

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 hydroxide ion		Lactone	<i>dl</i> -pan- tothenic acid	Total % con- version
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