

1-Cinnamoyl-1,2-dihydroquinaldonitrile was prepared from 12 g. of freshly made cinnamoyl chloride in exactly the same manner as the benzoyl compound; needles from alcohol, m. p. 149–150°; yield, 16 g.

Anal. Calcd. for $C_{19}H_{14}ON_2$: C, 79.75; H, 4.93; N, 9.73. Found: C, 79.62; H, 5.02; N, 9.80.

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COMMUNICATIONS TO THE EDITOR

ELECTROPHORETIC ISOLATION OF CONSTITUENTS OF RAGWEED POLLEN EXTRACTS*

Sir:

Dialyzed extracts of giant ragweed pollen were studied with the Tiselius¹ moving boundary technique at approximately pH 7.4 and 1.5°. Employing the Philpot-Svensson² cylindrical lens system to visualize the boundaries, we have found a major constituent which is negatively charged, unpigmented and migrates more slowly than the pigmented constituents. The latter are also negatively charged. The major unpigmented constituent may constitute as much as 75% of the material in fresh extracts when estimated by the criterion of the integration of the Philpot-Svensson curves. Similar Longworth³ diagrams have been obtained. The unpigmented fraction is highly skin reactive in individuals with ragweed hay fever. It may be introduced into the skin by electrophoresis in these cases by the positive pole even though the substance is negatively charged at the pH employed. The electrical mobility of the unpigmented constituent is 0.5×10^{-5} cm. sec.⁻¹ in 0.05 M phosphate buffer at pH 7.0.⁴ Variations have been observed in the pigmented portions of the electrophoretic diagrams and apparently depend on the extent and nature of the dialysis as well as the age and treatment of the pollen grains.

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* This investigation has been aided by a grant from the Josiah Macy, Jr., Foundation.

(1) A. Tiselius, *Trans. Faraday Soc.*, **33**, 524 (1937).

(2) H. Svensson, *Kolloid-Z.*, **87**, 190 (1939).

(3) L. G. Longworth and D. A. MacInnes, *Chem. Rev.*, **24**, 271 (1939).

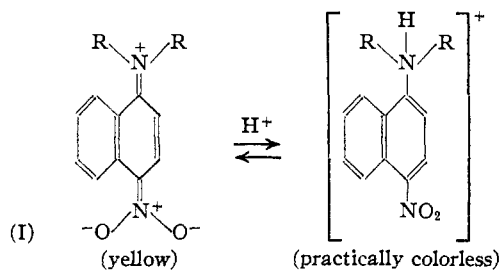
(4) H. A. Abramson, A. Sookne and L. S. Moyer, *J. Allergy*, **10**, 317 (1939); H. A. Abramson and M. H. Gorin, *Chem. Prod.*, **3**, 37 (1940).

THE STERIC INHIBITION OF RESONANCE

Sir:

It has been shown recently¹ that the concept of the steric inhibition of resonance offers an adequate explanation for the differences in acidity observed with trinitrotriphenylmethanes.

Using exactly the same reasoning, we have attacked this problem from a different point of view, *i. e.*, by a consideration of the basic strengths of substituted 4-nitro-1-naphthylamines.



The electron pair of the amino nitrogen atom (upon which depends the basicity of the molecule) is no longer present in the resonance isomer I. If the alkyl groups in I are large, they will inhibit the ability of the group R_2N- and the benzene ring to become coplanar. The result of this must be a diminution in resonance. This reduction in resonance by steric hindrance should result in an increase in the electron density at the amino nitrogen atom and thus lead to an increase in basicity. We have shown that the basicity of the substituted amine (I, $R = CH_3$) is much greater than that of the unsubstituted amine (I, $R = H$) and that this difference is far too great to be explained by an inductive effect of the methyl groups.

The decrease in resonance reduces the polar character of these molecules² and should consequently lower the melting points (if other crystal

(1) Wheland and Danish, *THIS JOURNAL*, **62**, 1125 (1940).

(2) Birtles and Hampson, *J. Chem. Soc.*, 10 (1937).

structure factors remain essentially constant). The values in Table I show that the melting points decrease markedly with increasing size of the alkyl groups.

