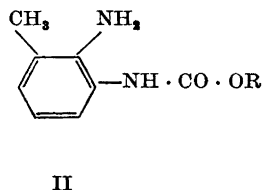
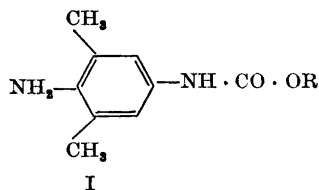


Note on the Preparation of Some
4-Amino-3,5-dimethyl- and
2-Amino-3-methyl-
phenylurethanes

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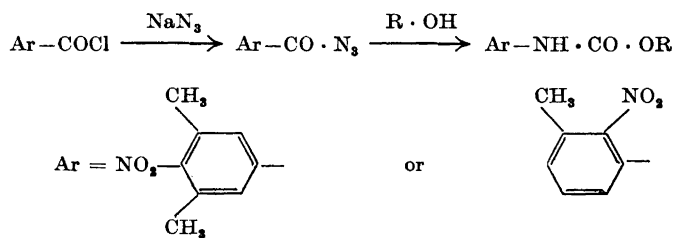
Several amino- and methyl-substituted phenylurethanes (Types I and II) were required as starting material for certain syntheses in the field of local anesthetics.



R = C₂H₅, n-C₃H₇, n-C₄H₉, and n-C₆H₁₁.

These compounds were obtained by the Curtius degradation of the appropriate nitro-substituted carboxylic acid.

(93 %), m.p. 82–83° (decomp.). Without purification the product was used for further syntheses.



Degradation was followed by hydrogenation of the nitro group to the amino compound.

Experimental. 4-Nitro-3,5-dimethylbenzoyl chloride was obtained from 4-nitro-3,5-dimethylbenzoic acid according to the method of Löfgren *et al.*¹ B.p. 144–145°/9 mm, yield 86 %.

2-Nitro-3-methylbenzoyl chloride was similarly prepared by refluxing 2-nitro-3-methyl-

benzoic acid* (45 g, 0.25 mole) and thionyl chloride (89 g, 0.75 mole) for 4 h. The thionyl chloride was removed *in vacuo* and the residue (without purification) was used for further syntheses. An attempt to distill this compound *in vacuo* led to a violent explosion.

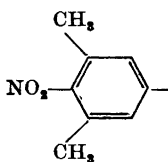
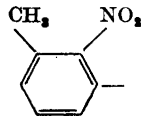
4-Nitro-3,5-dimethylbenzoyl azide. 4-Nitro-3,5-dimethylbenzoyl chloride (42.7 g, 0.2 mole) was dissolved in acetone (80 ml) and cooled to 10°. Sodium azide (14.3 g, 0.22 mole) in water (45 ml) was then added dropwise with stirring over a period of 15 min.; the temperature was maintained at 25° by external cooling. After one hour, water (100 ml) was added, and the reaction product which separated was collected and dried in a vacuum desiccator. Yield 40.8 g

2-Nitro-3-methylbenzoyl azide was prepared as above. Yield 98 %, m.p. 86–87° (dec.).

4-Nitro-3,5-dimethyl- and 2-nitro-3-methylphenylurethanes. A solution of the appropriate azide (0.05 mole) in an alcohol (50 ml) containing the desired alkyl group was heated on the water bath until nitrogen evolution had ceased (2 h). Excess of the alcohol was removed *in vacuo*, leaving an oil which in most instances quickly solidified. The resulting product, obtained in yields of 95–100 %, was practically pure. A sample was recrystallised for analysis.

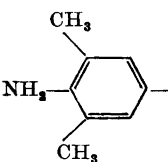
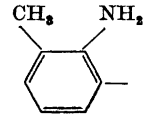
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Table 1. Nitro-substituted phenylurethanes, Ar-NH · CO · OR

