

333. *Reactions of $\alpha\beta$ -Unsaturated Cyclic Aldehydes and Ketones.
Part I. Their Conversion into Anilines.*

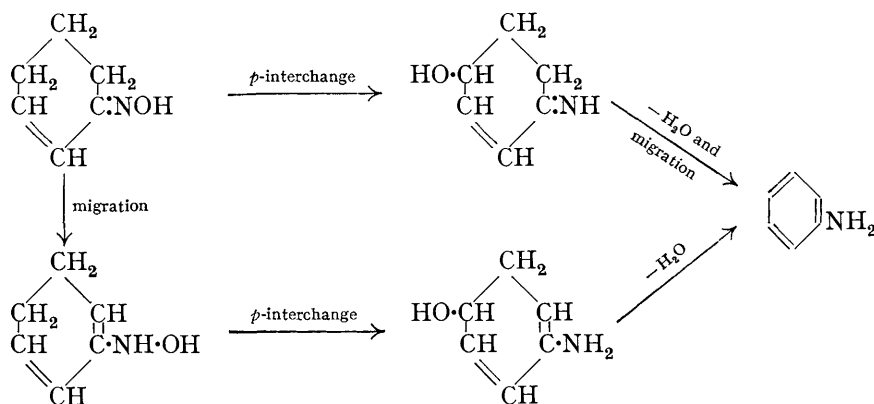
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The product of the action of acetic anhydride on the oxime of *l*-4-isopropyl- Δ^2 -cyclohexen-1-one has been identified as 4-isopropylacetanilide, and the corresponding base has been isolated and identified by means of derivatives. The action is parallel to that described by Kotz and Grethe, who obtained aniline from Δ^2 -cyclohexenone-

oxime. Similar reactions have been found to occur with the oximes of piperitone and carvone, but these are much more stable and the yields of bases are much lower than in the preceding cases.

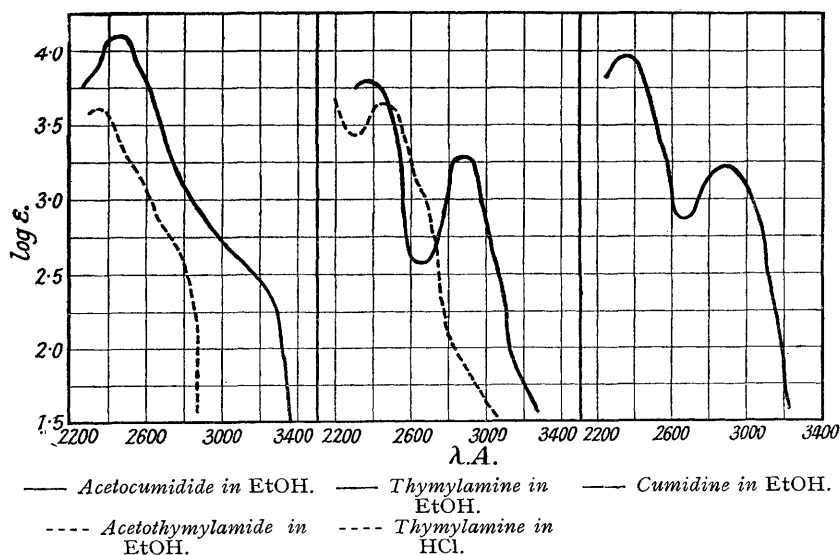
The absorption spectra of cumidine and thymylamine and their acetates have been examined and compared with those previously recorded for simple aromatic bases.

THE action of acetic anhydride on the oxime of 4-isopropyl- Δ^2 -cyclohexen-1-one gives a white crystalline product (Berry, Macbeth, and Swanson, this vol., p. 986) which has now been shown to be 4-isopropylacetanilide. Hydrolysis of the product, followed by steam-distillation, gives the corresponding base, cumidine (I), and the reaction thus finds a parallel in the work of Kotz and Grethe (*J. pr. Chem.*, 1909, **80**, 500), who isolated aniline when the oxime of Δ^2 -cyclohexenone was similarly treated. The mechanism of the reaction proposed by these workers involves *para*-interchange of a hydrogen atom and a hydroxyl group, followed by elimination of water, as formulated below :



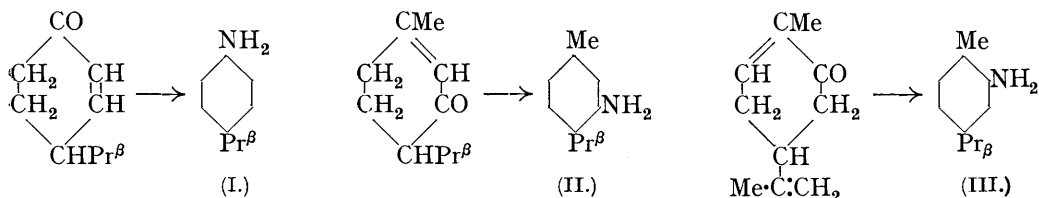
The oximes of piperitone and carvone undergo a similar change, giving rise to the bases thymylamine (II) and carvacrylamine (III) respectively. The reaction with these sub-

FIG. 1.



stances does not, however, proceed as readily as in the case of 4-isopropyl- Δ^2 -cyclohexen-1-one, and the yields of the bases are much lower.

