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Registry No. 1, 24397-89-5; **1a**, 88549-75-1; **3**, 88549-76-2; **4**, 88549-78-4; **5**, 88549-79-5; **6**, 88549-80-8; **7**, 88549-81-9; **8**, 88549-82-0; **9**, 88549-83-1; **10**, 88549-84-2; **11**, 88549-85-3; **12**, 88549-86-4; **12a**, 88549-94-4; **13**, 88549-87-5; **14**, 88549-88-6; **15**, 88549-89-7; **16**, 88549-90-0; **16** (*exo*-methylene derivative), 88549-91-1; **17**, 88549-92-2; **18**, 88549-93-3; **18a**, 88549-95-5; (*E*)-EtOCCH=CHCOCl, 26367-48-6; Z-Ala, 1142-20-7; L-threonine, 72-19-5; acrolein, 107-02-8.

Supplementary Material Available: Structural and physical data for Scheme I and X-ray data (9 pages). Ordering information is given on any current masthead page.

Complete Intramolecular Transfer of a Central Chiral Element to an Axial Chiral Element. Oxidation of (*S*)-4-Naphthyldihydroquinolines to (*S*)-4-Naphthylquinolines

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Asymmetric induction has become one of the cornerstones in modern synthetic methodology leading to a host of enantiomerically enriched compounds (EEC) and enantiomerically pure compounds (EPC).[1] The use of so-called chiral auxiliaries to induce biased stereochemical changes has allowed investigators to form C–H, C–C, C–O, and C–N bonds with high enantioselectivity (>90%) and enantiomerically pure compounds after removal of the auxiliary. Rare among these enantioselective processes is the *inter*molecular transfer of chirality[2] or the *intra*molecular transfer of chiral elements or stereogenic units[3] (that portion of the molecule where the symmetry is perturbed).[4]

In 1955 Berson[5] proposed an experiment to transform a chiral 4-aryl-1,4-dihydropyridine to a 4-arylpyridine with simultaneous destruction of the chiral element at C-4 in the former to an axial chiral element in the latter. Due to experimental difficulties the postulate that transfer of these chiral elements should occur could not be verified. Since that time, processes that involve conservation of chirality with simultaneous creation and destruction of chiral elements have come to be known as "self-immolative",[6] and examples are still rare. Although central to axial chiral element transfers (or vice versa) have been observed in allene systems[7] and a hetero-ene reaction,[8] we are unaware of any reports describing the type Berson sought to uncover, namely in the biaryl series.[9] We now report that this process indeed occurs, as Berson predicted, for the chiral dihydroquinoline *S*-**6a** to the quinoline *S*-**7** with >95% conservation of chirality. Our experiments were founded on an earlier observation in which pyridines and quinolines containing a chiral oxazoline in the 3-position led to high diastereoselective addition with organometallics to furnish 4-substituted-1,4-dihydropyridines or quinolines.[10,11] Thus, addition of naphthyllithium to the quinoline oxazoline **1** gave the dihydro derivative **2** (90%), which was analyzed for diastereomeric excess using HPLC. By converting an aliquot to the urethane **2a**, an 88:12 mixture of **2a**:**4a** was observed (reverse phase, 9:1 MeOH–H_2O, accuracy was ±1%). The remainder of **2** was then oxidized with dichlorodicyanoquinone (DDQ) in THF at −78 °C to give

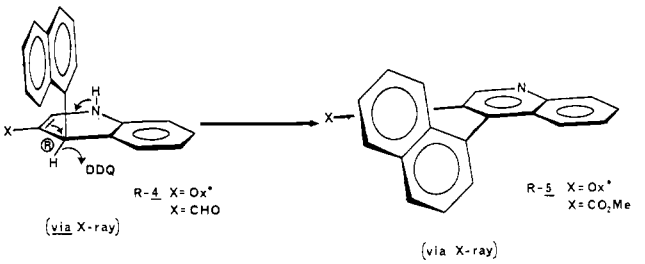
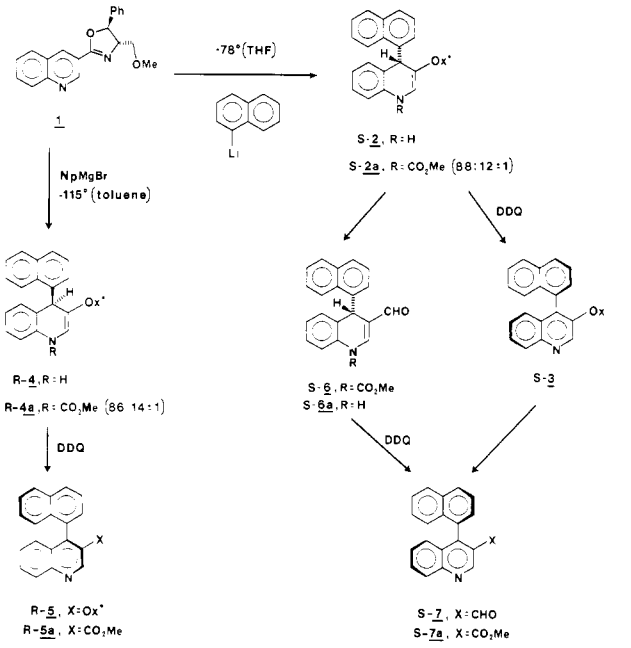


