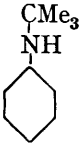
222. *The Preparation of Alkylanilines containing Tertiary Alkyl Groups.*

By W. J. Hickinbottom.

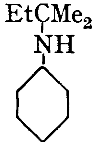
It became necessary, for an investigation on the addition of amines to olefins (Hickinbottom, J., 1932, 2646), to have specimens of alkylanilines containing *tert.*-alkyl groups. The preparation of such compounds from *tert.*-alkyl halides presents serious difficulties; for instance, Nef (*Annalen*, 1899, **309**, 164) prepared *tert.*-butylaniline in this way, but could not obtain pure *tert.*-amylaniline by a similar method.

By a suitable modification of Nef's procedure, it has now been possible to obtain not only *tert.*-butyl- (I) but also tert.*-amyl-* (II) and tert.*-hexyl-aniline* (III) in a state of purity. The yield of each amine is, however, comparatively small, for when a *tert.*-alkyl halide reacts with aniline, the principal product is an olefin. Indeed, this reaction has been found very convenient for the preparation of pure αβ-dimethyl-α-ethylethylene (V) from *tert.*-hexyl iodide.

No examination of the reactions of these alkylanilines has hitherto been made, nor have derivatives of them been previously reported. Each of the amines now described has been characterised by a well-crystallised *hydrochloride*, a *picrate*, and a p*-toluenesulphonyl* derivative. The *nitrosoamines* from *tert.*-butyl- and *tert.*-amyl-aniline are crystalline, but that from *tert.*-hexylaniline is liquid at room temperature. Methyl iodide reacts with *tert.*-butyl- and with *tert.*-hexyl-aniline to furnish the corresponding tertiary amines, although the *tert.*-alkyl group is partially eliminated during the reaction.



(I.)



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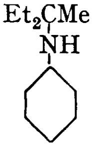
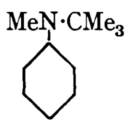
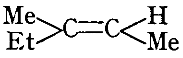


(III.)



(IV.)



$$\begin{matrix}\text{Me}\\ \text{Et}\end{matrix}\!\!>\!C{=}C\!<\!\!\begin{matrix}\text{H}\\ \text{Me}\end{matrix}$$

(V.)

It is noteworthy that both *methyl-*tert.*-butylaniline* (IV) and *methyl-*tert.*-hexylaniline* are indifferent to aqueous solutions of nitrous acid and therefore do not furnish *p*-nitroso-derivatives. Similarly, attempts to obtain such derivatives from the nitrosoamines of the *tert.*-alkylanilines by the Fischer–Hepp reaction were unsuccessful. Instead, the nitroso-group was eliminated, with formation of the hydrochlorides of the *tert.*-alkylanilines. It is already known that the nitrosoamines derived from certain other alkylanilines sometimes fail to give any appreciable amount of the *p*-nitroso-compound by the Fischer–Hepp reaction, but this is stated to be due to the solubility relationships of the hydrochlorides of the secondary amine and the potential *p*-nitrosoamine (O. Fischer, *Ber.*, 1912, **45**, 1099). It is doubtful if such an explanation can be applied to the examples now described, in view of the failure of methyl-*tert.*-butyl- and -hexyl-aniline to yield *p*-nitroso-derivatives. A more probable hypothesis is that, owing to abnormal conditions prevailing at the amino-group, the reactivity of the para-position is reduced. Specific evidence of the abnormality of the *tert.*-alkyl group in these amines will be presented later (see Hickinbottom, *Nature*, 1933, **131**, 762). There are several observations on record which suggest that the reactivity of the amino-group and of the para-position are interdependent; for instance, dimethyl-*o*-toluidine and dimethylamino-*p*-xylene do not readily combine with methyl iodide, nor do they yield *p*-nitroso-derivatives by the action of nitrous acid (von Braun, Arkuszewski, and Köhler, *Ber.*, 1918, **51**, 282). *o*-Chlorodimethylaniline is similarly indifferent to aqueous nitrous acid, and reacts very sluggishly with methyl iodide (Friedländer, *Monatsh.*, 1898, **19**, 625; von Braun, *Ber.*, 1916, **49**, 1101). The low reactivity of the para-position of the amines just cited is also exhibited in reactions with benzaldehyde and formaldehyde, although the regularities are not so striking as with nitrous acid.

