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## Synthesis of 4-Allyl- and 4-Benzyl-2,6-dimethylbromobenzene from 2,6-Xylidine

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N-Allyl-2,6-xylidine was unchanged when heated alone, but rearranged to 4-allyl-2,6-xylidine with zinc chloride in refluxing xylene. When the hydrochloride was heated alone, the principal reaction was dissociation to allyl chloride and xylidine, and only a trace of 4-allyl compound was formed. In contrast, N-benzyl-2,6-xylidine did not rearrange in the presence of zinc chloride but the required 4-benzyl-2,6-xylidine was obtained by direct benzylation of 2,6-xylidine. The 4-allyl- and 4-benzyl-2,6-xylidines were converted smoothly to the corresponding bromobenzenes by the Sandmeyer reaction.

DOERING and BRAGOLE<sup>1</sup> recently commented that there are few examples of reactions analogous to the Claisen rearrangement of phenyl allyl ethers where other groups or atoms replace oxygen. We report here the use of a reaction related to the para-Claisen rearrangement of O-allyl-2,6-dimethyl phenol,<sup>2</sup> with nitrogen instead of oxygen.

The rearrangement of N-allyl-2,6-xylidine (II) to 4-allyl-2,6-xylidine (IV) was investigated as one stage in the development of a satisfactory synthesis of 4-allyl-2,6-dimethylbenzyl alcohol, needed for other work.<sup>3</sup>



N-Allyl-2,6-xylidine was obtained from allyl chloride and 2,6-xylidine (I) (2 moles). Like N-allylaniline,<sup>4</sup> it gave no C-allyl compound when heated alone. This agrees with theoretical considerations by Marcinkiewicz et  $al.,^5$  which suggested that N-allylanilines would cleave rather than rearrange, in contrast to N-allylnaphthylamines which were shown to undergo a Claisen-type rearrangement.

Previous workers found that, when other reagents were added, N- to C-alkenyl migrations were promoted in the aniline series. Thus, aniline hydrochloride or hydrobromide converts N-but-2-enylaniline to 4-but-2-envlaniline <sup>6</sup> and with zinc chloride in refluxing xylene, N-allylaniline gives 2-allylaniline in 40% yield.<sup>7</sup> Acids cause cyclisation after rearrangement so that N-alkenylanilines finally give 2-methyl-indoles and -indolines.8

These considerations indicated that, provided the

two ortho-substituents of N-allyl-2,6-xylidine were not displaced, indoles and indolines would not be formed and the 4-position would be the most probable goal for the migrating group. In confirmation, zinc chloride in refluxing xylene converted N-allyl-2,6-xylidine to 4allyl-2,6-xylidine in 73% yield in 2 hr. Isolation of the intermediate N-allyl-2,6-xylidine could be avoided by subjecting the crude mixture of primary and secondary amines to rearrangement with zinc chloride in xylene, when the higher boiling 4-allyl-2,6-xylidine was easily separated.

Because indoles and indolines were not obtained, it seemed possible that rearrangement of N-allyl-2,6xylidine hydrochloride might be induced simply by heating. However, only a trace of 4-allyl compound (IV) was obtained, and the principal reaction under the conditions used, which allowed the escape of volatile material, was elimination of allyl chloride to give 2,6xylidine. In contrast, 4-benzyl-2,6-xylidine (V), also required as an intermediate, could be made by this method; it was formed in 68% yield together with 3,4-dibenzyl-2,6-xylidine (17%) when a 1 : 1 mixture of benzyl chloride and 2,6-xylidine was heated at 250° for 2 hr. Presumably, the conditions which allowed allyl chloride to escape retained the higher boiling benzyl chloride, and, at the higher temperature consequently attained, the aromatic nucleus was directly alkylated. Such reactions have often been observed; <sup>9</sup> for example, the action of heat on NN-dibenzylaniline hydrochloride gives a mixture of mono, di-, and tri-C-benzylanilines.<sup>10</sup> The rearrangement by zinc chloride in refluxing xylene seems to be specific for allyl derivatives, because 4-benzyl-2,6-xylidine was not formed when the rearrangement of N-benzyl-2,6-xylidine was attempted. Analogously, benzyl aryl ethers do not rearrange under Claisen conditions.<sup>11a</sup>

Both 4-allyl- (IV) and 4-benzyl-2,6-xylidine (V) were converted by the Sandmeyer reaction to the required

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<sup>1961, 438.</sup> 

<sup>&</sup>lt;sup>6</sup> W. J. Hickinbottom, J. Chem. Soc., 1934, 1981.

<sup>7</sup> C. D. Hurd and W. W. Jenkins, J. Org. Chem., 1957, 22, 1418.

