2. Synthetic ephedrine has been resolved into its dextro- and levorotatory antipodes, one of which is identical with the base obtained from the Chinese drug, Ma Huang.

3. The resolution was effected by means of *d*- and *l*-mandelic acid and, conversely, natural *l*-ephedrine lends itself admirably to the preparation of pure *l*-mandelic acid.

NEW HAVEN, CONNECTICUT

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF ZION COLLEGE AND OF THE COLLEGE OF LIBERAL ARTS, NORTHWESTERN UNIVERSITY]

PHENYLISOTHIOCYANATE AND ORTHO-TOLYLISOTHIOCYANATE AS REAGENTS FOR PRIMARY AROMATIC AMINES

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Isothiocyanates (mustard oils) react with primary amines to form substituted thioureas suitable for purposes of identification. They are easily crystallized and have convenient melting points. The two isothiocyanates studied in the present work are readily available. They do not react readily with water or alcohol.

The reactions were carried out in alcohol solution. In some cases they took place spontaneously with the evolution of heat, while in others the mixture had to be heated to induce reaction. Since there were no by-products and since the products crystallized well, they were easily purified to constant melting points by crystallization from alcohol. The yields were almost quantitative.

Phenylhydrazine was also treated with phenylisothiocyanate. It reacted violently with two molecules of the mustard oil.

Hydrazobenzene also reacted with two molecules of mustard oil.

Experimental Part

The substituted thiocarbanilides were prepared by dissolving the calculated amounts of the amine and mustard oil in a convenient quantity of alcohol. From 10 to 50 g. of the amines were used as the thiocarbanilides were desired for another purpose. If no reaction took place in the cold, the contents of the flask were heated to boiling. After gentle boiling for a minute or two, the reaction mixture was allowed to cool. If the product did not separate, even when the wall of the tube was rubbed with a glass rod, the process was repeated until the desired effect was produced. (All of the amines will react in the cold if allowed to stand long enough.) The substituted thiocarbanilide was then filtered off and dissolved in boiling alcohol, filtered while hot and the material separating from the filtrate on cooling was recrystallized again from boiling alcohol. This was usually sufficient to give a sharp melting product. The yields of recrystallized products were 65–80%. The nitrogen content was determined by the Kjeldahl method.

TABLE I

o-TOLYL MUSTARD OIL DERIVATIVES

Amine	Compound	M. p., °C.	Nitrogen, %		Heat required
			Calcd.	Found	
p-Toluidine	$C_{15}H_{16}N_2S$	132	10.9	10.65	–
o-Toluidine	$C_{15}H_{16}N_2S$	158	10.9	10.7	–
m-Toluidine	$C_{15}H_{16}N_2S$	140	10.9	10.5	–
p-Bromo-aniline	$C_{14}H_{13}N_2SBr$	143	8.7	8.75	+
o-Bromo-aniline	$C_{14}H_{13}N_2SBr$	128	8.7	8.8	+
m-Bromo-aniline	$C_{14}H_{13}N_2SBr$	101	8.7	8.65	+
p-Chloro-aniline	$C_{14}H_{13}N_2SCl$	134.5	10.12	10.2	+
o-Chloro-aniline	$C_{14}H_{13}N_2SCl$	140	10.12	10.2	+
m-Chloro-aniline	$C_{14}H_{13}N_2SCl$	124	10.12	10.2	+
p-Iodo-aniline	$C_{14}H_{13}N_2SI$	150	7.6	7.3	+
3-Bromo-4-aminotoluene	$C_{15}H_{15}N_2SBr$	132	8.3	8.2	+
4-Amino-1,3-dimethylbenzene	$C_{16}H_{18}N_2S$	143.5	10.3	10.2	–
2-Amino-5-hydroxytoluene	$C_{15}H_{16}ON_2S$	182.5	10.3	10.3	+
p-Aminophenol	$C_{14}H_{14}ON_2S$	158	10.8	10.7	+
Ammonia	$C_8H_{10}N_2S$	160	16.3	16.71	+
p-Anisidine	$C_{15}H_{16}ON_2S$	138	10.3	10.2	+
o-Anisidine	$C_{15}H_{16}ON_2S$	126	10.3	10.6	+

