Pergamon

Tetrahedron: Asymmetry Vol. 6, No. 7, pp. 1535-1538, 1995
Elsevier Science Ltd
Printed in Great Britain
0957-4166/95 $9.50+0.00

0957-4166(95)00192-1

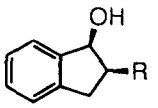
Synthesis of Enantiomerically Pure *cis* and *trans*-2-Amino-1-indanol.

Anton Mitrochkine †, Gérard Gil ‡, and Marius Réglier †*.

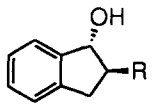
† Laboratoire de Bioinorganique Structurale and ‡ Laboratoire de Bioconversions-URA CNRS 1409 C12,
Faculté des Sciences de Saint Jérôme, Avenue Escadrille Normandie-Niemen 13397 Marseille Cedex 20, France.

Abstract: Enantiomerically pure *cis* and *trans*-2-amino-1-indanols **1** and **2** were synthesized *via* a highly enantioselective lipase catalyzed transesterification of racemic *cis*-2-azido-1-indanol **3**.

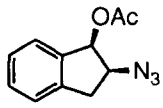
Enantiomerically pure aminoindanols constitute widely studied structures of interest for pharmacophore producing dopamimetic activity,[1] as metabolites of aminoindane in urine of rabbits and rats,[2] as components of the inhibitor of a key enzyme in the human immunodeficiency virus (HIV),[3] and as highly efficient chiral ligands in titanium catalyzed asymmetric Diels Alder reactions [4] or borane reductions of aromatic ketones.[5] Moreover, we have observed that 2-amino-1-indanol is a metabolite[6] of dopamine β-hydroxylase (DBH),[7] a copper-containing monooxygenase which catalyses the transformation of dopamine into noradrenaline. In the course of these studies, the need for preparing useful quantities of the four enantiomerically pure aminoindanols **1** and **2** became apparent.



1 (R = NH_2)
3 (R = N_3)



2 (R = NH_2)
4 (R = N_3)
5 (R = Br)



6

Enantiomerically pure 2-amino-1-indanols **1** and **2** have been prepared by reduction of 2-hydroxyimino-1-indanone followed by resolution with tartaric acid [8] or by Friedel-Crafts cyclisation of (-) and (+) phenylalanine.[9]

Recently, we have described the preparation of (1*S*, 2*R*)-2-amino-1-indanol **1a** by reduction of (1*S*, 2*R*)-2-azido-1-indanol **3a** obtained *via* enantioselective lipase catalyzed transesterification of racemic *trans*-2-bromo-1-indanol **5**.[10] By this way it was not possible to obtain enantiomer (1*R*, 2*R*)-**5** in higher enantiomeric excess than 70%. A preparative kinetic resolution of racemic *cis*-2-azido-1-indanol **3** with lipases has been considered instead. Results obtained with seven lipases in organic solvent and vinyl acetate as acyl donor are shown in table 1.[11] After 4 days, LP 237.87 lipase gave 75% of acetate (1*R*, 2*S*)-**6a** with low enantiomeric

excess (e. e. = 21%) but the 25% of remaining azidoalcool (1*S*, 2*R*)-**3a** were obtained in high enantiomeric purity (e. e. 95%; 99% after recrystallization from carbon tetrachloride). On the other hand, the lipase of *Mucor Javanicus* produced acetate (1*R*, 2*S*)-**6a**. with 95% e. e. and 20% yields. The results with the lipase of *Candida Antartica* A which gave the opposite diastereoisomer (1*R*, 2*S*)-2-azido-1-indanol **3b** in 93% e. e. (99% after recrystallization from carbon tetrachloride) after 10 days and 66% conversion were more interesting.

Table 1. Lipase catalyzed transesterification of racemic *cis*-2-azido-1-indanol **3**.

Lipases	Reaction Times in days	*cis*-1-acetoxy-2-azidoindane 6			*cis*-2-azido-1-indanol 3		
		Yields	Config.	e. e. [i]	Yields	Config. [ii]	e. e. [i]
LP 237.87 [iii]	4	75%	(1*R*, 2*S*)	21%	25%	(1*S*, 2*R*)	95%(99%)
Mucor Miehi	20	15%	(1*R*, 2*S*)	2%	85%	(1*S*, 2*R*)	4%
Mucor Javanicus	20	20%	(1*R*, 2*S*)	95%	80%	(1*S*, 2*R*)	6%
Mucor Genevenis	20	6%	(1*R*, 2*S*)	20%	94%	(1*S*, 2*R*)	5%
LCC	3	3%	(1*S*, 2*R*)	2%	2%	(1*R*, 2*S*)	2%
C. Antartica A [iv]	10	66%	(1*S*, 2*R*)	35%	34%	(1*R*, 2*S*)	93% (99%)
C. Antartica B [iv]	5	6%	(1*S*, 2*R*)	12%	94%	(1*R*, 2*S*)	5%