<sup>&</sup>lt;sup>8</sup> J. E. Hyre and A. R. Bader, *J. Amer. Chem. Soc.*, 1958, **80**, 437; A. R. Bader, R. J. Bridgewater, and P. R. Freeman, *ibid.*,

<sup>1961, 83, 3319.
&</sup>quot; Chemistry of Carbon Compounds," ed. Rodd, Elsevier,

 <sup>&</sup>lt;sup>10</sup> P. J. Drumm, W. F. O'Connor, and J. Reilly, J. Amer. Chem. Soc., 1949, 62, 1241.
 <sup>11</sup> D. S. Tarbell, Org. Reactions, 1944, 2, (a) p. 4; (b) p. 28.

bromobenzenes. A side product of the reaction with the 4-allyl compound, which confirmed its structure, was 4-allyl-2,6-xylenol, identical with a sample made by rearrangement of O-allyl-2,6-xylenol.<sup>2</sup>

## EXPERIMENTAL

Ultraviolet spectra were measured in ethanol on a Unicam SP 500 spectrophotometer, infrared spectra on a Perkin-Elmer Infracord spectrophotometer, and n.m.r. spectra on a Perkin-Elmer R10 spectrometer. In the work-up procedure, the ether solutions were washed with saturated sodium chloride solution, dried  $(Na_2SO_4)$ , and concentrated at 20 mm. on a steam-bath, to give the reaction product.

4-Allyl-2,6-xylidine.—(a) Allyl chloride (76.5 g., 1 mole) and 2,6-xylidine (242 g., 2 moles) were heated on steam in a flask with an efficient condenser for 8 hr. After being set aside overnight, the product was poured into water, made alkaline with sodium hydroxide, and extracted into ether. (This step was necessary because the precipitate contained N-allyl-2,6-xylidine hydrochloride as well as 2,6-xylidine hydrochloride; in contrast, aniline and allyl chloride gave only aniline hydrochloride.<sup>7</sup>) The ether extract was worked-up and the product was distilled at 0.25mm. using a column (50  $\times$  1 cm.) packed with glass helices. After the collection of starting material and an intermediate fraction (131.8 g.), b. p. 43-50°,  $n_{\rm D}^{20}$  1.5568, N-allyl-2,6-xylidine was obtained as a liquid (129.9 g., 81% based on allyl chloride), b. p. 50–53°,  $n_{\rm p}^{20}$  1.5343,  $\lambda_{\rm max}$  240 mµ ( $\epsilon$  5500);  $\nu_{max}$  3400 (NH), 990, and 920 cm.<sup>-1</sup> (CH=CH<sub>2</sub>), pure enough for rearrangement. The lower boiling fraction contained ca. 5% of N-allyl compound, which was recycled. The N-benzoyl derivative of N-allyl-2,6-xylidine had m. p. 71° (from hexane) (Found: C, 81.8; H, 7.3; N, 6.0. C<sub>18</sub>H<sub>19</sub>NO requires C, 81.5; H, 7.2; N, 5.3%).

(b) N-Allyl-2,6-xylidine (300 g., 1.86 mole) was stirred in refluxing xylene (800 ml.) with zinc chloride (300 g., 2.20 mole) during 4 hr. The mixture thickened and stopped the stirrer towards the end of this period. After cooling, the product was stirred with sodium hydroxide (200 g., 5 mole) in water (700 ml.). The upper layer was separated; residual undissolved solid was taken into warm hydrochloric acid (6N) and added to the aqueous alkaline layer. The additional organic material which separated was collected in ether and the combined amine fractions in ether were workedup and distilled at 0.5 mm. Distillate (23.8 g.), b. p. 50-83°,  $n_{\rm p}^{20}$  1.5472 contained ca. 8% of product and was recycled. 4-Allyl-2,6-xylidine (218 g., 73%) had b. p. 83—85°,  $n_{\rm D}^{20}$  1.5543,  $\lambda_{\rm max}$  240 and 290 mµ ( $\varepsilon$  8600 and 2000),  $\nu_{\rm max}$  doublet at *ca*. 3400, 1630 (NH<sub>2</sub>), 998, and 915 cm<sup>-1</sup>  $(CH=CH_2)$  (Found: C, 81.95; H, 9.4; N, 8.7.  $C_{11}H_{15}N$ requires C, 81.9; H, 9.4; N, 8.4%). N-Benzoyl derivative, m. p. 166° (from benzene-hexane) (Found: C, 80.9; H, 6.8; N, 5.9%).

