patten for their assistance in the preparative work.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, FACULTY OF SCIENCE, CAIRO UNIVERSITY]

On the Reactivity of the Unsaturated System in *N*-Arylmaleimides

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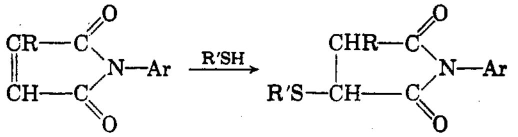
The unsaturated system in *N*-arylmaleimides (I) undergoes addition reactions with aromatic thiols and with piperidine to give the adducts (IIa–b) and (IIIa–d and IV) respectively. Similarly, addition of aromatic hydrocarbons takes place to the C=C bond in Ia–b in the presence of aluminum chloride, without opening of the hetero-ring, to yield the products Va–h, thus establishing an easy method for the preparation of substituted *N*-arylsuccinimides.

N-Arylmaleimides add a number of reagents to give substituted derivatives of *N*-arylsuccinimides. Thus, addition products are obtained with diazoalkanes[1,2] and with arylazides,[1] and they function as dienophiles in the Diels-Alder synthesis.[3]

In conjunction with a study of the pharmacological action of sulfur-containing compounds against *Belharziasis* snails, Mustafa and coworkers[4] have recently described a number of new β-nitrosulfides, prepared by the addition of aromatic thiols to ω-nitrostyrenes in the presence or absence of piperidine. We now have extended our study to the addition of aromatic thiols, *e.g.*, thiophenol and *p*-thiocresol, to *N*-phenylmaleimide (Ia) to obtain the sulfides needed for the pharmacological investigation.[4]



Ia. Ar = C_6H_5; R = H
b. Ar = $p\text{-}CH_3C_6H_4$; R = H
c. Ar = $p\text{-}CH_3OC_6H_4$; R = H
d. Ar = $p\text{-}C_2H_5OC_6H_4$; R = H
e. Ar = C_6H_5; R = CH_3
IIa. Ar = R' = C_6H_5; R = H
b. Ar = C_6H_5; R' = $p\text{-}CH_3C_6H_4$; R = H

The sulfides (IIa–b) are colorless crystalline products, obtained in good yields, and are believed to have structures like II. The addition of thiols to the double bond in Ia finds analogy with the well established addition of the same reagents to unsaturated compounds.[5,6]

Reaction of N-arylmaleimides with piperidine. We now have also investigated the addition of piperidine to the unsaturated system in *N*-arylmaleimides. Thus, when benzene solutions of Ia–e were treated with piperidine at room temperature, the piperidinium adducts (IIIa–d and IV, respectively) were obtained in good yields.

The piperidinium adducts are sharp melting crystalline compounds and are stable under normal conditions, but decompose to the original components when heated above their melting points.[7]

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(1) A. Mustafa, S. M. A. D. Zayed, and S. Khattab, *J. Am. Chem. Soc.*, **78**, 145 (1956).

(2) *N*-Phenylmaleimide adds diazomethane to give the corresponding pyrazoline derivative, which upon thermal decomposition yields cyclopropane-2,3-(*N*-phenyl)dicarboximide (*cf.* ref. No. 1). The latter compound was erroneously formulated by Gregory and Perkin (T. W. D. Gregory and W. H. Perkin, *J. Chem. Soc.*, 780 (1903) as hexahydropyromellitic acid di(*N*-phenyl)carboximide, and was later corrected by Perkin (W. H. Perkin, *J. Chem. Soc.*, 359 (1905); *Beilstein*, Vol. **21**, 411) as cyclopropane-2,3-(*N*-phenyl)dicarboximide.

(3) *Cf.* A. Mustafa and M. Kamel, *J. Am. Chem. Soc.*, **77**, 1328 (1955), A. Mustafa and M. I. Ali, *J. Org. Chem.*, **21**, 849 (1956); A. Mustafa, M. Kamel, and M. A. Allam, *J. Am. Chem. Soc.*, **78**, 4692 (1956).

(4) The pharmacological results will be published elsewhere.