Figure 1.

Scheme I



(1) "Asymmetric Synthesis–A Multivolume Treatise", Morrison, J. D., Ed.; Academic Press: New York, 1984. "Modern Synthetic Methods"; Scheffold, R., Ed.; Verlag Sauerlander: Frankfurt, **1979**. Scott, J.; Valentine, D. *Synthesis* **1978**, 329. Apsimon, J. W.; Segun, R. P. *Tetrahedron* **1979**, *35*, 2797.

(2) The first example of a true chirality transfer in an intermolecular process was described for the reaction of (*S*)-2-octanol and (*S*)-pinacolyl alcohol with a bridged biphenyl ketone in the presence of aluminum *tert*-butoxide to give an optically active biphenyl: Newman, P.; Rutkin, P.; Mislow, K. *J. Am. Chem. Soc.* **1958**, *80*, 465. For a related example, see: Morrison, J. D.; Ridgway, R. W. *J. Org. Chem.* **1974**, *39*, 3107.

(3) For a discussion on these and other terms and their usage to define stereochemical properties, see: Prelog, V.; Helmchen, G. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 567. Mislow, K.; Siegel, J. *J. Am. Chem. Soc.*, submitted for publication.

(4) Warnhoff, E. W.; Lopez, S. V. *Tetrahedron Lett.* **1967**, 2723.

(5) Berson, J. A., Brown, E. *J. Am. Chem. Soc.* **1955**, *77*, 450.

(6) Mislow, K. "Introduction to Stereochemistry"; W. A. Benjamin: New York, 1966; p 12. Morrison, J. D.; Mosher, H. S. "Asymmetric Organic Reactions"; Prentice-Hall: Englewood Cliffs, NJ, 1971; pp 384–390.

(7) Hayashi, T.; Okamoto, Y.; Kumada, M. *Tetrahedron Lett.* **1983**, *24*, 807. Elsevier, C. J.; Stehouwer, P. M.; Westmijze, H.; Vermeer, P. *J. Org. Chem.* **1983**, *48*, 1103. "Stereochemistry"; Kagan, H., Ed.; Georg Thieme Verlag: Stuttgart, 1977; Vol. 3, pp 10–11.

(8) Bertrand, M.; Roumestant, M. L.; Sylvestre-Panthet, P. *Tetrahedron Lett.* **1981**, *22*, 3589.

(9) The transformation of thebaine to phenyldihydrothebaine wherein four asymmetric centers are destroyed to give an optically active biphenyl was studied by: Berson, J. A. *J. Am. Chem. Soc.* **1956**, *78*, 4170. However, this is a special case where the complexity of the molecule may play a significant role. Berson, realizing this problem, attempted to study an unencumbered system in simple 4-arylpyridines.[5]

(10) Meyers, A. I.; Natale, N. R.; Wettlaufer, D. G. *Tetrahedron Lett.* **1981**, *22*, 5123.

(11) For the synthesis of chiral binaphthyls using chiral or achiral oxazolines by direct substitution of alkoxy by organometallics, see: Meyers, A. I.; Lutomski, K. A. *J. Am. Chem. Soc.* **1982**, *104*, 879. Cram, D. J.; Wilson, J. *Ibid.* **1982**, *104*, 881.