TABLE I
MELTING POINTS OF VARIOUS ALKYLATED AMINO NITRO
COMPOUNDS

Substance	M. p., °C.
Nitroaminodurene	161
Nitrodimethylaminodurene	90
1-Amino-4-nitronaphthalene	191
1-Methylamino-4-nitronaphthalene	184
1-Ethylamino-4-nitronaphthalene	176
1-Benzylamino-4-nitronaphthalene	156
1-Dimethylamino-4-nitronaphthalene ^a	65
1-Diethylamino-4-nitronaphthalene ^a	Liquid

^a There is no chance for a preferred position of the alkyl groups in this case.

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THE BIOLOGICAL ACTIVITY OF SYNTHETIC PANTOTHENIC ACID

Sir:

The lactone of the "acid fragment" of pantothenic acid has been identified as α -hydroxy- β,β -dimethylbutyrolactone by Stiller, Keresztesy and Finkelstein.¹ The coupling of the synthetic *dl*-lactone with β -alanine in 50% yields, as determined by microbiological assay, and assuming the inactivity of one isomer, has been reported by Weinstock and co-workers.² In the present investigation the yield from the coupling reaction was 88%, and definite evidence was found for the inertness of the unnatural isomer.

When equimolecular amounts of 1 *N* sodium hydroxide, β -alanine and the lactone³ are mixed at 0°, 50% coupling takes place almost immediately as determined by a Sørensen formol titration for free amino nitrogen. Upon standing no further coupling occurs. Instead, the remaining hydroxide ion disappears during the course of an hour, due probably to the saponification of the uncoupled lactone. If instead of equimolecular amounts, the ratio of lactone to β -alanine to 1 *N* sodium hydroxide is made 3:1:1, a 55% coupling occurs immediately, again followed by the disappearance of hydroxide ion. If now to this same

(1) As reported by Williams and Major, *Science*, **91**, 246 (1940).

(2) Weinstock, Arnold, May and Price, *ibid.*, **91**, 411 (1940).

(3) Prepared according to the directions of Kohn and Neustadter, *Monatsh.*, **39**, 295 (1918).

solution an amount of 10 *N* sodium hydroxide equivalent to the amount of free β -alanine remaining is added, 51% of this remainder likewise couples. Upon repetition of the procedure, the % of the remainder of the β -alanine which couples falls off rapidly. The results of a typical experiment are summarized in Table I.

TABLE I

	Milliequivalents of			<i>dl</i> -pantothenic acid	Total % conversion
	β -alanine	hydroxide ion	Lactone		
Present at start	540	540	1680	0	..
Present after 1 hr.	235 ^a	< 1 ^b	..	305 ^c	55
Added at end of 1 hr.	0	235	0	0	..
Present at end of 2 hr.	115 ^a	< 1 ^b	..	425 ^c	79
Added at end of 2 hr.	0	115	0	0	..
Present at end of 3 hr.	78 ^a	< 1 ^b	..	462 ^c	85
Added at end of 3 hr.	0	100	0	0	..
Present at end of 4 hr.	68 ^a	< 1 ^b	..	472 ^c	88

^a By Sørensen formol titration. ^b Acid to phenolphthalein. ^c By difference.

At the end of the experiment, the solution was biologically assayed with chicks,⁴ and found to contain 3,680,000 chick filtrate factor units, corresponding to 36 units per mg. of *dl*-pantothenic acid. Natural pantothenic acid has been stated to contain 71 chick units per mg.⁵ This points to the inactivity of one enantiomorph in the synthetic preparation.

At the same time a mixture of 10 g. of the *dl*-lactone and 7 g. of β -alanine was incorporated in 1000 g. of heated diet and biologically assayed. Slight but definite activity was observed, calculated to correspond roughly to a coupling *in vivo* of 0.06% of the mixture. This indicates that none of the activity of the pantothenic acid solution at the level fed (corresponding to 2.1 mg. of *dl*-pantothenic acid per 100 g. of diet) may be attributed to the presence of unchanged starting materials.

(4) Jukes, *J. Biol. Chem.*, **117**, 11 (1937).

(5) Jukes, *ibid.*, **129**, 225 (1939).

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NAPHTHOQUINONE OXIDES

Sir:

Since 2-methyl-1,4-naphthoquinone oxide can be converted very easily and efficiently [Fieser, *J. Biol. Chem.*, **133**, 391 (1940)] into the isomer phthiocol, it was somewhat surprising to discover