It is significant that this low reactivity of the para-position is accompanied by a comparatively low reactivity of the amino-group, in regard to acylation. Reaction with acetic anhydride takes place sufficiently slowly to enable a mixture of aniline and one of these amines to be separated by treating it with an aqueous suspension of acetic anhydride; with care, the aniline is acetylated completely while the alkylaniline can be recovered almost unchanged by adding sodium carbonate. The arylsulphonyl chlorides react with these amines even more sluggishly than acetic anhydride, a mixture of *tert.*-butylaniline and *p*-toluenesulphonyl chloride showing no appreciable reaction in several hours; further, measurements showed that the following proportions of *p*-toluenesulphonyl chloride (1 mol.) had reacted with *tert.*-amylaniline (2 mols.) after definite times at room temperature: 72 hrs., 46%; 120 hrs., 56%; 288 hrs., 77%. On the other hand, 96% of the chloride had reacted with *iso*amylaniline under similar conditions in 2 hours.

Although the reaction between these amines and arylsulphonyl chlorides is so sluggish, it proceeds fairly readily in pyridine solution and this method is the most convenient. Even in this solvent, however, *tert.*-hexylaniline does not readily form a toluenesulphonyl derivative at room temperature, as do its lower homologues, heating being required.

EXPERIMENTAL.

Preparation of tert.-*Butylaniline.*—The following modification of Nef's procedure (*loc. cit.*) was found to be satisfactory. *tert.*-Butyl iodide (37 g.) and aniline (38 g.) were mixed in a 1-l. round-bottomed flask fitted with a reflux condenser. The upper end of the condenser was closed by a cork through which passed a wide tube leading to an aspirator full of water, to serve as a receiver for the gas liberated during the reaction.

There was no obvious sign of reaction for about 6 mins., but then there was a rapidly increasing evolution of gas. The following table records the volume of gas collected after various periods from the initial mixing of the reactants:

t (mins.)	6	14	18	21	22	23	26
Vol. (c.c.)	—	100	200	660	1000	2000	2300

The reaction mixture was shaken continuously during the evolution of the gas; otherwise, this became so violent as to project the product from the flask. The gas liberated in this preparation was identified as *iso*butylene by the formation of its dibromide, b. p. 148—149°.

The addition of aqueous sodium hydroxide to the brownish solid remaining in the flask liberated a mixture of aniline and *tert.*-butylaniline. After the usual treatment, the dried mixture of amines was carefully fractionated to remove some of the excess of aniline. The remainder of the aniline was removed by suspending the mixture in water, and then adding acetic anhydride to the well-stirred suspension till a definite odour of the anhydride persisted after 3 or 4 mins. Excess of sodium carbonate solution was added after several hours, and the *tert.*-butylaniline removed from the mixture by steam distillation. The amine in the distillate was taken up in ether, and the ethereal solution dried and fractionated. Approximately pure *tert.*-butylaniline was collected at 203—206° (uncorr.). The yield from 80 g. of *tert.*-butyl iodide and 81 g. of aniline was 22 g. with 5·5 g. of b. p. up to 203°.

The separation of aniline was effected, in the preliminary experiments, by treatment of the mixture of amines with aqueous zinc chloride (Hickinbottom, J., 1930, 992), followed by extraction of the resultant mass with light petroleum. Although it gave pure *tert.*-butylaniline, this process was more laborious than that described above.

The main fraction of *tert.*-butylaniline, which gave only a faint test for a primary amine, yielded the pure secondary amine after two fractionations under reduced pressure. Alternatively, it was purified through its *hydrochloride* or *picrate*. It is a liquid with a faint straw-yellow tint, b. p. 92·5—93°/19·5 mm., 214—216°/753 mm. (corr.) (Nef gives b. p. 208—210° i.d.) (Found : C, 80·5; H, 10·2. Calc. for $C_{10}H_{15}N$: C, 80·5; H, 10·1%). It has a distinct and not altogether agreeable odour resembling that of aniline and is miscible with most of the common organic solvents. The hydrochloride separates from the dilute aqueous acid as large four-sided tabular crystals; for analysis it was crystallised from ethyl acetate (Found : HCl, 19·6. $C_{10}H_{15}N,HCl$ requires HCl, 19·65%). The *hydrobromide* was obtained as massive tabular crystals with bevelled edges from aqueous-alcoholic hydrobromic acid (Found : HBr, 35·5. $C_{10}H_{15}N,HBr$ requires HBr, 33·3%). The sulphate was precipitated as a white mass by addition of *N*-sulphuric acid to the amine. It is sparingly soluble in alcohol.

