

The Preparation of [ $^{15}\text{N}$ ,  $^{15}\text{N}'$ ]- and [ $4,4'$ - $^{13}\text{C}_2$ ]-4,4'-  
Dichloroazobenzene and [ $^{15}\text{N}$ ,  $^{15}\text{N}'$ ]-4-Chloroazobenzene

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ABSTRACT

Syntheses of specifically labelled [ $^{15}\text{N}$ ,  $^{15}\text{N}'$ ]- and [ $4,4'$ - $^{13}\text{C}_2$ ]-4,4'-dichloroazobenzene and [ $^{15}\text{N}$ ,  $^{15}\text{N}'$ ]-4-chloroazobenzene have been accomplished.

Key Words: Nitrogen and carbon doubly-labeled azobenzenes.

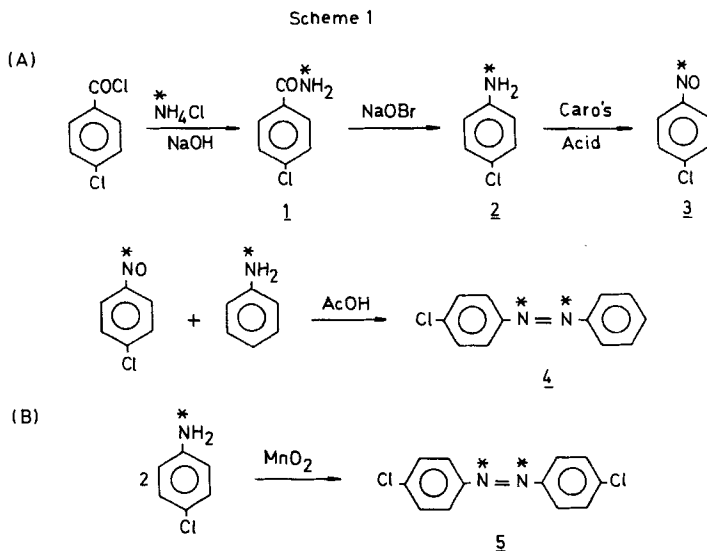
INTRODUCTION

For studying the mechanism of rearrangement of 4,4'-dichlorohydrazobenzene, specifically labelled [ $^{15}\text{N}$ ,  $^{15}\text{N}'$ ]- and [ $4,4'$ - $^{13}\text{C}_2$ ]-4,4'-dichloroazobenzene were needed. Similarly, [ $^{15}\text{N}$ ,  $^{15}\text{N}'$ ]-4-chloroazobenzene was made for rearrangement of 4-chlorohydrazobenzene.

EXPERIMENTAL

[ $^{15}\text{N}$ ,  $^{15}\text{N}'$ ]-4-Chloroazobenzene and [ $^{15}\text{N}$ ,  $^{15}\text{N}'$ ]-4,4'-Dichloroazobenzene  
(Scheme 1)

[ $^{15}\text{N}$ ]-4-Chlorobenzamide (1). A solution of 4.0 g (73.4 mmol) of [ $^{15}\text{N}$ ] ammonium chloride (Stohler, 99%  $^{15}\text{N}$ ) was made in 36 mL of water. Benzene (3 mL) was layered on top of the solution which was kept at 6°C. A solution of 6.8 g of sodium hydroxide in 30 mL of water, cooled to 6°C, was added slowly from a pipette tip which was kept under the surface of the benzene layer. A solution of 12.85 g (73.4 mmol) of 4-chlorobenzoylchloride in 300 mL of cold benzene was added quickly. The reaction mixture was stirred vigorously for 2 h at room temperature, during which time the product precipitated. This



was filtered to give 11.3 g (98%) of [ $^{15}\text{N}$ ]-4-chlorobenzamide, mp 178-179°C.

[ $^{15}\text{N}$ ]-4-Chloroaniline (2). Bromine (13.3 g) was added dropwise to an ice-cold, stirred solution of 19.4 g of sodium hydroxide in 320 mL of water. After 5 min, 11.3 g (72.1 mmol) of 1 was added and mixture was stirred at 0°C for 20 min. The mixture was then slowly heated to 95°C and maintained at that temperature for 1.5 h. After the reaction mixture was cooled to room temperature, the dark-brown product was filtered, giving 7.8 g, mp 60-64°C. The filtrate was extracted three times with ether, and the extract was dried over sodium sulfate and evaporated to leave 0.51 g of [ $^{15}\text{N}$ ]-4-chloroaniline, mp 65-69°C. The total yield of crude product was 8.3 g (90%).