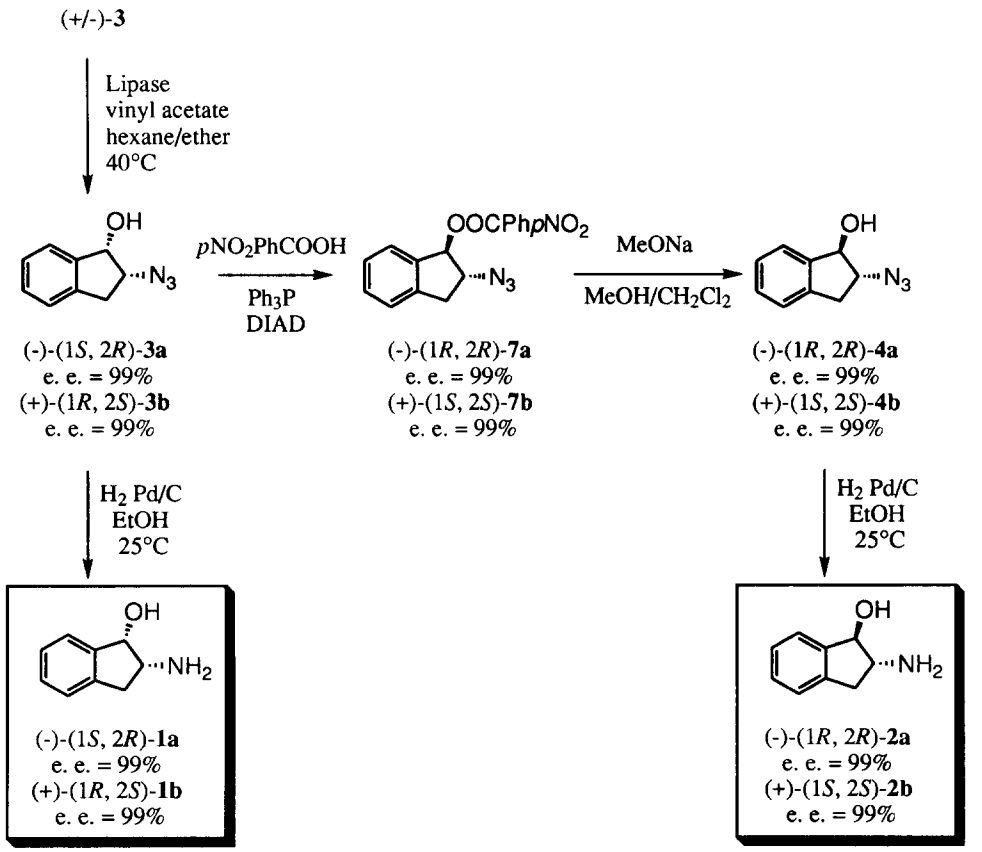
[i] In parentheses, e. e. after recrystallization from carbon tetrachloride. e. e determined by HPLC using Chiralcel column OD-H (Daicel) with hexane/isopropyl alcohol (98:2) as eluant. [ii] From the $[\alpha]_D^{25} = +53$ (*c* 1, $CHCl_3$) for (1*R*, 2*S*) enantiomer (Ref. 4). [iii] Gist Brocades. [iv] Novo.

The transformations outlined in scheme 1 were performed with enantiomerically pure *cis*-2-azido-1-indanol **3a** and **3b**[12] resulting from, respectively, the reaction of lipases LP 237.87 and *Candida Antartica A*. Hydrogenation of *cis*-2-azido-1-indanol **3a** and **3b** in ethanol catalyzed by palladium on charcoal gave, respectively, enantiomerically pure *cis*-2-amino-1-indanol **1a** and **1b**[13] in quantitative yields (99%). The reaction of cis-2-azido-1-indanol **3a** and **3b** with *para*-nitrobenzoic acid under Mitsunobu conditions,[14] afforded respectively *trans*-benzoic esters **7a** and **7b**[15] in good yields. By treatment with MeONa in $MeOH/CH_2Cl_2$, *trans*-benzoic ester **7a** and **7b** were transformed into enantiomerically pure *trans*-2-azido-1-indanol **4a** and **4b**[16] in quantitative yields and 99% e. e. (determined by HPLC on Daicel Chiralcel column OD-H with hexane/isopropyl alcohol (98:2) as eluant). Hydrogenation in ethanol catalyzed by palladium on charcoal gave *trans*-2-amino-1-indanol **2a** and **2b**[17] quantitatively and enantiomerically pure form.