(c) 2,6-Xylidine (1452 g., 12 moles) was heated at  $100^{\circ}$  for 8 hr. with allyl chloride (459 g., 6 moles) and then xylene (4.5 l.) was added. The solution was washed with 20% sodium hydroxide (1500 ml.), with saturated sodium chloride (3 × 500 ml.), and then dried by distillation of some of the xylene. Powdered zinc chloride (1636 g., 12 moles) was added and the mixture was stirred and heated under reflux for 2 hr.; it was cooled to room temperature and then decomposed with sodium hydroxide (1800 g.) in water (6 l.).

The alkaline layer was separated from the amine and extracted with ether (2 × 500 ml.). The combined organic layers were washed with saturated sodium chloride, dried by distillation of the solvents, and fractionated to give 4-allyl-2,6-xylidine (728 g., 73% based on unrecovered 2,6-xylidine), b. p. 80–82°/0·3 mm.,  $n_{\rm p}^{20}$  1·5534 after separation of fractions, b. p. 52–80°/0·3 mm. (706 g.), suitable for recycling.

Investigation of Rearrangement of N-Allyl-2,6-xylidine.— (a) The spectra of N-allyl-2,6-xylidine were unchanged after it had been heated alone at  $220^{\circ}$  for 2 hr.

(b) Action of heat on hydrochloride. N-Allyl-2,6-xylidine (16·1 g.) was heated gently with concentrated hydrochloric acid (10 ml.) until all the water had been driven off. At 230° (bath temperature) the solid melted. After maintaining this temperature for 15 min., the product was cooled, diluted with water, decomposed with 10% sodium hydroxide (100 ml.), extracted into ether, worked-up, and distilled at 15 mm. to give (identifications by i.r. spectra) mainly 2,6-xylidine and N-allyl-2,6-xylidine, with only a little 4-allyl-2,6-xylidine in the last fraction.

(c) 2,6-Xylidine (60.5 g., 0.5 mole), allyl chloride (38.3 g., 0.5 mole), and zinc chloride (75 g., 0.55 mole) were heated together under reflux for 6 hr. Work-up as before gave very little of the required product.

(d) Similarly, 2,6-xylidine (60.5 g., 0.5 mole), N-allyl-2,6-xylidine (80.5 g., 0.5 mole), and zinc chloride (75.0 g., 0.55 mole) in xylene (200 ml.) heated and stirred under reflux for 5 hr. gave only a low yield of 4-allyl-2,6-xylidine, together with much unchanged N-allyl-2,6-xylidine. Experiments (c) and (d) showed that zinc chloride equivalent to all the amine (primary and secondary) present was necessary.

N-Benzyl-2,6-xylidine.—Benzyl chloride (12·7 g., 0·1 mole) and 2,6-xylidine (24·2 g., 0·2 mole) were heated at 100° for 16 hr., after which the mixture was cooled and shaken with ether (100 ml.) and 10% sodium hydroxide (100 ml.) until dissolution was complete. The ether layer was worked-up and distilled to give 2,6-xylidine (13·4 g.) and N-benzyl-2,6-xylidine (14·4 g., 76% based on unrecovered starting material), b. p. 106—109°/0·1 mm.,  $n_{\rm D}^{20}$  1·5806,  $\lambda_{\rm max}$  244 m $\mu$  ( $\varepsilon$  7700),  $\nu_{\rm max}$  3400 cm.<sup>-1</sup> (NH) (Found: C, 84·6; H, 8·2; N, 7·1. C<sub>15</sub>H<sub>17</sub>N requires C, 85·3; H, 8·1; N, 6·6%).

Attempted Rearrangement with Zinc Chloride.—N-Benzyl-2,6-xylidine (10.5 g., 0.05 mole) and zinc chloride (7.5 g., 0.055 mole) were heated in refluxing xylene (50 ml.) for 5 hr. with stirring and then worked-up as in the corresponding N-allyl experiment. Distillation gave a 75%recovery of N-benzyl-2,6-xylidine but no 4-benzyl-2,6xylidine.

4-Benzyl-2,6-xylidine.—Benzyl chloride (126.5 g., 1 mole) and 2,6-xylidine (121 g., 1 mole) in a flask immersed to the neck in an oil-bath and protected by an air condenser were heated, cautiously at first to minimise sublimation, and then at 250° for 2 hr., when the reaction mixture crystallised. Prolonged trituration of the cooled reaction mixture with 10% sodium hydroxide (600 ml.), and then with ether (600 ml.) gave two liquid layers. The organic layer was worked-up and distilled to give 2,6-xylidine (17.5 g.), b. p. 54—58°/0·3 mm., 4-benzyl-2,6-xylidine (122.5 g., 68% based on unrecovered 2,6-xylidine), b. p. 143—150°/0·3 mm.,  $n_{\rm D}^{20}$ 1·6005,  $\lambda_{\rm max}$  243 and 293 mµ ( $\varepsilon$  9800 and 2200),  $\nu_{\rm max}$  1620, doublet at *ca.* 3400 cm.<sup>-1</sup> (NH<sub>2</sub>). The n.m.r. spectrum of a solution in CCl<sub>4</sub> had peaks at  $\tau 2.95$ 