The addition of *tert.*-butylaniline to a concentrated solution of picric acid in benzene produced a red coloration, which soon became lighter with the deposition of rosettes of golden-yellow platelets of the *picrate*, which separates from benzene containing a little alcohol, or from ethyl acetate–light petroleum (b. p. 40—60°) as small, golden-yellow, compact crystals, m. p. 191—192° (decomp.) (Found : C, 50·8; H, 5·0. $C_{10}H_{15}N,C_6H_3O_7N_3$ requires C, 50·8; H, 4·8%). It is fairly soluble in alcohol, ethyl acetate, and acetone, not readily in ether, and sparingly in light petroleum (b. p. 40—60°).

Acetyl derivative. A mixture of *tert.*-butylaniline (1·74 g.) and acetic anhydride (10 g.) was kept at room temperature for 4 days, and the excess of anhydride then distilled off. The residue was treated with water, taken up in ether, and the solution washed several times with very dilute hydrochloric acid, then with sodium carbonate and finally water. After drying, the solvent was removed, leaving an oil which soon solidified (yield 1·7 g.). It was purified by dissolving in light petroleum (b. p. 40—60°) at room temperature and then cooling to 0°. The *acetyl* derivative separated as coarse prisms, m. p. 55—56°, b. p. 124—125°/22 mm., readily soluble in light petroleum or alcohol (Found : C, 75·4; H, 8·8. $C_{12}H_{17}ON$ requires C, 75·3; H, 9·0%).

p-*Toluenesulphonyl derivative.* *p*-Toluenesulphonyl chloride (5·1 g., 1·25 mols.) and 3·26 g. (1 mol.) of the amine were mixed. There was no apparent reaction till pyridine (6 c.c.) was added. The mixture then became warm, assumed a red colour, and on cooling, commenced to deposit a fine crystalline precipitate. After 2 days at room temperature, it was poured into an excess of dilute acid, and the insoluble semi-solid mass thus obtained was taken up in ether. The ethereal solution was washed with dilute hydrochloric acid several times, then with sodium hydroxide solution, and the ether evaporated. The residue was heated for a short time with alcoholic sodium hydroxide to hydrolyse any unchanged sulphonyl chloride, the alcohol removed by distillation, and the purified p-*toluenesulphonyl* derivative extracted with ether; yield 2·24 g., m. p. 78—80°. It separates from alcohol as a white felted mass of needles, m. p. 82—83° (Found : C, 67·8, 67·4; H, 6·9, 7·1; N, 4·8. $C_{17}H_{21}O_2NS$ requires C, 67·3; H, 7·0; N, 4·6%).

The m-*nitrobenzenesulphonyl derivative* was prepared in pyridine solution; it crystallises from glacial acetic acid as masses of radially-grouped, cream-coloured needles, m. p. 100—101° (Found : C, 57·9; H, 5·6; N, 8·5. $C_{16}H_{18}O_4N_2S$ requires C, 57·45; H, 5·4; N, 8·4%).

*Phenyl-*tert.*-butylnitrosoamine*, prepared by addition of the calculated amount of sodium nitrite to a solution of *tert.*-butylaniline hydrochloride in very dilute hydrochloric acid, separates from light petroleum (b. p. 40—60°) as tabular prisms, m. p. 61—62° (Found : C, 67·8, 67·6; H, 7·8, 7·9; N, 16·1. $C_{10}H_{14}ON_2$ requires C, 67·4; H, 7·9; N, 15·7%).

The following crystallographic measurements have kindly been supplied by Mr. E. G. Cox of this department : " Phenyl-*tert.*-butylnitrosoamine crystallises from petroleum in large transparent crystals of a very slight greenish-yellow colour; density 1·15 g./c.c. They are monoclinic prismatic, exhibiting the forms *c*{001}, *m*{110}, *n*{120} and very infrequently, *a*{100}. The prism *m* predominates, although its faces are frequently very unequally developed; the crystals are usually somewhat elongated in the vertical direction. The elements are $a : b =$ 1·191; β = 93° 27′. (The development of the crystals does not allow the ratio $c : b$ to be calculated.)