In summary, enantioselective lipase catalyzed transesterification of racemic *cis*-2-azido-1-indanol **3** followed by simple chemical transformations (Mitsunobu inversion, hydrogenation) provides all four stereoisomers of 2-amino-1-indanol in good yields and high enantiomeric excess.

Acknowledgments: We are grateful to C. N. R. S. for financial support, the French Government for a grant to A. Mitrochkine and Gist Brocades and Novo companies for the lipases. We are indebted to the Pr. C. Roussel (ENSSPICAM, Marseilles) for suggestions concerning the enantiomeric excess determinations.

Scheme 1. Synthesis of enantiomerically pure *cis* and *trans*-2-amino-1-indanols **1a,b** and **2a,b**.



References and Notes:

1 Hagishita, S.; Shiro, M.; Kuriyama, K. *J. Chem. Soc. Perkin Trans. I* **1984**, 1655.

2 Irino, O.; Tateishi, M.; Miura, C.; Fukawa, K. *Chem. Pharm. Bull.* **1972**, *20*, 734.

3 Tompson, W. J.; Fitzgerald, P. M. D.; Holloway, M. K.; Emini, E. A.; Darke, P. L.; McKeever, B. M.; Schleif, W. A.; Quintero, J. C.; Zugay, J. A.; Tucker, T. J.; Schwering, J. E.; Hommick, C. F.; Numberg, J.; Spinger, J. P.; Huff, J. R. *J. Med. Chem.* **1992**, *35*, 1685.
Moon Kim, B.; Guare, J. P.; Hanifin, C. M.; Arford-Bickerstaff, D. J.; Vacca, J. P.; Ball, R. G. *Tetrahedron Lett.* **1994**, *35*, 5135.

4 Corey, E. J.; Roper, T. D.; Ishihara, K.; Sarakinos, G. *Tetrahedron Lett.* **1993**, *34*, 8399.

5 Hong, Y.; Gao, Y.; Nie, X.; Zepp, C. M. *Tetrahedron Lett.* **1994**, *35*, 6631.
Di Simone, B.; Savoia, D.; Tagliavini, E.; Umani-Ronchi, A. *Tetrahedron: Asymmetry* **1995**, *6*, 301.

6 Mitrochkine, A.; Eydoux, F.; Réglier M. to be published.

7 Klinman, J. P. *Ann. Rev. Biochem.* **1988**, *57*, 551.

8 Rimek, H-J.; Yupraphat, T.; Zymalkowski, F. *Liebigs Ann. Chem.* **1969**, *725*, 116.
Desimondi, G.; Faita, G.; Mellerio, G.; Righetti, P. P.; Zanelli, C. *Gazz. Chim. Ital.* **1992**, *122*, 269.

9 Dornhege, E. *Liebigs Ann. Chem.* **1971**, *743*, 42.
McClure, D. E.; Arison, B. H.; Jones, J. H.; Baldwin, J. J. *J. Org. Chem.* **1981**, *46*, 2433.

10 Mitrochkine, A.; Eydoux, F.; Martres, M.; Gil, G.; Heumann, A.; Réglier, M. *Tetrahedron: Asymmetry* **1995**, *6*, 59.

11 Faber, K.; Riva, S. *Synthesis* **1992**, 895.
Chen, C. S.; Sih, C. J. *Angew. Chem. Int. Ed. Eng.* **1989**, *28*, 695.
Boland, W.; Frössl, C.; Lorenz, M. *Synthesis* **1991**, 1049.

12 *cis*-2-azido-1-indanol **3**. ^{1}H N.M.R. (200 MHz, $CDCl_3$, δ in ppm/TMS): 2.42 (d; *J* 8,3 Hz; 1H); 3.14 (d; *J* 4.6 Hz; 2); 4.32 (dt; *J* 4.6, 4.0 Hz; 1H); 5.13 (d; *J* 4 Hz; 1); 7.20-7.50 (m; 4H). ^{13}C N.M.R. (50 MHz, $CDCl_3$, δ in ppm/TMS): 35.2 (CH_2), 65.7 (CH), 76.4 (C_1), 124.7 (CH), 125.1 (CH), 127.6 (CH), 129.0 (CH), 139.0 (C), 141.6 (C). (-)-(1*S*, 2*R*)-**3a** $[\alpha]_D^{25}$ - 112.0 (*c* 11 $CHCl_3$). (+)-(1*R*, 1*S*)-**3b** $[\alpha]_D^{25}$ +109.8 (*c* 11, $CHCl_3$).

