

A CONVENIENT PROCEDURE FOR THE SYNTHESIS OF ^{15}N -LABELED DIPHENYLAMINE AND DIPHENYLNITROSAMINE

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Procedures are described for the synthesis on a 5 m mole scale of ^{15}N -labeled diphenylnitrosamine in four steps from aniline ^{15}N .

Diphenylamine(^{15}N) and its ^{15}N -nitroso derivative were required in this laboratory for mechanism studies in nitramine chemistry and for obtaining the ^{15}N -nuclear magnetic resonance data including coupling constants. For the coupling constants between directly bonded ^{15}N nuclei it was essential to have high ^{15}N -enrichment in spite of the availability of Fourier-transform techniques.

The obvious commercial compound to start with was the expensive ^{15}N -aniline (95% enriched) and it was apparent that the yields at the several steps involved would be low resulting in a poor overall yield. Considerable experimentation was done, therefore, in order to optimize the conditions and details of the procedure which gave an overall yield of 81% of diphenylnitrosamine are presented in this paper.

Diphenyl- ^{15}N -amine

The more common methods are (a) heating together^(1,2) aniline and its hydrochloride at 150° or higher, and (b) by an Ullmann type reaction on aniline

and bromo (or iodo) benzene⁽³⁾. However, the first method had to be discarded for ^{15}N synthesis since it would necessarily result in 50% loss of ^{15}N as $^{15}\text{NH}_4\text{Cl}$. The second method in several trial runs led to the formation of triphenylamine. Recourse had to be made, therefore, to preventing the further condensation of diphenylamine by prior acetylation. The procedure finally adopted was, with some changes, the one described by Hickinbottom⁽⁴⁾ and more recently by Chen, et al,⁽⁵⁾ and Hatano & Yamamoto⁽⁶⁾.

Acet- ^{15}N -anilide⁽⁷⁾: A solution of aniline- ^{15}N (1 g) in carbon tetrachloride (15 ml) was treated with 1 ml c.p. hydrochloric acid and 5 ml of acetic anhydride under reflux for 30 mins. Excess acetic anhydride and acetic acid are easily removed by the addition of 15 ml methanol and distillation of the methylacetate. The water formed in the reaction was removed by azeotropic distillation with CCl_4 which was itself finally evaporated leaving a flaky residue 1.43 g in 99% yield, m.p. 111-12°. The more conventional methods gave only about 70% yield in trial runs.

N-Acetyldiphenyl- ^{15}N -amine: Acetanilide- ^{15}N (1.02 g, 7.5 m moles), iodobenzene (2.25 g, 11 m moles), anhydrous K_2CO_3 (0.6 g) and cuprous iodide (15 mg.) were refluxed in nitrobenzene (4 ml) for about 20 hrs. At the end of refluxing, the nitrobenzene and the excess iodobenzene were removed by steam-distilling. The oily residue was then taken up in ether, the extract dried and evaporated to obtain 1.43 g (90% theory) crystalline acetyldiphenylamine- ^{15}N .

Diphenyl- ^{15}N -Amine: The N-acetyldiphenylamine- ^{15}N was then hydrolyzed by refluxing with 5 ml alcohol and 4 ml c.p. hydrochloric acid for 3 hrs. following which the diphenylamine was isolated by steam distillation (about 400 ml distillate). The yield of crystalline diphenylamine was 1.05 g (92%), m.p. 46-8.5° compared to the reported yield in the literature of 60% from acetanilide. This represents an overall yield of 82% based on aniline- ^{15}N .

^{15}N -Nitrosodiphenyl- ^{15}N -Amine

Because of the insoluble nature of diphenylamine hydrochloride in water, benzene was used as solvent in the procedure described here. Somewhat better yields were obtained by this method than the one due to Chen, et al⁽⁵⁾ using alcohol as the solvent.

Diphenyl- ^{15}N -amine (0.85 g.) dissolved in 10 ml benzene and sodium nitrite- ^{15}N (0.5 g.) dissolved in 5 ml water were stirred vigorously at about 5° and 1.5 ml c.p. HCl was added dropwise over 30 min. The mixture was stirred 1 hr longer and extracted with excess benzene (60-70 ml). The extract was washed with water, dried and evaporated under N_2 to yield 0.98 g. (99% theory), representing an 81% overall yield of nitrosamine. This was crystallized from pentane and alcohol mixture, m.p. 62.5-3.5°, Nmr(H) (CDCl_3 -TMS: δ , 8, 7.45.

Major bands in I.R. (KBr pellet), cm^{-1}

1590 (s), 1488 (s), 1460 (s), 1420 (s), 1314 (m), 1298 (s), 1187 (s)
1160 (s), 1080 (s), 1050 (s), 1000(d),(m), 970(d),(m), 920 (m), 910 (m),
835 (m) 760 (s), 742 (s), 692 (s), 620(d),(m), 565 (m), 523 (m), 505 (m),
443 (w), 400 (w).

The underlined frequencies showed substantial isotopic shifts ranging from 5 to 20 cm^{-1} .

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¹⁵N-Labeled Diphenylamine and Diphenylnitrosamine

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