NOTES

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Absolute Configuration of 3-Amino-1-phenylbutane

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Synopsis. The absolute configuration of (−)-3-amino-1-phenylbutane was established by the correlation to (*R*)-(−)-*N*-benzoylalanine methylester *via* (+)-*trans*-3-amino-1-phenylbut-1-ene.

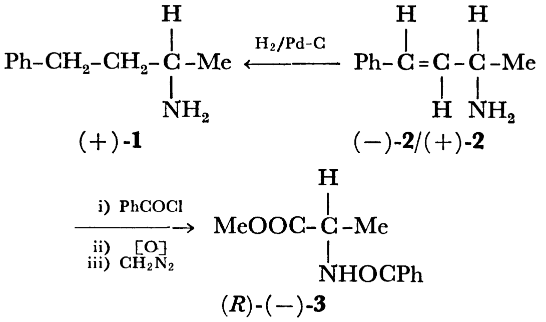
As regards the chirality of 3-amino-1-phenylbutane (**1**), two conflicting assignments have been made. Červinka[1] inferred the *R*-configuration to (+)-**1** by converting it into (+)-γ-*N*-benzoylaminovaleric acid whose configurational correlation had been achieved by the homologation of (*R*)-(−)-alanine.[2] In contrast, the opposite *S*-configuration was claimed for the same enantiomer (+)-(**1**) by Terent'ev based on chiroptical data.[3]

We were therefore inextricably confused by this situation and did not know which of these assignments should be relied upon as the correct one. Since the binary nature of chirality dictates *a priori* a 50 : 50 chance of predicting the correct configuration to a given chiral compound no matter what means one may employ, great caution must be exercised in drawing any conclusion on chirality. This is even more true because the deduced configuration may possibly divert one to an erroneous stereochemistry of asymmetric synthesis.[4]

In connection with the studies on self-immolative asymmetric synthesis, we established the absolute configuration of (+)-*trans*-3-amino-1-phenylbut-1-ene (+)-(**2**) by means of the independent chemical transformations[5] and, by virtue of this assignment, settled the disputed problem of the chirality of 3-amino-1-phenylbutane. (+)-3-Amino-1-phenylbut-1-ene (+)-(**2**) was converted to the *N*-benzoyl derivative and then was oxidized by the use of barium permanganate eventually to give (−)-*N*-benzoylalanine methylester (−)-(**3**). Since the *R*-configuration of the latter has been unequivocally established,[6] the parent amine (+)-(**2**) can be assigned the same configuration in view of the present conversion process, which does not jeopardize the chiral center.

Since the unsaturated amine (−)-(**2**) afforded the corresponding saturated amine with dextrorotation (+)-(**1**) on catalytic hydrogenation over palladium carbon[4], which is generally accepted to proceed without disturbing the chiral center, (−)-3-amino-1-phenylbutane (−)-(**1**) should be allotted the *R*-configuration in support of Terent'ev.[3]

The present transformations, when linked to those by Červinka,[1] Fischer,[7] and Balenović,[2] constitute a triligostatic stereochemical cycle[8] which involves (−)-*N*-benzoylalanine as one of the chiromers. The ligand metathesis is *a priori* ruled out for a triligostatic cycle and all the unit reactions involved in the cycle are of such a nature that no inversion of configuration occurs, so that this cycle is podal. In consequence, the disagreement between Červinka's configurational assignment and ours to **1** suggests a probable experimental fault committed in either the Červinka, Fischer, or Balenović process, inasmuch as the present chemical transformations are convincingly faultless.



$$\mathrm{Ph\text{-}CH_2\text{-}CH_2\text{-}\overset{\displaystyle H}{\underset{\displaystyle NH_2}{C}}\text{-}Me} \xleftarrow{\mathrm{H_2/Pd\text{-}C}} \mathrm{Ph\text{-}\overset{\displaystyle H}{C}{=}\underset{\displaystyle H}{C}\text{-}\overset{\displaystyle H}{\underset{\displaystyle NH_2}{C}}\text{-}Me}$$

(+)-**1** (−)-**2**/(+)-**2**

$$\xrightarrow[\mathrm{ii)\ [O]\quad iii)\ CH_2N_2}]{\mathrm{i)\ PhCOCl}} \mathrm{MeOOC\text{-}\overset{\displaystyle H}{\underset{\displaystyle NHOCPh}{C}}\text{-}Me}$$

(*R*)-(−)-**3**

Experimental

(+)-3-Amino-1-phenylbutane (+)-(***1***). (*S*)-(−)-*trans*-3-Amino-1-phenylbut-1-ene[5] (−)-(**2**) (5.0 g, $[\alpha]_D^{25}$ −8.9° (*c*, 10.0, benzene) was hydrogenated over palladium carbon in ethanol and an equivalent amount of hydrogen (830 ml at 25 °C) was absorbed. The resulted amine (**1**) distilled at 108—109 °C/18 Torr.; n_D^{27} 1.5081, $[\alpha]_D^{27}$ 10.1° (neat), (lit,[1] bp 110—115 °C/14 Torr., (lit,[9] bp 101—102 °C/14 Torr., n_D^{20} 1.5152 for the racemate). The acetylation of (+)-**1** (4.6 g) with acetic anhydride in pyridine afforded (−)-3-acetamido-1-phenylbutane (5.6 g, 95%); bp 149 °C/2 Torr., mp 68—69 °C, $[\alpha]_D^{26}$ −35.2° (*c*, 0.7, ethanol), (lit,[1] bp 142—150 °C/3 Torr., mp 55 °C). Found: C, 75.33; H, 9.11; N, 7.38%. Calcd for $C_{12}H_{17}NO$: C, 75.35; H, 8.96; N, 7.32%.

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