[CONTRIBUTION FROM THE ORGANIC RESEARCH DEPARTMENT, ABBOTT LABORATORIES]

1-PHENYL-2-TETRALONE AND 1-PHENYL-2-NAPHTHYLAMINE

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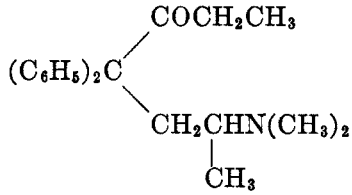
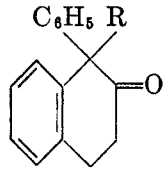
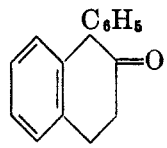
In the structure of the potent analgesic methadon, ring-closure between the propionyl and one of the phenyl groups would result in the β-tetralone structure I (R = 2-dimethylaminopropyl). In the present work attempted synthesis of this type led to the preparation of 1-phenyl-2-tetralone (II) by perbenzoic acid oxidation of 1-phenyl-3,4-dihydronaphthalene.





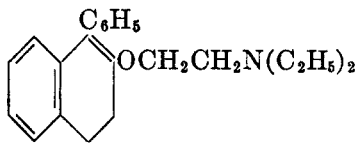
I



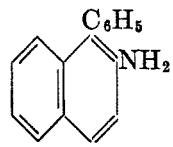
II

Unlike previously reported (1) alkylations of β-tetralones, alkylation of II with diethylaminoethyl chloride, using sodamide as a condensing agent resulted in O-alkylation to give the enol ether III isolated as the acid oxalate, m.p. 155–156°.

Further anomalous behavior in this series was encountered when attempts were made to hydrogenate (in acid solution) the oxime of 1-phenyl-2-tetralone (II) to the corresponding 1-phenyl-1,2,3,4-tetrahydro-2-naphthylamine. Instead of reduction, dehydroisomerization occurred and the sole product isolated was 1-phenyl-2-naphthylamine (IV).



III



IV

The identity of this compound was established by conversion to a diacetylimino derivative and by other properties described in the experimental section. The same product was obtained from the oxime of II by acid treatment in the absence of catalytic reducing conditions as well as by catalytic dehydrogenation. Similar transformations of cyclic oximes have already been noted. The most recent report (2) seems to be that of the acid-catalyzed dehydroisomerization of several substituted thiophanone oximes to the corresponding aminothiophenes. However, the tendency for this type of reaction to take place appears to be unpredictable. In the present work, unsubstituted β-tetralone oxime could not be converted to β-naphthylamine either under the conditions used for the conversion of the oxime of II or by the procedure of Cheney and Piening (2).

EXPERIMENTAL

1-Phenyl-2-tetralone (II). The perbenzoic acid oxidation was an adaptation of the method of English and Cavaglieri (3). To a solution of 24 g. (0.116 mole) of 1-phenyl-3,4-dihydronaphthalene (4) in 200 cc. of chloroform cooled to −10° was added dropwise with stirring a solution of 17.4 g. (0.126 mole) of perbenzoic acid (5) (determined iodometrically) in 485 cc. of chloroform. The temperature was not allowed to rise above −4° and after addition was complete, the mixture was kept in the ice-bath for 2½ hours. Iodometric titration of a sample indicated nearly complete consumption of the perbenzoic acid. The solution was then washed with excess 2 *N* sodium hydroxide and water, and dried over magnesium sulfate. Distillation of the chloroform *in vacuo* gave 27 g. of a viscous oil which could not be crystallized. This oil was then refluxed for 3½ hours with 200 cc. of 30% sulfuric acid, taken up in ether, washed with bicarbonate, and dried. Distillation of the ether gave 26 g. of the viscous oil which still could not be crystallized. It was then fractionally distilled *in vacuo* through a nine-inch helix-packed column. There was obtained 18 g., b.p. 141–142°/0.5 mm. Redistillation of a sample for analysis gave b.p. 156–158°/1 mm., n_D^{24} 1.6089.

Anal. Calc'd for $C_{16}H_{14}O$: C, 86.45; H, 6.34.
Found: C, 86.06; H, 6.30.

Phenylhydrazone, prepared from the ketone in the usual manner, m.p. 146–147.5° (from ethanol-methanol mixture).

Anal. Calc'd for $C_{22}H_{20}N_2$: N, 8.96. Found: N, 9.09.

During the distillation of the phenyltetralone, a solid material came over in the first fraction. Crystallization from 95% ethanol gave a small amount of a compound, m.p. 124–125.5°.

Anal. Calc'd for $C_{16}H_{14}O_2$: C, 80.64; H, 5.91.
Found: C, 80.35, 80.25; H, 5.67, 5.81.

This corresponds to a structure containing one more oxygen atom than the 1-phenyl-2-tetralone. This by-product is very likely one of the two possible isomeric lactones formed by further oxidative rearrangement of ketone (6). Since insufficient material was at hand, the compound was not investigated further.

1-Phenyl-2-tetralone oxime. A mixture of 10 g. of 1-phenyl-2-tetralone, 25 g. of hydroxylamine hydrochloride, 100 cc. of 10% sodium hydroxide, 150 cc. of water, and 200 cc. of 95% ethanol was heated to boiling for ten minutes. Cooling in ice gave 7 g. of crude oxime. Recrystallization from 200 cc. of hot alcohol by the addition of 10 cc. of hot water gave 5 g., m.p. 184–185°.

Anal. Calc'd for $C_{16}H_{15}NO$: C, 80.98; H, 6.37; N, 5.90.
Found: C, 81.01; H, 6.35; N, 5.96.