## J. Chem. Soc. (C), 1967

(s, 5H; C<sub>6</sub>H<sub>5</sub>); 3·41 (s, 2H; equivalent aromatic H's); 6·27 (s, 2H; benzylic CH<sub>3</sub>); 6·75 (s, 2H, disappeared on adding D<sub>2</sub>O; NH<sub>2</sub>); 7·99 (s, 6H; two equivalent aromatic Me's) (Found: C, 85·3; H, 8·0; N, 7·0. C<sub>15</sub>H<sub>17</sub>N requires C, 85·3; H, 8·1; N, 6·6%). The crude residue from this distillation was recrystallised from ethanol to give 3,4-*dibenzyl*-2,6-*xylidine* (43·0 g., 17%), m. p. 110°,  $\lambda_{max}$  243 and 294 mµ ( $\varepsilon$ 10,200 and 2900),  $\nu_{max}$ . 1620, doublet at *ca*. 3400 cm.<sup>-1</sup> (NH<sub>2</sub>). The n.m.r. spectrum of a solution in CDCl<sub>3</sub> had peaks at  $\tau$  2·9 (multiplet, 10H; 2 × C<sub>6</sub>H<sub>5</sub>); 3·22 (s, 1H; aromatic H); 6·02 (s, 2H) and 6·14 (s, 2H) (benzylic CH<sub>2</sub>'s); 6·63 (s, 2H, disappeared on adding D<sub>2</sub>O; NH<sub>2</sub>); 7·82 (s, 3H) and 7·99 (s, 3H) (two non-equivalent aromatic Me's) (Found: C, 87·4; H, 7·6; N, 4·4. C<sub>22</sub>H<sub>23</sub>N requires C, 87·7; H, 7·7; N, 4·6%).

4-Allyl-2,6-Dimethylbromobenzene.—Sodium nitrite (315 g.) in water (600 ml.) was added to 4-allyl-2,6-xylidine (726 g.) in water (825 ml.) and hydrobromic acid (48%, 1350 ml.) at 0° with stirring. This solution was then added at room temperature with stirring to cuprous bromide (648 g.) in hydrobromic acid (1620 ml.) and benzene (750 ml.). After warming to complete nitrogen evolution, the upper benzene layer was separated and combined with a benzene extract of the lower layer. The benzene solution was washed with water (2 × 11.), dried (Na<sub>2</sub>SO<sub>4</sub>), and evaporated to remove benzene. The product was stirred with Claisen alkali <sup>11b</sup> (4·5 l.) at 50° for 30 min., then taken up in benzene (3 × 1500 ml.). The benzene solution was washed with 10% sulphuric acid (1500 ml.), and saturated

sodium chloride (2 × 1500 ml.), dried (Na<sub>2</sub>SO<sub>4</sub>), and the solvent evaporated; the residue was distilled to give 4-allyl-2,6-dimethylbromobenzene (600 g., 60%), b. p. 63—67°/0·1 mm.,  $n_{\rm D}^{20}$  1·5542 (Found: C, 58·9; H, 6·0. C<sub>11</sub>H<sub>18</sub>Br requires C, 58·7; H, 5·8%). A portion of the Claisen alkali was neutralised (H<sub>2</sub>SO<sub>4</sub>) and the liberated product taken up in benzene. The solution was washed (saturated sodium chloride), dried, and then distilled; only 4-allyl-2,6-xylenol was obtained, b. p. 132—134°/18 mm.,  $n_{\rm D}^{20}$  1·5389, identical (u.v., i.r., and other physical constants) with a specimen made from O-allyl-2,6-xylenol.<sup>2</sup>

4-Benzyl-2,6-dimethylbromobenzene.—A mixture of 4-benzyl-2,6-xylidine (42.2 g.), 48% hydrobromic acid (60 ml.), and water (100 ml.) was stirred at 0° and treated dropwise with sodium nitrite (14 g.) in water (25 ml.), when the slurry gradually became homogeneous. This solution was added to cuprous bromide (28.8 g.), 48% hydrobromic acid (36 ml.), and benzene (100 ml.) to give a mixture which was worked-up as in the preparation of 4-allyl-2,6-dimethylbromobenzene. Distillation gave 4-benzyl-2,6-dimethylbromobenzene (39.6 g., 72%), b. p. 117—120°/0·1 mm., m. p. 63° (Found: C, 65.7; H, 5.7; Br, 28.4. C<sub>15</sub>H<sub>15</sub>Br requires C, 65.5; H, 5.5; Br, 29.1%).

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