(5) *Cf.* T. Posner [*Ber.*, **35**, 809 (1902)] and B. H. Nicolet [*J. Am. Chem. Soc.*, 3066 (1931)] in the case of α,β-unsaturated ketones; R. M. Ross and F. W. Raths [*J. Am. Chem. Soc.*, **73**, 129 (1951)] in the case of 1-cyano-1-cyclohexene; and R. M. Ross, H. L. Bushey, and R. J. Rolih [*J. Am. Chem. Soc.*, **73**, 540 (1951)] and R. M. Ross [*J. Am. Chem. Soc.*, **71**, 3458 (1949)] in the case of alkylacrylonitriles.

(6) For the addition of thioglycollic acid to Ia, *cf.* D. H. Marrian, [*J. Chem. Soc.*, 1515 (1949)]. E. Friedmann, D. H. Marrian, and Simon-Reuss [*I. Brit. J. Pharmacol.*, **4**, 105 (1949)].

(7) A. Mustafa, W. Asker, A. F. A. Shalaby, S. A. Khattab, and Z. Selim, *J. Am. Chem. Soc.*, **81**, 6007 (1959).

TABLE I

PIPERIDINIUM ADDUCTS FROM *N*-ARYLMALEIMIDES

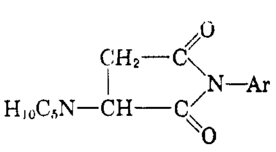
Maleimide Derivatives	Adduct	M.P.[a]	Yield, %	Formula	Carbon, %		Hydrogen, %		Nitrogen, %	
					Calcd.	Found	Calcd.	Found	Calcd.	Found
Ia	IIIa	131	90	$C_{15}H_{18}N_2O_2$	69.76	69.90	6.97	7.10	10.85	10.55
b	b	162	85	$C_{16}H_{20}N_2O_2$	70.58	70.31	7.35	7.55	10.29	10.11
c	c	144	80	$C_{16}H_{20}N_2O_3$	66.66	66.68	6.94	6.89	9.72	9.47
d	d	151	85	$C_{17}H_{22}N_2O_3$	67.54	67.42	7.28	7.19	9.26	9.25
e	IV	119	90	$C_{16}H_{20}N_2O_2$	70.58	70.15	7.35	7.18	10.29	10.25

[a] All melting points are uncorrected.

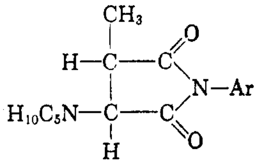
TABLE II

Compound	Solvent[a] of Crystallization	M.P.[b]	Yield, %	Formula	Carbon, %		Hydrogen, %		Nitrogen, %	
					Calcd.	Found	Calcd.	Found	Calcd.	Found
Va	A	140	85	$C_{16}H_{13}NO_2$	76.49	76.48	5.18	5.00	5.57	5.51
b	B	138	68	$C_{17}H_{15}NO_2$	76.98	76.70	5.66	5.59	5.28	5.21
c	B	118	82	$C_{18}H_{17}NO_2$	77.42	77.39	6.09	5.97	5.02	4.96
d	C	144	76	$C_{18}H_{17}NO_4$	69.45	69.41	5.46	5.42	4.50	4.46
e	A	142	85	$C_{17}H_{15}NO_2$	76.98	76.90	5.66	5.61	5.28	5.21
f	B	152	72	$C_{18}H_{17}NO_2$	77.42	77.38	6.09	6.00	5.02	4.99
g	B	145	86	$C_{19}H_{19}NO_2$	77.81	77.78	6.48	6.41	4.77	4.72
h	D	130	75	$C_{19}H_{19}NO_4$	70.15	70.10	5.84	5.78	4.31	4.27

[a] A = mixture of benzene and petroleum-ether (b.p. 80–100°); B = petroleum-ether (b.p. 80–100°); C = methyl alcohol; D = ethyl alcohol. [b] All melting points are uncorrected.



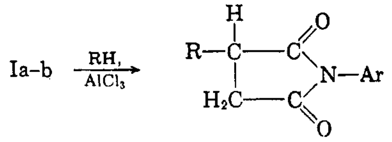
IIIa. Ar = C_6H_5
b. Ar = p-$CH_3C_6H_4$
c. Ar = p-$CH_3OC_6H_4$
d. Ar = p-$C_2H_5OC_6H_4$



IV (or its isomer)

In view of the well established mechanism for the addition of secondary amines, *e.g.*, piperidine to analogous unsaturated compounds,[8] structures III and IV are preferable. The ease of removal of the addend indicates that the substance is the result of simple addition and that no unexpected reaction has occurred.