The absorption spectra of the pure bases were examined for comparison with those of the simple bases already recorded. The results are summarised in Table I and shown in



Figs. 1 and 2. Cumidine and thymylamine show the two maxima characteristic of aromatic bases and of similar intensity (aniline : λ_{\max} . 2340 and 2845 A., $\log \epsilon$ 4.06 and 3.24; *p*-toluidine : λ_{\max} . 2357 and 2905 A., $\log \epsilon$ 4.01 and 3.3). The absorption of cumidine in 10% hydrochloric acid closely resembles that of *p*-toluidine in the same solvent, but one of the toluidine bands is represented by an inflexion only in the cumidine curve. In the case of acid solutions of thymylamine similar maxima are recorded, but the $\log \epsilon$ values are higher.

The absorption of acetocumidide resembles that of aceto-*p*-toluidide (λ_{\max} . ca. 2450 A., $\log \epsilon$ 4.28). In the aceto-*o*- and -*m*-toluidides the maxima are somewhat displaced towards shorter wave-lengths and the $\log \epsilon$ values are lower (Morton and McGoekin, J., 1934, 907) : and similar effects are observed in the case of acetothymylamide, in which no substituent is present in the *p*-position to the amino-group.

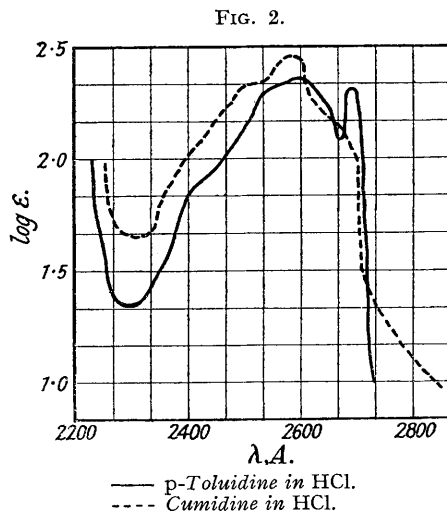


TABLE I.

	In alcohol.				In 10% hydrochloric acid.			
	λ_{\max} , A.	$\log \epsilon$.	λ_{\max} , A.	$\log \epsilon$.	λ_{\max} , A.	$\log \epsilon$.	λ_{\max} , A.	$\log \epsilon$.
Cumidine	2348	3.99	2882	3.23	2585	2.43	ca. 2660	2.19
Thymylamine	2381	3.81	2865	3.27	2451	3.64	ca. 2670	3.08
Acetocumidide	2445	4.12						
Acetothymylamide	ca. 2320	3.63						
<i>p</i> -Toluidine	2357	4.01	2905	3.3	2599	2.36	2688	2.32

Italicised figures represent inflexions.

EXPERIMENTAL.

4-isoPropylacetamide.—The oxime of 4-*isopropyl*- Δ^2 -cyclohexen-1-one (Berry, Macbeth, and Swanson, *loc. cit.*) was refluxed for 4 hours with acetic anhydride (10 parts) and anhydrous sodium acetate. After cooling, the mixture was poured into water, an ethereal extract of the product dried and evaporated, and the residual red-brown oil fractionated under reduced pressure. The high-boiling fraction, 195—210°/25 mm., soon solidified, and after drying on a porous tile yielded white needles, m. p. 103°, on recrystallisation from light petroleum (b. p. 60—80°). The product also separated in glistening leaves, m. p. 102°, from water. It was remarkably stable towards alkalis, and was precipitated unchanged from its solution in concentrated acids on dilution. It was, however, hydrolysed on refluxing with 70% sulphuric acid, and the solution yielded a scarlet dye with β -naphthol after diazotisation. After the addition of sodium hydroxide, a base was recovered from the hydrolysed solution by extraction with ether or by steam-distillation. The base was found to be cumidine (*p*-*isopropylaniline*) and the white crystalline material has been identified as acetocumidide (4-*isopropylacetanilide*) (Found : C, 74.8; H, 8.6; N, 7.9; *M*, 178. Calc. for $C_{11}H_{15}ON$: C, 74.6; H, 8.5; N, 7.9%; *M*, 177).

In further experiments the red-brown oil instead of being fractionated was forthwith sub-

jected to hydrolysis by 70% sulphuric acid (20 mins. refluxing) and, after cooling, the undissolved oil was extracted with ether. The residue was steam-distilled after the addition of sodium hydroxide; cumidine extracted from the distillate, after drying over solid potassium hydroxide, distilled as a clear refractive oil, b. p. 220—222°/765 mm. It gave the isonitrile reaction, formed azo-dyes after diazotisation, gave on treatment with acetyl chloride an acetyl derivative identical with that described above, yielded on benzylation benzocumidide, which crystallised in white woolly needles, m. p. 160°, from alcohol (Found: C, 80.2; H, 7.3. Calc. for $C_{16}H_{17}ON$: C, 80.3; H, 7.1%), and on treatment with saturated aqueous oxalic acid gave an oxalate, m. p. 159° after recrystallisation from water (compare Constam and Goldschmidt, *Ber.*, 1888, 21, 1157; Sachs and Weigert, *Ber.*, 1907, 40, 4360).