"The classification angles are : *c*(001) : *a*(100) = 86° 33′, *a*(100) : *m*(110) = 49° 57′. From a Laue photograph the elements were found to be approximately $a : b : c =$ 1·18 : 1 : 1·20; β = 87·0°. Mean refractive index = 1·56 approx. Optic axial angle $2V$ = 31°.

" The plane of the optic axes is *b*(010); the bisectrix lies in the acute angle and makes an angle of 46° with the *c*-axis. Dispersion $\rho > \upsilon$, strong; no appreciable dispersion of the bisectrices."

The nitrosoamine gave the Liebermann test, but the coloration was less intense than that usually observed with nitrosoamines from *n*- and *sec.*-alkylanilines.

Attempts to prepare *p*-nitroso-*tert.*-butylaniline by the action of solutions of hydrogen chloride in alcohol or acetic acid were unsuccessful, the hydrochloride of *tert.*-butylaniline being the principal product.

The nitrosoamine (1·03 g.) in 2·8 c.c. of dry ether was mixed with 5 c.c. of dry alcohol saturated with dry hydrogen chloride at 0°. The solution immediately assumed a cherry-red colour, and a small amount of crystalline material commenced to separate. A mild effervescence commenced about 2 or 3 mins. after mixing, but it gradually subsided. At the same time the colour of the solution gradually diminished in intensity till, after 2 hours, it was only a pale golden-yellow, and ultimately (over-night) yellow with a greenish tint. A large volume of ether was added to complete the precipitation of the hydrochloride, which was shown by analysis (Found : HCl, 19·5. Calc. : HCl, 19·65%) and by formation of the crystalline nitrosoamine to be pure *tert.*-butylaniline hydrochloride (yield 0·66 g.; 60%). Control experiments carried out under precisely the same conditions with phenylethylnitrosoamine and phenyl*iso*butylnitrosoamine gave the corresponding *p*-nitroso-compounds in good yield.

During the action of alcoholic hydrogen chloride on phenyl-*tert.*-butylnitrosoamine some of the alcohol was oxidised to acetaldehyde. To avoid side reactions of this type, experiments were made with acetic acid as a solvent instead of alcohol. A solution of phenyl-*tert.*-butylnitrosoamine (0·34 g.) in 1 c.c. of ether was mixed with acetic acid saturated with dry hydrogen chloride (2 c.c.). The solution became cherry-red in colour and small crystals commenced to separate. Over-night a dense crystalline deposit was formed and the supernatant liquid was still cherry-red. The crystals were collected, and washed with ether. They consisted for the most part of small white glistening prisms with some few of a pale orange colour (yield 0·29 g.; 87%). The material thus obtained was practically pure *tert.*-butylaniline hydrochloride (Found : HCl, 19·5. Calc. : 19·65%) and was identified by conversion into the corresponding nitrosoamine (m. p. and mixed m. p.). Phenylethylnitrosoamine, under similar conditions, gave *p*-nitroethylaniline hydrochloride (65% yield) (m. p. and mixed m. p. of free base).

*αβ-Diphenyl-β-*tert.*-butylurea* is formed by warming phenylcarbimide with *tert.*-butylaniline. It separates from light petroleum as slender needle-like crystals, m. p. 81° (Found : C, 76·1; H, 7·6. $C_{17}H_{20}ON_2$ requires C, 76·1; H, 7·5%).

Reaction of tert.*-Butylaniline with Methyl Iodide : Formation of Methyl-*tert.*-butylaniline.*—A mixture of *tert.*-butylaniline and a moderate excess of methyl iodide gradually sets to a solid gummy mass containing a quaternary ammonium iodide, and salts of secondary and tertiary amines. The following conditions were found to give a tertiary amine in fairly satisfactory yield. *tert.*-Butylaniline (3·8 g.) and methyl iodide (4·6 g.) were heated together under reflux at 100°, and 30 c.c. of *N*-sodium carbonate added gradually. After 1¼ hrs., the aqueous layer was removed, the amine taken up in ether, and heated under reflux with a further quantity of sodium carbonate solution and 2 c.c. of methyl iodide. The ethereal layer was separated after 2 hours, washed with alkali, dried, and distilled. As it still contained a small amount of a secondary amine, it was heated on a steam-bath for ½ hour with phenylcarbimide, and then steam distilled after heating under reflux with water for a short time. The amine which passed over still contained some dimethylaniline. It was purified by conversion into a sparingly soluble *picrate* in ether, which separates from benzene or alcohol as small, bright, canary-yellow crystals, m. p. 162—163° (decomp.) (Found: C, 52·1; H, 5·2. $C_{11}H_{17}N,C_6H_3O_7N_3$ requires C, 52·0; H, 5·1%).