13 *cis*-2-amino-1-indanol **1**. ^{1}H N.M.R. (200 MHz, $CDCl_3$, δ in ppm/TMS): 2.15 (bs; 1H), 2.75 (dd; *J* 15.8, 5.1 Hz; 1H), 3.15 (dd; *J* 15.8, 6.6 Hz; 1H), 3.75 (dt; *J* 6.6, 5.5, 5.1 Hz; 1H), 4.82 (d; *J* 5.5 Hz; 1H), 7.15-7.6 (m; 4H). ^{13}C N.M.R. (50 MHz, $CDCl_3$, δ in ppm/TMS): 41.1 (CH_2), 56.8 (CH); 77.2 (CH), 126.7 (CH), 126.8 (CH), 129.0 (CH), 130.5 (CH), 143.0 (C), 145.4 (C). (-)-(1*S*, 2*R*)-**1a** $[\alpha]_D^{25}$ - 60.6 (*c* 5, $CHCl_3$). (+)-(1*R*, 2*S*)-**1b** $[\alpha]_D^{25}$ + 63.0 (*c* 5, $CHCl_3$).

14 Mitsunobu, O. *Synthesis* **1981**, 1.
Hughes, D. L. *Organic Reactions* **1992**, *42*, 335.
Warmerdam, E. G. J. C.; Brussee, J.; Kruse, C. G.; van der Gen, A. *Tetrahedron* **1993**, *49*, 1063.

15 *para*-nitrobenzoic-*trans*-2-azido-1-indanyl ester **7**. ^{1}H N.M.R. (200 MHz, $CDCl_3$, δ in ppm/TMS): 3.0 (dd; *J* 16, 5.6 Hz; 1H), 3.5 (dd; *J* 16, 7.7 Hz; 1H), 4.35 (dt; *J* 7.7, 5.6, 4.3 Hz; 1H), 6.43 (d; *J* 4.3 Hz; 1H), 7.3-7.4 (m; 4H), 8.2-8.3 (m; 4H). ^{13}C N.M.R. (50 MHz, $CDCl_3$, δ in ppm/TMS): 30.4 (CH_2), 60.6 (CH), 70.7 (CH), 117.9 (2 CH), 125.2 (2 CH), 119.4 (CH), 119.9 (CH), 122.1 (CH), 124.3 (CH), 129.3 (CH), 131.9 (CH), 134.6 (C), 144.9 (C), 158.7 (C). (-)-(1*R*, 2*R*)-**7a**: $[\alpha]_D^{25}$ - 106.7 (*c* 9, $CHCl_3$). (+)-(1*S*, 2*S*)-**7b**: $[\alpha]_D^{25}$ + 112.0 (*c* 11, $CHCl_3$)

16 *trans*-2-azido-1-indanol **4**. ^{1}H N.M.R. (200 MHz, $CDCl_3$, δ in ppm/TMS): 2.30 (s; 1H); 2.75 (dd; *J* 16.0, 8.0 Hz; 1H); 3.2 (dd; *J* 16.0, 8.0 Hz; 1H); 4.0 (dt; *J* 8.0, 6.0 Hz; 1H); 5.0 (d; *J* 6.0 Hz; 1H); 7.1-7.3 (m; 4H). ^{13}C N.M.R. (50 MHz, $CDCl_3$, δ in ppm/TMS): 35.1 (CH_2), 69.2 (CH), 80.3 (CH), 123.9 (CH), 124.9 (CH), 127.6 (CH), 128.9 (CH), 138.4 (C), 141.5 (C). (-)-(1*R*, 2*R*)-**4a** $[\alpha]_D^{25}$ -34 (*c* 11, $CHCl_3$). (+)-(1*S*, 2*S*)-**4b** $[\alpha]_D^{25}$ + 32 (c 11, $CHCl_3$).

17 *trans*-2-amino-1-indanol **2**. ^{1}H N.M.R. (200 MHz, $CDCl_3$, δ in ppm/TMS): 2.0 (bs; 3H), 2.65 (dd; *J* 15.3, 8.0 Hz; 1H), 3.25 (dd; *J* 15.3, 8.0 Hz; 1H), 3.45 (dt; *J* 8.0, 6.5 Hz; 1H), 4.82 (d; *J* 6.5 Hz; 1H), 7.15-7.60 (m; 4H). ^{13}C N.M.R. (50 MHz, $CDCl_3$ δ in ppm/TMS), 38.8 (CH_2), 62.9 (CH), 82.4 (CH), 123.7 (CH), 124.7 (CH), 126.9 (CH), 128.1 (CH), 139.5 (C), 143.3 (C). (-)-(1*R*, 2*R*)-**2a** $[\alpha]_D^{25}$ - 15.0 (*c* 5 $CHCl_3$). (+)-(1*S*, 2*S*)-**2b** $[\alpha]_D^{25}$ + 13.4 (*c* 5 $CHCl_3$).

(*Received in UK* 15 *May* 1995)