Thymylamine from Piperitoneoxime.—Piperitone isolated from *E. Dives* by hot sodium sulphite solution (Read and Smith, *J. Soc. Chem. Ind.*, 1923, 42, 339 τ) had $\alpha_D - 12.5^\circ$ after fractionation under reduced pressure. It was converted into the oxime by 5 hours' refluxing with alcoholic hydroxylamine hydrochloride (1 mol.) and anhydrous sodium acetate. After removal of the greater part of the alcohol the product was steam-distilled; the oxime which collected in the distillate had m. p. 117° after recrystallisation from alcohol (compare Simonsen, *J.*, 1921, 119, 1647).

The oxime (50 g.) was refluxed with acetic anhydride (300 c.c.) and anhydrous sodium acetate for 2 hours, but the resulting oil, worked up in the usual way, did not give a high-boiling fraction which solidified. The total distillates were therefore mixed and subjected to hydrolysis by 70% sulphuric acid. The product, after extraction with ether on cooling, was made strongly alkaline and steam-distilled. A solid which collected was found to be unchanged oxime, which is therefore not only resistant to the action of acetic anhydride, but is also soluble in the acid solution employed for hydrolysis.

When the work was repeated with longer refluxing with acetic anhydride (8 hours), a base was obtained, b. p. 230—234°/765 mm., but some piperitoneoxime still persisted unchanged and separated as a solid towards the end of the steam-distillation. The yield of oil obtained in the best experiments did not equal those experienced in the case of 4-isopropyl- Δ^2 -cyclohexen-1-one. The product gave the reactions of a primary aromatic base, and on treatment with acetyl chloride gave an acetyl derivative which crystallised from water or light petroleum in long silky needles, m. p. 111° (Found: N, 7.35. Calc. for $C_{12}H_{17}ON$: N, 7.3%). The base is therefore thymylamine (3-methyl-6-isopropylaniline) (compare Widman, *Ber.*, 1882, 15, 169).

Thymylamine oxalate was precipitated on addition of a saturated aqueous solution of oxalic acid to the base and obtained in fine white needles, m. p. 169°, on recrystallisation from dilute alcohol (Found: C, 68.2; H, 8.3; N, 7.25. $2C_{10}H_{15}N, H_2C_2O_4$ requires C, 68.0; H, 8.2; N, 7.2%).

Carvacrylamine from Carvoxime.—Carvoxime was best prepared by refluxing carvone (55 g.) with hydroxylamine hydrochloride (28 g.) for 4 hours in alcoholic solution with anhydrous sodium acetate. After removal of the major part of the alcohol and steam-distillation the oxime collected as a solid, which separated in glistening plates (50 g.), m. p. 73°, on recrystallisation from dilute alcohol.

The oxime was refluxed for 8 hours with acetic anhydride (10 parts) and anhydrous sodium acetate; the oil which was precipitated when the mixture was poured into water soon solidified. Part of the solid, recrystallised from water (norit), separated in white needles, m. p. 64°, which after recrystallisation from aqueous acetone gave glistening plates, m. p. 65—66°. It was identified as carvoxime acetate (Found: C, 69.6; H, 8.2; N, 6.8. Calc.: C, 69.6; H, 8.2; N, 6.8%) (compare Rupe, *Annalen*, 1913, 395, 137).

When the major part of the crude solid was submitted to the usual hydrolytic and steam-distillation treatment, only a small quantity of an oily base was obtained. It was identified as carvacrylamine (2-methyl-5-isopropylaniline) by the preparation of its benzoyl derivative, which crystallised from dilute alcohol and then from light petroleum, separated in fine white needles, m. p. 98° (Found: C, 80.3; H, 7.6; N, 5.6. Calc. for $C_{17}H_{19}ON$: C, 80.6; H, 7.5; N, 5.5%). The isopropenyl group becomes saturated in this case as in several other reactions with this oxime.

The large yield of carvoxime acetate shows this oxime to be extremely resistant to the action of acetic anhydride.

A slightly improved yield of the base was obtained in a further experiment in which refluxing with the anhydride was continued for 24 hours, but even under these conditions unchanged carvoxime acetate persisted. The base was further identified by its hydrochloride, obtained in glistening plates, m. p. 210°, and by the *oxalate* (prepared as described in the preceding case), which separated in glistening plates, m. p. 150°, from dilute alcohol (Found: N, 7.25. $2C_{10}H_{15}N, H_2C_2O_4$ requires N, 7.2%).