ASYMMETRIC SYNTHESIS USING α -SULFINYLCARBANIONS. II. SYNTHESIS OF OPTICALLY ACTIVE AMINES

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Recently we have reported the synthesis of optically active alcohols from aldehydes, ketones, and oxiranes using optically active p-tolylsulfinylcarbanion(2) which is easily prepared from the corresponding sulfoxide (1) by the action of lithium diethylamide.¹⁾ Now we would like to describe the synthesis of optically active amines from imines and nitriles by the extension of the same method.



Addition of N-benzylideneaniline(3) to a solution of p-tolylsulfinylcarbanion(2) which was prepared from (R)-(+)-methyl p-tolyl sulfoxide(1), $(\alpha)_{\rm D}$ +181.9°,²⁾ with lithium diethylamide in tetrahydrofuran at -10 to -20°C produced, after the usual work-up, the adduct(4) as yellowish crystals. The NMR spectrum of the crude 4 disclosed that only one isomer was obtained stereospecifically. Recrystallization from chloroform-benzene-cyclohexane furnished (R_S, S_C)-(+)-N-phenyl-2-amino-2-phenylethyl p-tolyl sulfoxide(4), mp 216-217°C, $(\alpha)_{\rm D}$ +209.7°(CHCl₃), in a 70% yield. Keductive desulfurization of 4 with Raney-nickel produced (R)-(-)-N-phenyl- α -phenethylamine(5), mp 45.5-47°C(lit.³⁾ mp 48.5-50°C), $(\alpha)_{\rm D}$ -18.1°(MeOH), in an 81% yield, after alumina chromatography. Since the specific rotation of optically pure 5 is reported to be $(\alpha)_{578}$ 17.7, 18.5, or 19.5°,³⁾ the amine(5) was obtained in high optical purity by this method.



It is noteworthy that in this reaction only one isomer of two possible diastereomers was produced stereospecifically by asymmetric induction of the chiral tricoordinate sulfinyl sulfur and easily isolated in a 70% yield by recrystallization.

Reaction of p-tolylsulfinylcarbanion(2) from the corresponding sulfoxide $((\alpha)_D + 186.9^{\circ})^{2})$ with benzonitrile(6) gave 2-imino-2-phenylethyl p-tolyl sulfoxide(7) quantitatively as yellowish crystals. As 7 was unstable at room temperature, the crude 7 was immediately reduced with NaBH₄ in methanol to give a (1:1) diastereomeric mixture of 2-amino-2-phenylethyl p-tolyl sulfoxide(8a,b) in an 82.5% yield.⁴⁾ The amine(8a,b) was acetylated with acetic anhydride in pyridine to produce 2-acetylamino-2-phenylethyl p-tolyl



sulfoxide (9a,b) quantitatively. By fractional recrystallizations from chloroform-hexane and benzene-hexane, (R_S , R_C)-(+)-isomer(9a), mp 200-202°C, (α)_D +70.2°(CHCl₃), was isolated in a 27.4% yield,⁴) while by concentration of the mother liquor followed by fractional recrystallizations from chloroformhexane and chloroform-ethyl acetate, (R_S , S_C)-(+)-isomer(9b), mp 203-206°C, (α)_D +182.5°(CHCl₃), was isolated in a 27.4% yield.⁴) Desulfurization of 9a with Raney-nickel gave (S)-(-)-N-acetyl- α -phenethylamine(10a), mp 99-101°C (lit.⁵) mp 104°C), (α)_D -152.5°(EtOH), in a 66.5% yield, and desulfurization of 9b gave (R)-(+)-isomer(10b), mp 103-104°C, (α)_D +148.1°(EtOH), in a 64.7% yield. As the reported specific rotation of optically pure N-acetyl- α phenethylamine is (α)_D 168.1°,⁵) 10a was obtained in a 91% optical purity while 10b was obtained in an 88% optical purity.

Reaction of p-tolylsulfinylcarbanion($(\alpha)_D$ +184°)²) with hexanenitrile (11) followed by NaBH₄-reduction in methanol furnished in a 44% yield^{4,6}) a (1:1) diastereometric mixture of 2-aminoheptyl p-tolyl sulfoxide(12a,b) which was acetylated with acetic anhydride in pyridine to give 2-acetylaminoheptyl p-tolyl sulfoxide(13a,b) quantitatively. By fractional recrystallizations of 13a,b from benzene-hexane, 13a, mp 138.5-140°C, $(\alpha)_D$ +132.7°(CHCl₂), was





isolated in an 18% yield,⁴⁾ while by silica gel chromatography of the mother liquor, 13b, mp 122.5-124.5°C, $(\alpha)_D$ +205.1°(CHCl₃), was isolated in a 12% yield.⁴⁾ Desulfurization of 13a and 13b with Raney-nickel produced (R)-(-)-2-acetylaminoheptane(14a),⁷⁾ mp 53-54°C, $(\alpha)_D$ -8.6°(EtOH), and (S)-(+)-isomer (14b),⁷⁾ mp 53.5-54.5°C, $(\alpha)_D$ +11.2°(EtOH), in 69% yields, respectively.

Thus, the optically active p-tolylsulfinylcarbanion(2) is a versatile reagent for the synthesis of optically active amines from imines and nitriles as well as optically active alcohols from aldehydes, ketones, and oxiranes.¹⁾

REFERENCES AND REMARKS

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- 3. G. Wittig and U. Thiele, Ann. Chem., <u>726</u>, 1(1969).
- 4. The yields are based on 1.
- 5. A. Campbell and J. Kenyon, J. Chem. Soc., 25(1946).
- 6. Since 47.2% of the starting sulfoxide(<u>1</u>) was recovered with high optical purity($(\alpha)_D$ +188°), the conversion yield is 93%.⁴) The low isolation yield may be due to the formation and side-reaction of α -anion of hexanonitrile (11).
- 7. The absolute configuration of the asymmetric center of 14a or 14b is unknown, but (R)- and (S)-configurations were tentatively assigned to 14a and 14b respectively, on the basis of the fact that N-benzoylation of (S)-(+)-2-aminohexane([α]_D +4.30°) gave (S)-(+)-2-benzoylaminohexane ((α)_D +14.3°) of the same sign. See P. A. Levene, A. Rothen, and M. Kuna, J. Biol. Chem., 120, 759(1937) and J. H. Brewster, J. Amer. Chem. Soc., 81, 5475(1959).