TABLE II

PHENYL MUSTARD OIL DERIVATIVES

Amine	Compound	M.p., °C.	Nitrogen, %		Heat required
			Calcd.	Found	
p-Toluidine	$C_{14}H_{14}N_2S$	141	11.55	11.6	–
o-Toluidine	$C_{14}H_{14}N_2S$	136	11.55	11.65	–
m-Toluidine	$C_{14}H_{14}N_2S$	94	11.55	11.4	–
p-Bromo-aniline	$C_{13}H_{11}N_2SBr$	148	9.1	9.1	+
o-Bromo-aniline	$C_{13}H_{11}N_2SBr$	146	9.1	9.0	+
m-Bromo-aniline	$C_{13}H_{11}N_2SBr$	97	9.1	9.15	+
p-Chloro-aniline	$C_{13}H_{11}N_2SCl$	152	10.6	10.7	+
o-Chloro-aniline	$C_{13}H_{11}N_2SCl$	156	10.6	10.7	+
m-Chloro-aniline	$C_{13}H_{11}N_2SCl$	116	10.6	10.75	+
p-Iodo-aniline	$C_{13}H_{11}N_2SI$	153	7.9	8.0	+
Phenylhydrazine	$C_{20}H_{18}N_4S_2$	172	14.8	14.7	–
Hydrazobenzene	$C_{26}H_{22}N_4S$	168	12.3	12.0	stand
3-Bromo-4-aminotoluene	$C_{14}H_{13}N_2SBr$	154.5	8.7	8.6	+
4-Amino-1,3-dimethylbenzene	$C_{15}H_{16}N_2S$	133.5	10.93	10.9	–
2-Amino-5-hydroxytoluene	$C_{14}H_{14}ON_2S$	167.5	10.80	10.5	+
p-Aminophenol	$C_{13}H_{12}ON_2S$	150	11.5	11.6	–
Ammonia	$C_7H_8N_2S$	154	18.40	18.3	–

Summary

1. Phenyl mustard oil and *o*-tolyl mustard oil are satisfactory reagents for many primary aromatic amines, forming well-crystallizing and sharply melting thiocarbanilides in good yields.

2. The reagents do not react with water or alcohol, and a determination may be made in their presence.

3. There are no by-products of the reaction.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY, CASE SCHOOL OF APPLIED SCIENCE]

SOME UREAS AND THIOUREAS DERIVED FROM VANILLYLAMINE. RELATIONS BETWEEN CONSTITUTION AND TASTE OF PUNGENT PRINCIPLES

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Capsaicin, the pungent principle of cayenne pepper, and piperin or chavicin, the pungent principle of black pepper, are both acid amides; capsaicin (I) is the vanillyl amide of Δ^6-8-methylnonenic acid; piperin, δ-piperonylvinylacrylopiperidide, is the piperidine amide of piperic acid; spilanthol, the reduction product of the pungent principle of para-cress is *n*-deco*iso*butyl amide.[1]

Since these natural pungent principles are acid amides, it is naturally conceivable that a relation might exist between pungency and the amide structure. The synthesis of a number of more or less closely related amides has indeed shown this relation to exist and has also led to conclusions as to the effect on pungency which accompanies changes in the molecular structure. Thus in compounds similar to capsaicin it has been found that a free phenolic group (preferably in the para position to the side chain) in the amine portion is necessary to produce pungency, that the methoxy group in the meta position exerts a favorable influence toward pungency (aromatic bases resembling aniline when replacing the hydroxy benzylamine bases diminish pungency), that the pungency is a maximum when the acid portion consists of nine to ten carbon atoms and that the pungency is not influenced by the position of the double bond in the acid portion. As to the effect of the presence or absence of un-

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[1] Nelson, THIS JOURNAL, **41**, 1115 (1919); *ibid.*, **41**, 2121 (1919); Nelson and Dawson, *ibid.*, **45**, 2179 (1923); Ott and Eichler, *Ber.*, **55**, 2653 (1922); Ott and Lüdemann, *ibid.*, **57**, 214 (1924); Ott and Zimmermann, *Ann.*, **425**, 314 (1921); Jones and Pyman, *J. Chem. Soc.*, **127**, 2588 (1925); Kobayashi, *Rikagaku Kenkyujo Iho*, **4**, 527 (1925); Kobayashi, *Inst. Phys. Chem. Research* (*Tokyo*), **6**, 166 (1927); Staudinger and Schneider, *Ber.*, **56**, 699 (1923); Staudinger and Müller, *ibid.*, **56**, 711 (1923); Lapworth and Royle, *J. Chem. Soc.*, **115**, 1109 (1919); Asahina and Asano, *J. Pharm. Soc. Japan*, **1922**, 85.