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the 1-naphthyl-4-quinoline *S*-**3** (87%). The latter, on HPLC (reverse phase, 8.2:1 MeOH-H_2O) gave an 84:16 ratio of diastereomers indicating that the oxidation proceeded with virtually complete conservation of chirality albeit in the presence of the chiral oxazoline. When the process was repeated using **1** and naphthylmagnesium bromide, the epimeric dihydroquinoline **4** was the major product as determined by HPLC analysis of the urethane **4a**. The ratio of **4a**:**2a** was 86:14. Oxidation of **4** with DDQ (THF, -78 °C) gave the biaryl **5** (80%) whose diastereoisomeric composition was assessed (HPLC) as 88:12 ± 1% indicating once again that **5** was formed with virtually complete conservation of chirality (Scheme I). Thus, a synthesis enriched in either diastereomer was in hand, and each was oxidized with virtually complete destruction of the stereochemistry at C-4 and the creation of the axial chiral element in **3** and **5**, respectively. An X-ray structure determination was performed on the pure *t*-Boc derivative of **4**[12] after removal of the contaminating epimer **2** by radial chromatography (EtOAC-hexane) and then crystallization (CH_2Cl_2-pentane). HPLC analysis confirmed the total purity of **4** (R = *t*-Boc) and complete absence of **2**.

The X-ray structure of **4** indicates that the absolute configuration of the newly created chiral element is *R*. Since the *R* center in **4** came from Grignard addition, the *S* center in **2** undoubtedly arose from naphthyllithium addition. An X-ray structure determination was also performed on the biaryl **5**,[13] which was purified from its epimer **3** by chromatography and crystallization as above. The configuration due to the axial chiral element in **5** was shown to be *R* (Figure 1).[14] The oxazoline was removed from **5** by hydrolysis (6MH_2SO_4, reflux) to the carboxylic acid and immediately transformed into the methyl ester *R*-**5a** [mp 101-102.5 °C, $[\alpha]_D$ +13.16° (*c* 1.1, $CHCl_3$)].

The oxidation of **4** to **5** with complete conservation of chirality raised a concern over whether the naphthalene addition to **1** gave rise to *two* elements of chirality and oxidation merely removed the chirality element at C-4, leaving the naphthalene ring in the observed configuration. This concern arises if there is hindered rotation of the naphthalene ring in **2** and **4**. However, NMR studies at temperatures between +45 and -80 °C indicate clearly that the barrier to naphthalene rotation is below 18 kcal and therefore it is free to rotate[15] in agreement with other studies on 9-arylxanthyls,[16a] 9-arylthioxanthyl,[16b] and 9-arylfluorenes.[17] Furthermore, oxidation of **2** or **4** gave identical ratios of **3** and **5** at all temperatures in the range of -78 to +40 °C. This is strong support that, although naphthalene rotation is occurring, access to the hydrogen at C-4 in *R*-**4** is only possible when the nonconnective benzene ring is as far as possible from the hydride to be removed, thus leading to *R*-**5**. The previous results may be considered adequate proof of the Berson postulate for central to axial transfer by conversion of *S*-**2** to *S*-**3** (or *R*-**4** to *R*-**5**). However, the presence of the oxazoline in **2** and **4** could have been responsible for the efficient transfer observed. It was therefore critical to see if this process could be repeated in the absence of any chiral element other than that which is destroyed or created during the oxidation.

The oxazoline in **2a** (88:12 diastereomeric mixture, ±1%) was removed ($MeOSO_2F$, CH_2Cl_2; $NaBH_4$, MeOH-THF; oxalic acid-silica gel) to the aldehyde *S*-**6** in 96% yield ($[\alpha]_D$ +149.6°, $CHCl_3$) and transformed to the aldehydo dihydroquinoline *S*-**6a** (KOH-H_2O-THF-EtOH). Due to the tendency of **6a** to deteriorate on standing, it was directly oxidized (DDQ, -78 to 25 °C) to the biaryl aldehyde *S*-**7** in 90% yield ($[\alpha]_D$ -93.3°, $CHCl_3$). In order to assess the enantiomeric purity of *S*-**7** and the efficiency of the transfer, the aldehyde was oxidized (90%) and esterified (98%) to the ester, *S*-**7a**, already prepared pure and with known absolute configuration. To our delight *S*-**7a** showed $[\alpha]_D$-10.60° ($CHCl_3$), which corresponds to a 90:10 ±1% enantiomeric ratio in good agreement with the 88:12 ratio in **2a**. This confirmed that the stereochemical transfer from C-4 to the biaryl in the absence of any external chiral elements was virtually complete. It may, therefore, be concluded that the DDQ oxidation occurred in a manner that precluded any racemization (Figure 1) and verified the Berson prediction. Studies to utilize these chiral substances as reagents for asymmetric syntheses are in progress.