Reaction of N-arylmaleimides with aromatic hydrocarbons. In connection with another problem, it now becomes of interest to investigate the addition of aromatic hydrocarbons to the unsaturated system in *N*-arylmaleimides. The C=C bond in maleic anhydride, which is analogous to that in Ia–b, undergoes addition reactions with aromatic hydrocarbons having at least one saturated side-chain in the absence of Friedel-Crafts type catalysts to give substituted derivatives of succinic anhydride, *e.g.*, benzylsuccinic anhydride in the case of toluene[9] and with *m*-dimethoxybenzene in the presence of aluminum chloride to give α-(2,4-dimethoxyphenyl)succinic anhydride.[10] When Ia–b were treated with benzene, toluene, *m*-xylene, and/or *m*-dimethoxybenzene, independently, in the presence of aluminum chloride, 3(4)-aryl derivatives of *N*-arylsuccinimides (Va–h) were obtained. Va gave, upon treatment with barium hydroxide, phenylsuccinanilic acid. It was readily transformed to Va by the action of acetyl chloride.



Va. Ar = R = C_6H_5
b. Ar = C_6H_5; R = C_7H_7
c. Ar = C_6H_5; R = C_8H_9
d. Ar = C_6H_5; R = $C_8H_9O_2$
e. Ar = p-$CH_3C_6H_4$; R = C_6H_5
f. Ar = p-$CH_3C_6H_4$; R = C_7H_7
g. Ar = p-$CH_3C_6H_4$; R = C_8H_9
h. Ar = p-$CH_3C_6H_4$; R = $C_8H_9O_2$

EXPERIMENTAL

Reaction with Ia *with:* (a) *Thiophenol.* A mixture of equimolecular amounts of Ia and thiophenol, contained in a dry test tube-shaped vessel, was heated on a steam bath for 4 hr. The cooled reaction mixture was washed several times with hot petroleum ether (b.p. 50–70°) and the resulting solid

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[8] *Cf.* J. Loevenich and H. Gerber [*Ber.*, **63**, 1707 (1930)]; J. Loevenich, J. Koch, and U. Pucknat [*Ber.*, **63**, 636 (1930)]; R. L. Heath and J. D. Rose [*J. Chem. Soc.*, 1486 (1947)]; V. E. Stewart and C. B. Pollard [*J. Am. Chem. Soc.*, **58**, 1980 (1936); **59**, 2702 (1937)]; N. H. Cromwell and J. S. Burch [*J. Am. Chem. Soc.*, **66**, 872 (1944)]; and N. H. Cromwell [*Chem. Revs.*, **38**, 83 (1946)].

[9] G. P. Rice, Ger. Patent **607,380**, Jan. 1935, to I. G.; *Chem. Abstr.*, **29**, 1834 (1935).

[10] G. P. Rice, *J. Am. Chem. Soc.*, **53**, 3153 (1931).

was crystallized from a mixture of benzene and petroleum ether (b.p. 50–70°) to give colorless crystals of IIa, m.p. 144°; yield *ca.* 80%.

Anal. Calcd. for $C_{16}H_{13}NO_2S$: C, 67.84; H, 4.59; N, 4.94; S, 11.30. Found: C, 67.61; H, 4.62; N, 4.91; S, 11.45.

IIa is insoluble in petroleum ether (b.p. 50–70°), but is soluble in hot benzene. It gives no color with concentrated sulfuric acid.

(b) *p-Thiocresol.* The reaction was carried out as mentioned above. The corresponding adduct IIb was obtained as colorless crystals from a mixture of benzene and petroleum ether (b.p. 50–70°), m.p. 135°; yield *ca.* 82%.

Anal. Calcd. for $C_{17}H_{15}NO_2S$: C, 68.68; H, 5.05; N, 4.71; S, 10.77. Found: C, 68.81; H, 5.20; N, 4.81; S, 10.82.

IIb is insoluble in petroleum ether (b.p. 50–70°) but soluble in hot benzene. It gives no color with concentrated sulfuric acid.

Action of piperidine on Ia–e. *General procedure.* A mixture of 0.01 mole of each of Ia–e and 0.01 mole of piperidine in dry benzene (30 ml.) was allowed to stand at room temperature for a few minutes. The yellow color of the benzene solution soon disappeared and, on addition of petroleum ether (b.p. 50–70°), the colorless adducts (listed in TableI) separated. The product was filtered, washed with petroleum ether (b.p. 50–70°), and finally recrystallized from petroleum ether (b.p. 90–120°).

