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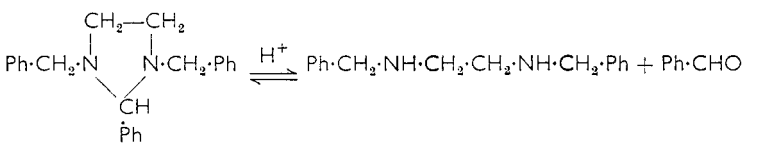
Estimation of 1,3-dibenzyl-2-phenyltetrahydroimidazole in *NN'*-dibenzylethylenediamine diacetate

A. W. ARCHER

A simple spectrophotometric method is described for the estimation of 1,3-dibenzyl-2-phenyltetrahydroimidazole in *NN'*-dibenzylethylenediamine diacetate. The imidazole is quantitatively hydrolysed by dilute sulphuric acid to benzaldehyde and *NN'*-dibenzylethylenediamine; the benzaldehyde is estimated spectrophotometrically after extraction into n-hexane.

THE diamine, *NN'*-dibenzylethylenediamine (II), is used as its diacetate in the preparation of benzathine penicillin (Szabo, Edwards & Bruce, 1951). The diamine is normally obtained by the reduction of *NN'*-dibenzylidene-ethylenediamine (Van Alphen, 1935; Lob, 1936; Szabo & others, 1951); in the course of this reaction some 1,3-dibenzyl-2-phenyltetrahydroimidazole (I) is produced as a by-product (Szabo & others, 1951). This water-insoluble compound is an undesirable impurity as, unless removed, it will be present in the precipitated benzathine penicillin; it was therefore desirable to be able to determine this compound quantitatively.



(I) (II)

Experimental

Lob (1936) reported that (I) was hydrolysed by acids to benzaldehyde and (II). This reaction has been found to be complete within 1 min at room temperature in the presence of dilute sulphuric acid; the resulting benzaldehyde may be extracted with n-hexane and determined spectrophotometrically; *NN'*dibenzylethylenediamine is retained in the acid layer and does not interfere. A sample of (I) was prepared by the method of Van Alphen (Van Alphen, 1935) as a white, microcrystalline solid (m.p. 99°, quoted melting-point 100°; found: C, 83·6; H, 7·4; N, 8·5; calculated for $C_{23}H_{24}N_2$: C, 84·1; H, 7·4; N, 8·5%) and subjected to hydrolysis as described under Procedure; one extraction with an equal volume of n-hexane was sufficient to remove the benzaldehyde produced; a second extract showed negligible absorption at 241 mμ. The results are shown in Table 1.

The ultraviolet spectrum of the material produced by hydrolysis and extracted by hexane was identical to that of benzaldehyde (Analar grade, British Drug Houses, nominal assay: not less than 99%) λ_{max} = 241 mμ,

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$E(1\%, 1\text{ cm}) = 1{,}400$, shoulder at 247 m$\mu$, and different to that of the imidazole, $\lambda_{max} = 248$ mμ, $E(1\%, 1\text{ cm}) = 441$. Hydrolysis and recovery of (I) added to *NN'*dibenzylethylenediamine diacetate were found to be satisfactory, as shown in Table 2.

TABLE 1. HYDROLYSIS OF 1,3-DIBENZYL-2-PHENYLTETRAHYDROIMIDAZOLE

Imidazole, μg	Calculated yield of benzaldehyde, μg	Benzaldehyde found, μg*	Hydrolysis %
50	16·15	16·0	99·4
50	16·15	15·3	95·0
100	32·3	30·7	95·0
100	32·3	30·5	94·4
100	32·3	31·2	96·6
100	32·3	33·1	102·5
100	32·3	31·7	98·1
			Average: 97·3%

* Calculated from $E(1\%, 1\text{ cm})$ of benzaldehyde in n-hexane.

TABLE 2. RECOVERY OF 1,3-DIBENZYL-2-PHENYLTETRAHYDROIMIDAZOLE ADDED TO 200 mg *NN'*-DIBENZYLETHYLENEDIAMINE DIACETATE*

Added μg	Found μg	Recovered μg (corrected for blank)	Recovery %
0	33·0	0	—
50	84·7	51·7	103·4
50	85·1	52·1	104·2
100	132·4	99·4	99·4
100	133·5	100·5	100·5
100	134·3	101·3	101·3
		Average recovery: 101·8%	

* Commercial material recrystallised twice from ethyl acetate.

To avoid very small sample weights for material containing larger quantities of the imidazole, it was necessary to prepare a solution containing about 1 mg of the imidazole and to take a suitable aliquot.

PROCEDURE

Weigh accurately a quantity of sample expected to contain about 1 mg of (I) into a 100 ml volumetric flask and dilute to volume with dilute sulphuric acid (10% v/v). Pipette 10 ml of this solution into a stoppered test-tube (25 ml capacity), add 10 ml n-hexane (spectroscopic grade), shake vigorously for 1 min and allow to separate; measure the extinction of the upper layer in a 1 cm cell at 241 mμ, using hexane as a blank. Determine the $E(1\%, 1\text{ cm})$ of benzaldehyde in n-hexane.

$$\%\ \text{1,3-dibenzyl-2-phenyltetrahydroimidazole} = \frac{100 \times E_{241} \times \text{molecular weight of the imidazole}}{E(1\%, 1\text{ cm}) \text{ of benzaldehyde} \times W \times \text{molecular weight of benzaldehyde}}$$

where W = weight taken in g.

Results

The method was applied to four different batches with the results shown in Table 3.

TABLE 3. RESULTS OBTAINED USING THE PROPOSED METHOD

Batch A	0·0506	0·0509	0·0508	0·0513%	Average 0·0509%
B	0·0369	0·0373	0·0370	0·0371%	0·0370%
C	0·0182	0·0184	0·0177	0·0176%	0·0180%
D	0·0311	0·0319	0·0322	0·0325%	0·0319%

References

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