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Supplementary Material Available: X-ray structures and data along with spectral properties of **1-7** (12 pages). Ordering information is given on any current masthead page.

(12) **4** (R = *t*-Boc): mp 148.5-151.5 °C, $[\alpha]_D$ -91.4° (*c* 1.1, $CHCl_3$). Anal. C, H. X-ray details are given as supplementary material.

(13) **5**: mp 203-206 °C, $[\alpha]_D$ -51.26° (*c* 1.1, $CHCl_3$). Anal. C, H. X-ray details are given as supplementary material.

(14) The scheme in Figure 1 is shown for the *R* enantiomers, taken from the X-ray structures for these same substances.

(15) Additional support for naphthalene rotation in the aldehyde **6a** prior to oxidation to **7** was gathered by use of the 7′-methoxy derivative of **6a**. Only a single 7′-methoxy and a single C-4 proton in the quinoline were observed in the ^1H NMR at temperatures down to -50 °C. Below this (-60 to -75 °C) both signals separated into the two conformers.

(16) (a) McKinley, S. V.; Grieco, P. A.; Young, A. E.; Freedman, H. H. *J. Am. Chem. Soc.* **1970**, *92*, 5900. (b) Maryanoff, B. E.; Stackhouse, J.; Senkler, G. H., Jr.; Mislow, K. *Ibid.* **1975**, *97*, 2718.

(17) Mori, T.; Oki, M. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 1199. Siddall, T. H.; Stewart, W. E. *J. Org. Chem.* **1969**, *34*, 233.

Modification of the Free-Radical Thermolysis of Bibenzyl by Surface Immobilization[1,2]

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We report initial observations concerning thermolysis of 1,2-diphenylethane immobilized on a silica surface. Although there have been studies of decomposition of free-radical precursors physisorbed on silica gel,[4] we are not aware of studies in which the precursor was covalently attached. We present evidence that *surface immobilization can lead to enhancement of unimolecular radical decay pathways relative to bimolecular ones.*

Determination of the mechanisms of thermolysis of α,ω-diphenylalkanes, $Ph(CH_2)_nPh$, in the fluid state has been stimulated recently[3,5-7] because they serve as models of reactive sites during thermal conversions of coal.[8] However, initially formed reactive

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(2) Paper 4 in the series "Thermolysis of Model Compounds for Coal"; for paper 3 see ref 3.

(3) Poutsma, M. L.; Dyer, C. W. *J. Org. Chem.* **1982**, *47*, 4903.

(4) Leffler, J. E.; Barbas, J. T. *J. Am. Chem. Soc.* **1981**, *103*, 7768. Leffler, J. E.; Zupanic, J. J. *Ibid.* **1980**, *102*, 259. deMayo, P.; Nakamura, A.; Tsang, P. W. K.; Wong, S. K. *Ibid.* **1982**, 104, 6824. Baretz, B. H.; Turro, N. J. *Ibid.* **1983**, *105*, 1309.

(5) Poutsma, M. L. *Fuel* **1980**, *59*, 335.

(6) (a) Miller, R. E.; Stein, S. E. *J. Phys. Chem.* **1981**, *85*, 580. (b) Stein, S. E.; Robaugh, D. A.; Alfieri, A. D.; Miller, R. E. *J. Am. Chem. Soc.* **1982**, *104*, 6567.

(7) Gilbert, K. E.; Gajewski, J. J. *J. Org. Chem.* **1982**, *47*, 4899.

(8) Gavalas, G. R. "Coal Pyrolysis"; Elsevier: Amsterdam, 1982. Whitehurst, D. D.; Mitchell, T. O.; Farcasiu, M. "Coal Liquefaction"; Academic Press: New York, 1980. Wender, I.; Heredy, L. A.; Neuworth, M. B.; Dryden, I. G. C. In "Chemistry of Coal Utilization"; Elliott, M. A., Ed.; Wiley-Interscience: New York, 1981, Suppl. Vol. 2, Chapter 8. Davidson, R. M. In "Coal Science"; Gorbaty, M. L., Larsen, J. W., Wender, I., Eds.; Academic Press: New York, 1982; Vol. 1.

0002-7863/84/1506-1136$01.50/0