[ $^{15}\text{N}$ ]-4-Chloronitrosobenzene (3) was made as described for *p*-chloronitrosobenzene by Ingold,<sup>1</sup> but with some modification. Finely-powdered potassium persulfate (22.9 g) was used, instead of the ammonium salt, in 11.5 mL of conc. sulfuric acid, and poured onto 10 mL of ice and water. After neutralization with solid sodium carbonate, 4 g (31.1 mmol) of powdered 2 was added and the mixture was stirred for 1 h at 5°C. The solid product was filtered,

and washed with water and 1 N hydrochloric acid to give 2.35 g (53%) of crude 3, mp 80–85°C. The product was used without steam distilling.<sup>1</sup>

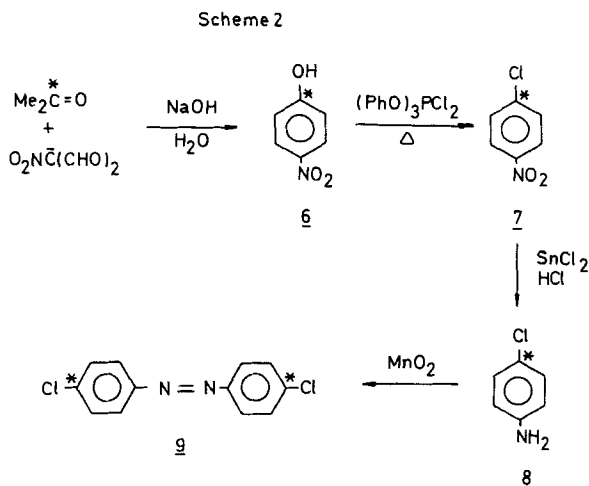
[<sup>15</sup>N, <sup>15</sup>N']-4-Chloroazobenzene (4). Condensation of p-chloroaniline with nitrosobenzene has been described by Jacobson and Loeb.<sup>2</sup> The method was adapted to our need as follows. A solution of 1.85 g (13.0 mmol) of [<sup>15</sup>N]-4-chloronitrosobenzene in 5 mL of acetic acid was added to a solution of 1.22 g (13.0 mmol) of [<sup>15</sup>N]-aniline (Stohler, 99% <sup>15</sup>N) in 3 mL of acetic acid. The mixture was stirred for 1 h, and allowed to stand for 7 h at room temperature. The solid product was filtered and dried to give 2.17 g (76%) of [<sup>15</sup>N, <sup>15</sup>N']-4-chloroazobenzene, mp 84–86°C. A further 0.3 g of product was obtained, mp 70–75°C., by adding water to the filtrate. Recrystallization from ethanol gave mp 87–88°C. Lit. mp 90–91°C.<sup>2</sup>

[<sup>15</sup>N, <sup>15</sup>N']-4,4'-Dichloroazobenzene (5). A suspension of 3.72 g (28.9 mmol) of [<sup>15</sup>N]-4-chloroaniline and 20 g of active manganese dioxide in 240 mL of benzene was stirred under reflux for 5 h in a Dean-Stark apparatus to remove water.<sup>3</sup> The hot solution was filtered and the manganese dioxide was washed with hot benzene. The filtrate was evaporated to give 3.2 g (87%) of [<sup>15</sup>N, <sup>15</sup>N']-4,4'-dichloroazobenzene, mp 170–185°C. Recrystallization from chloroform, gave mp 187–189°C. Lit. mp 185°C.<sup>3</sup>

[4,4'-<sup>13</sup>C<sub>2</sub>]-4,4'-Dichloroazobenzene (Scheme 2)

[1-<sup>13</sup>C]-4-Nitrophenol (6) was prepared by the method of Swartz and Gulick.<sup>4</sup> From 3.28 g (55.6 mmol, 99% <sup>13</sup>C) of [2-<sup>13</sup>C]-acetone (Merck) we obtained 5.0 g (64%) of crude, brownish-yellow 6. This was purified by flash chromatography on silica gel, eluting with a mixture of chloroform and ethanol (100:1), giving 4.3 g (55%), mp 109–112°C. Lit. mp 108–109°C.<sup>4</sup>

[4-<sup>13</sup>C]-4-Chloronitrobenzene (7). The general method of Coe et al.<sup>5</sup> of replacing phenolic OH with Cl was used as follows. Phosphorous pentachloride (6.4 g, 30.7 mmol) was heated for 4 h at 100°C with 8.6 g (91.5 mmol) of phenol. The [1-<sup>13</sup>C]-4-nitrophenol (4.3 g 30.7 mmol) was added to the cooled product,



which was then reheated for 4 h at 100°C. The crude tetraaryloxyphosphorous monochloride was then decomposed by heating at 200°C for 20 min. Vacuum distillation removed phenol first, and gave, next, 3.32 g (68%) of 7, mp 81–82.5°C.