| Ar | R | M.p. °C | Recryst. solvent. ^a | Formula | Calc. % | | | Found % | | |
|---|----------------------------------|-----------|--------------------------------|---|---------|------|------|---------|------|------|
| | | | | | C | H | N | C | H | N |
|  | C ₂ H ₅ | 77.5–78.5 | L–B | C ₁₁ H ₁₄ N ₂ O ₄ | 55.5 | 5.92 | 11.8 | 55.2 | 6.12 | 11.6 |
| | n-C ₃ H ₇ | 90.5–91.5 | L–B | C ₁₃ H ₁₆ N ₂ O ₄ | 57.1 | 6.39 | 11.1 | 57.0 | 6.63 | 10.9 |
| | n-C ₄ H ₉ | 104–105 | L | C ₁₃ H ₁₈ N ₂ O ₄ | 58.6 | 6.81 | 10.5 | 58.6 | 6.90 | 10.6 |
| | n-C ₅ H ₁₁ | 83–84 | L–B | C ₁₄ H ₂₀ N ₂ O ₄ | 60.0 | 7.19 | 10.0 | 60.1 | 7.10 | 9.90 |
|  | C ₂ H ₅ | 86–87 | L | C ₁₀ H ₁₂ N ₂ O ₄ | 53.6 | 5.39 | 12.5 | 53.5 | 5.86 | 12.5 |
| | n-C ₃ H ₇ | oil | | | | | | | | |
| | n-C ₄ H ₉ | oil | | | | | | | | |
| | n-C ₅ H ₁₁ | oil | | | | | | | | |

^a Aq, water; B, benzene; L, ligroin; M, methanol; P, petroleum ether.

Table 2. Amino-substituted phenylurethanes, Ar-NH · CO · OR

| Ar | R | M.p. °C | Recryst. solvent. ^a | Formula | Calc. % | | | Found % | | |
|---|----------------------------------|---------|--------------------------------|---|---------|------|------|---------|------|------|
| | | | | | C | H | N | C | H | N |
|  | C ₂ H ₅ | 97–98 | M–Aq | C ₁₁ H ₁₆ N ₂ O ₂ | 63.4 | 7.75 | 13.5 | 63.5 | 7.78 | 13.4 |
| | n-C ₃ H ₇ | 128–129 | M–Aq | C ₁₃ H ₁₈ N ₂ O ₂ | 64.8 | 8.16 | 12.6 | 64.9 | 8.14 | 12.5 |
| | n-C ₄ H ₉ | 117–118 | M–Aq | C ₁₃ H ₂₀ N ₂ O ₂ | 66.1 | 8.53 | 11.9 | 66.1 | 8.66 | 11.9 |
| | n-C ₅ H ₁₁ | 81–82 | L–B | C ₁₄ H ₂₂ N ₂ O ₂ | 67.2 | 8.86 | 11.2 | 67.7 | 9.10 | 10.9 |
|  | C ₂ H ₅ | 75–76 | L–B | C ₁₀ H ₁₄ N ₂ O ₂ | 61.8 | 7.27 | 14.4 | 62.0 | 7.41 | 14.1 |
| | n-C ₃ H ₇ | 69–70 | L–B | C ₁₁ H ₁₆ N ₂ O ₂ | 63.4 | 7.75 | 13.5 | 63.5 | 7.59 | 13.2 |
| | n-C ₄ H ₉ | 71–72 | L–B | C ₁₃ H ₁₈ N ₂ O ₂ | 64.8 | 8.16 | 12.6 | 64.9 | 7.71 | 12.7 |
| | n-C ₅ H ₁₁ | 72–73 | L–P | C ₁₃ H ₂₀ N ₂ O ₂ | 66.1 | 8.53 | 11.9 | 66.1 | 8.60 | 11.8 |

^a See Table 1.

crystallise were used directly in the next synthetic step.

4-Amino-3,5-dimethyl- and 2-Amino-3-methylphenylurethanes. The appropriate nitro compound (0.05 mole) was dissolved in ethanol (50 ml). It was then hydrogenated over Raney nickel in a Parr hydrogenation apparatus for 2 h at about 55°C with a pressure of about 5 atm. The solvent was evaporated *in vacuo* and the crystalline residue (95–100 %

of practically pure product) was recrystallised.

The amino compounds are listed in Table 2.

- Löfgren, N., Tegnér, C., Willman, N. and Dahlbom, R. *Unpublished results*.
- Tomisek, A., Graham, B., Griffith, A., Pease, C. S. and Christensen, B. E. *J. Am. Chem. Soc.* **68** (1946) 1587.

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