1-Phenyl-2-naphthylamine (IV) *A. By dehydroisomerization.* A solution of 6 g. of 1-phenyl-2-tetralone oxime in 200 cc. of absolute ethanol containing 2.8 g. of hydrogen chloride was treated with 0.6 g. of 20% palladium on charcoal and shaken with hydrogen at 35 pounds pressure and 55° for 36 hours. No hydrogen uptake was observed. The catalyst was filtered and the filtrate was concentrated *in vacuo* to 25 cc. This solution was treated with 200 cc. of water and 20 cc. of concentrated hydrochloric acid, heated to boiling and filtered from a small amount of insoluble oil. Cooling in ice and filtering gave 4.0 g. of crystalline powder, m.p. 235–236° (dec.). Recrystallization of a sample from ethanol-ether resulted in no change of melting-point.

Anal. Calc'd for $C_{16}H_{14}ClN$: N, 5.48. Found: N, 5.26.

Conversion to the free *base* gave small prisms (from Skellysolve B), m.p. 93–94°.

Anal. Calc'd for $C_{16}H_{13}N$: C, 87.64; H, 5.97; N, 6.39.
Found: C, 87.91; H, 5.90; N, 6.17.

This product could be diazotized and coupled with β-naphthol; with lithium aluminum hydride at 100° in the quantitative apparatus (7) it showed 1.94 active hydrogen atoms per mole of compound. (It is interesting to note that with the Grignard reagent, CH_3MgI, only one active hydrogen atom reacted under the same conditions.)

When the oxime (0.5 g.) was treated in the absence of catalyzed hydrogen with 100 cc. of dry alcohol containing 0.25 g. of hydrogen chloride for 65 hours at 40°, 0.27 g. of 1-phenyl-2-naphthylamine hydrochloride, m.p. 235–236° (dec.), was obtained. It formed a free base identical in every way with that reported above.

B. By catalytic dehydrogenation. A solution of 1.0 g. of the above oxime in 40 cc. of *p*-cymene was refluxed with 0.5 g. of 20% palladium on charcoal for four hours. The catalyst was filtered and the *p*-cymene was removed *in vacuo*. Working up of the residue in the usual way gave a very small amount of a hydrochloride which on conversion to the free base melted at 92–94° after recrystallization from Skellysolve B. When mixed with a sample of 1-phenyl-2-naphthylamine prepared by procedure A, it gave no melting point depression.

1-Phenyl-2-diacetyliminonaphthalene. The naphthylamine (V) (free-base) (0.6 g.) was refluxed for three hours with 7 cc. of acetic anhydride. The excess anhydride was decomposed with water and the residual solid (0.57 g., m.p. 98–102°) was recrystallized several times from Skellysolve B to give fine white needles, m.p. 105–107°.

Anal. Calc'd for $C_{20}H_{17}NO_2$: C, 79.18; H, 5.65; N, 4.62.

Found: C, 79.40; H, 5.85; N, 4.89.

Alkylation of 1-Phenyl-2-tetralone. A solution of 5 g. of 1-phenyl-2-tetralone and 3.9 g. of freshly distilled diethylaminoethyl chloride in 50 cc. of dry toluene was treated with stirring, in a nitrogen atmosphere, with a suspension of sodamide (prepared from 1.13 g. of sodium with liquid ammonia) in 30 cc. of dry toluene. The temperature was maintained below 35° during the addition. Then it was raised to 90° and maintained between 90° and 92° for five hours with continued stirring. After refluxing finally for one hour, the reaction mixture was cooled and extracted with excess dilute hydrochloric acid (1:5). The aqueous solution was then extracted with ether and made alkaline with excess 20% sodium hydroxide. The oil which separated was taken up in ether, washed, and dried over magnesium sulfate. Filtration and distillation of the ether gave 5.1 g. of an orange oil which could not be crystallized. However 6.5 g. of crude oxalate was obtained in solid form. Recrystallization from 40 cc. of absolute ethanol gave 4.0 g. of small shiny leaflets, m.p. 155–156°. Further recrystallizations for analysis did not improve the melting point.

Anal. Calc'd for $C_{22}H_{27}NO \cdot H_2C_2O_4$: C, 70.04; H, 7.10; N, 3.40.

Found: C, 69.93; H, 6.99; N, 3.52.

This product was not stable in warm dilute aqueous acid but decomposed to give a neutral substance; and no water insoluble basic material remained on prolonged heating.

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SUMMARY

1-Phenyl-2-tetralone has been prepared and its alkylation has been attempted. 1-Phenyl-2-tetralone oxime has been found to undergo acid-catalyzed dehydroisomerization to 1-phenyl-2-naphthylamine.

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REFERENCES

(1) BARLTROP, *J. Chem. Soc.*, 958 (1946); SALZER, *Z. physiol. Chem.*, **274**, 39 (1942); U. S. Patent 2,271,674.
(2) CHENEY AND PIENING, *J. Am. Chem. Soc.*, **67**, 729 (1945).
(3) ENGLISH AND CAVAGLIERI, *J. Am. Chem. Soc.*, **65**, 1085 (1943).
(4) WEISS *Org. Syntheses*, **24**, 84 (1944).
(5) BRAUN, *Org. Syntheses*, Coll. Vol. I, 431 (1941).
(6) TURNER, *J. Am. Chem. Soc.*, **72**, 878 (1950).
(7) ZAUGG AND LAUER, *Anal. Chem.*, **20**, 1022 (1948).