[4-<sup>13</sup>C]-4-Chloroaniline (8).<sup>6,7</sup> Stannous chloride dihydrate (15.4 g) in 12.6 mL of conc. hydrochloric was stirred while 3.21 g (20.3 mmol) of [4-<sup>13</sup>C]-4-chloronitrobenzene was added. Stirring was continued with gentle heating for 20 min, and 8 mL of 95% ethanol was added to give a clear solution. The reaction mixture was refluxed for 1 h, and after cooling to room temperature was made alkaline with 40% sodium hydroxide solution. A slightly-yellow precipitate formed; this was filtered and extracted with ether. Evaporation of the ether solution gave 667 mg of [4-<sup>13</sup>C]-4-chloroaniline, mp 64–68°C. The aqueous, alkaline filtrate was extracted with ether (6 x 25 mL). Drying over sodium carbonate and work up of the ether solution gave additionally 1.53 g of product, mp 65–68°C. The total yield was 84%.

[4,4'-<sup>13</sup>C<sub>2</sub>]-4,4'-Dichloroazobenzene (9) was prepared in 95% yield by the procedure described above for [<sup>15</sup>N,<sup>15</sup>N']-4,4'-dichloroazobenzene, and had mp 180–185°C. Recrystallization from chloroform gave mp 187–188.5°C.

Isotopic enrichments were determined by whole-molecule mass spectrometry. That is, enrichments in the (M + 1) or (M + 2) molecular ions were measured

by comparing the M/(M + 1) or M/(M + 2) abundances in the labelled compounds with those in the corresponding natural compounds.<sup>8</sup> The following results were obtained: [<sup>15</sup>N,<sup>15</sup>N']-4-chloroazobenzene, C<sub>12</sub>H<sub>9</sub>Cl<sup>15</sup>N<sub>2</sub>, 98.6% <sup>15</sup>N<sub>2</sub>, 1.0% <sup>15</sup>N<sub>1</sub>; [<sup>15</sup>N,<sup>15</sup>N']-4,4'-dichloroazobenzene, C<sub>12</sub>H<sub>8</sub>Cl<sub>2</sub><sup>15</sup>N<sub>2</sub>, 99.1% <sup>15</sup>N<sub>2</sub>, 0.49% <sup>15</sup>N<sub>1</sub>; [4-<sup>13</sup>C]-N-trifluoroacetylaniline, 98.2% <sup>13</sup>C prepared from 8. On the basis of this <sup>13</sup>C analysis the enrichment in our [4,4'-<sup>13</sup>C<sub>2</sub>]-4,4'-dichloroazobenzene should have been 96.5% <sup>13</sup>C<sub>2</sub>, 3.5% <sup>13</sup>C<sub>1</sub>, whereas direct analysis gave 95.4% <sup>13</sup>C<sub>2</sub> and 4.1% <sup>13</sup>C<sub>1</sub>. The difference reflects, we think, the difficulty of getting precise (M + 2) enrichment data for molecules containing two Cl atoms.

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## REFERENCES

1. Ingold, C. K. - J. Chem. Soc. 125: 87 (1924).
2. Jacobson, P. and Loeb, A. - Chem. Ber. 36: 4082 (1903).
3. Wheeler, O. H. and Gonzalez, D. - Tetrahedron 20: 189 (1964).
4. Swartz, G. L. and Gulick, Jr., W. M. - J. Labeled Compd. 11: 525 (1975).
5. Coe, D. G., Rydon, H. N. and Tonge, B. L. - J. Chem. Soc. 323 (1957).
6. Banthorpe, D. V. and Cooper, A. - J. Chem. Soc. (B) 627, (1968).
7. Horning, E. C. "Organic Syntheses", Coll. Vol. 3, John Wiley, New York, 1955, p. 453.
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