The amine liberated from the picrate by addition of aqueous ammonia distils at 81—82°/39 mm. (yield 2·1 g.) and is a colourless oil having a faint but not disagreeable odour (Found : C, 80·9; H, 10·1. $C_{11}H_{17}N$ requires C, 80·9; H, 10·5%). *Methyl-*tert.*-butylaniline* is not appreciably affected by aqueous nitrous acid. A solution of the amine (0·14 g.) in 2 c.c. of 3*N*-hydrochloric acid was treated with 1 c.c. of 10% sodium nitrite solution, but after ½ hour at room temperature, the mixture was worked up and afforded 0·295 g. of the picrate (m. p. and mixed m. p. 161—162°, decomp.) of the original base, corresponding to 83% recovered.

tert.*-Amylaniline.*—This amine was obtained by a method substantially the same as that used for the preparation of *tert.*-butylaniline, except that the amylene formed in the reaction was recovered by diluting the product with water and subsequent distillation. From *tert.*-amyl iodide (27 g.) and aniline (40 g.), 1·8 g. of amylene and 7·15 g. of tert.*-amylaniline* were obtained. This base is a refractive liquid with a faint yellow tint, miscible with the common organic solvents and insoluble in water; b. p. 227·5—229·5°/744 mm. (corr.); 112—114°/25 mm. (Found : C, 80·7; H, 10·3. $C_{11}H_{17}N$ requires C, 80·9; H, 10·5%). The *hydrochloride* separates from ethyl acetate as white plates, usually six-sided (Found : HCl, 18·1. $C_{11}H_{17}N,HCl$ requires HCl, 18·3%).

*Phenyl-*tert.*-amylnitrosoamine* separates from light petroleum (b. p. 40—60°) as thin buff-coloured plates, m. p. 47—48° (Found : C, 68·9; H, 8·4; N, 15·0. $C_{11}H_{16}ON_2$ requires C, 68·7; H, 8·4; N, 14·6%). It gives only a faint Liebermann test. Treatment of a solution of the nitrosoamine (0·46 g.) in ether (1·3 c.c.) with alcoholic hydrogen chloride saturated at 0° (2·3 c.c.) furnished a reddish-brown solution. On keeping for several days and subsequent evaporation of the solvent at room temperature, a crystalline residue was obtained. Treatment with ether freed it from most of the associated colouring matter and left a crystalline mass of *tert.*-amylaniline hydrochloride (0·19 g.) (Found : HCl, 18·1. Calc. : HCl, 18·3%).

The p-*toluenesulphonyl* derivative separates from aqueous alcohol or dilute acetic acid in small, stout, white prisms, m. p. 73—74° (Found : C, 68·3; H, 7·0; N, 4·7. $C_{18}H_{23}O_2NS$ requires C, 68·1; H, 7·3; N, 4·4%).

tert.*-Hexylaniline* (β-*Anilino*-β-*ethylbutane*).—The *tert.*-hexyl iodide required for this preparation was prepared by saturating methyldiethylcarbinol with hydrogen iodide. From 98 g. of carbinol, 189 g. of crude iodide were obtained, which yielded 157 g. of pure iodide, b. p. 47·5—48°/18 mm. The reaction with aniline was carried out in a manner similar to that employed for the preparation of *tert.*-amylaniline. In three preparations, a total of 152 g. of *tert.*-hexyl iodide and 150 g. of aniline yielded 44·25 g. of hexene (yield 74%) and tert.*-hexylaniline* (23%). The hexene boiled steadily at 69—70°, except for the first few drops, and is obviously identical with αβ-dimethyl-α-ethylethylene (b. p. 69·5—71°) described by Favorski (*J. Russ. Phys. Chem. Soc.*, 1918, **50**, 43), who obtained it by the action of alcoholic potash on γ-bromo-γ-methylpentane.