Thermal decomposition of IIIa. IIIa (0.3 g.) was heated in a dry test tube-shaped vessel, at 150° (bath temp.) for 1 hr. The yellow oily residue, left at the bottom of the vessel, solidified, and finally crystallized from petroleum ether (b.p. 50–70°) to give yellow crystals, m.p. 92°, identified as Ia, by melting point and mixed melting point determinations).

Friedel-Crafts reactions with N-arylmaleimides. General procedure. A solution of 0.01 mole of the *N*-arylmaleimide (Ia–b) and 0.015 mole of benzene, toluene, *m*-xylene and/or *m*-dimethoxybenzene in 20 ml. of dry carbon disulfide was stirred and warmed on a water bath, while 1.5 g. of finely powdered aluminum chloride were gradually added. Heating was continued for 6 hr. then the reaction mixture was poured into 40 ml. of dilute hydrochloric acid and heated to remove the carbon disulfide. It was then extracted with benzene, and the extract was dried (sodium sulfate) and evaporated. The oily residue left behind was washed with petroleum ether (b.p. 40–60°) and finally crystallized from the suitable solvent (*cf.* Table III).

The derivatives Va–h were colorless crystalline substances which melted without decomposition and gave no color with sulfuric acid.

Action of barium hydroxide on Va. A suspension of 0.4 g. of Va in 20 ml. of a saturated solution of barium hydroxide was refluxed for 4 hr. The resulting solution was cooled, acidified with ice-cold dilute hydrochloric acid and the precipitate formed was filtered off and crystallized from methyl alcohol, m.p. 169°, not depressed when admixed with an authentic specimen prepared after Hann and Lapworth.[11]

Action of acetyl chloride on phenylsuccinanilic acid. A solution of 0.5 g. of phenylsuccinanilic acid was heated in 5 ml. of acetyl chloride for 2 hr. The reaction mixture was cooled and decomposed with cold water. The precipitate formed was crystallized from methyl alcohol, m.p. 140° not depressed when admixed with Va.

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[11] A. C. O. Hann and A. Lapworth, *J. Chem. Soc.*, **85**, 1365 (1904).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, VANDERBILT UNIVERSITY]

The Swamping Catalyst Effect. III. The Halogenation of Pyridine and Picolines

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3-Chloropyridine and 3-chloro- and 3-bromo-4-picoline have been prepared in 30–40% yields by halogenation of the appropriate pyridine under swamping catalyst conditions. 3,5-Dichloro-4-picoline and 5-bromo-2-picoline have been prepared in lower yields. The above method is the best, if not the only, method of preparing these compounds in the laboratory. Further experiments showed that the maximum yield of halogenated pyridine, based on pyridine, is probably 50%.

The nuclear halogenation of aromatic aldehydes and ketones using large excesses of strong electrophilic reagents such as aluminum chloride has been reported recently.[1] The method has been termed the swamping catalyst effect and so defined as to include those reactions in which at least one equivalent of strong electrophilic reagent is used to complex the substrate material and a second equivalent is used to generate an active attacking species of reagent. The addition of the second equivalent of catalyst is sometimes simply a matter of convenience to accelerate the rate of reaction, but, as will be shown in this paper, it can be essential to the success of the completion of the reaction.

Pyridines are not easily halogenated. To summarize the review by Mosher,[2] substitution of pyridine by bromine or chlorine at 500°, tends to yield 2- or 4-substituted halopyridines- at 300° substitution by bromine yields 3-bromopyridine and some 3,5-dibromopyridine. Evidently the higher temperature favors a free radical rather than an ionic mechanism. The method of choice for synthesis of 3-bromo- or 3,5-dibromopyridine is the pyrolysis of pyridine perbromide hydrobromide at around 200°, the yield being 30–40%.[2] Interestingly enough, the preparation of 3-chloropyridine does not seem feasible by any direct chlo-

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[1] D. E. Pearson, H. W. Pope, W. W. Hargrove, and W. E. Stamper, *J. Org. Chem.*, **23**, 1412 (1958).

[2] H. S. Mosher in R. C. Elderfield, *Heterocyclic Compounds*, Vol. I, p. 504, John Wiley and Sons, New York 1950.