tert.-Hexylaniline is a liquid with a straw-yellow tint and a not unpleasant floral odour, b. p. 253—254°/759 mm. (corr.); 120—121°/17·5 mm. (Found : C, 81·3; H, 10·5. $C_{12}H_{19}N$ requires C, 81·3; H, 10·8%). The *hydrochloride*, prepared by evaporating a solution of the amine in dilute hydrochloric acid in a vacuum desiccator over soda-lime, separates from dry ethyl acetate as pyramidal crystals, which are fairly soluble in benzene (Found : HCl, 17·0. $C_{12}H_{19}N,HCl$ requires HCl, 17·1%). The picrate separates from benzene–light petroleum (b. p. 40—60°) as a mass of small golden-yellow crystals, m. p. 133—135°.

*Phenyl-*tert.*-hexylnitrosoamine* was obtained as an oil by adding the calculated amount of sodium nitrite solution to an aqueous solution of the foregoing hydrochloride. It was taken up in ether, the solution washed with water and sodium hydroxide, then steam distilled. The nitrosoamine was extracted from the distillate with ether, the ethereal solution dried (magnesium sulphate) and then evaporated under reduced pressure. Phenyl-*tert.*-hexylnitrosoamine was thus obtained as a pale yellow oil which solidified completely when, admixed with a little light petroleum, it was cooled in liquid air. The solid melted completely when warmed to 0°. For analysis, a sample of the steam-distilled nitrosoamine was kept in an evacuated desiccator over sulphuric acid for several days (Found : C, 70·0; H, 8·7. $C_{12}H_{18}ON_2$ requires C, 69·85; H, 8·8%).

Attempts to obtain the p-*toluenesulphonyl* derivative by reaction of the amine and the sulphonyl chloride in pyridine at room temperature gave very little of the required compound. The following procedure gave more satisfactory results. *tert.*-Hexylaniline (0·52 g.), *p*-toluenesulphonyl chloride (0·95 g.), and pyridine (2·5 c.c.) were mixed and kept at room temperature for 18 hours, then heated in a water-bath for 2 hours and poured into water. The oil thus precipitated was dissolved in ether and the ethereal solution washed successively with several quantities of dilute hydrochloric acid, sodium hydroxide, and water. After drying and evaporation of the solvent, moderately pure material was obtained (yield 0·3 g.); it crystallised from aqueous alcohol as needle-like prisms (Found : C, 68·6; H, 7·5; N, 4·5. $C_{19}H_{25}O_2NS$ requires C, 68·8; H, 7·6; N, 4·2%).

The m-*nitrobenzenesulphonyl* derivative of *tert.*-hexylaniline, prepared in pyridine at room temperature, formed flattened prisms from alcohol, m. p. 85—86° (Found : C, 59·7; H, 6·1; N, 8·0. $C_{18}H_{22}O_4N_2S$ requires C, 59·6; H, 6·1; N, 7·7%). It is sparingly soluble in the cold and more easily in the warm solvent, and readily soluble in benzene, acetone, or ether.

Methyl-*tert.*-hexylaniline was prepared by heating *tert.*-hexylaniline (1·52 g.) with methyl iodide (2 c.c.) and *N*-sodium carbonate solution (10 c.c.), following the procedure used for the corresponding *tert.*-butyl compound. After the second treatment, the amine was taken up in ether, the extract dried, and treated with a slight excess of picric acid, the *picrate* being precipitated (yield 0·97 g.); it separates from alcohol as bright yellow thin prisms or four-sided plates, m. p. 127—128° (Found : C, 54·5; H, 5·7. $C_{13}H_{21}N,C_6H_3O_7N_3$ requires C, 54·3; H, 5·8%).

The following attempt to obtain a *p*-nitroso-derivative was unsuccessful. The amine (0·11 g.) liberated from the purified picrate was dissolved in 3 c.c. of 3*N*-hydrochloric acid and 1 c.c. of 10% sodium nitrite solution added. There was no development of colour, and after standing for 2 hours at room temperature the solution had become slightly turbid. It was then made alkaline with ammonia and shaken with 3 successive portions of ether. Addition of picric acid to the dried ethereal solution precipitated the picrate of the unchanged base, m. p. and mixed m. p. 126—127°; yield 0·17 g. (70%).

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[*Received, May* 24*th*, 1933.]