from $OsO_4$, **1b**, and stilbene in toluene was determined by X-ray crystallographic analysis (Figure 1).[8,9] The stable octahedral complex **2** is free of toluene, and the diamine **1b** is chelating to osmium as clearly indicated by their N···Os distances (2.16 and 2.22 Å), which are very close to those reported for the pyridine[10] and the quinuclidine[11] osmate complexes. Each osmate phenyl group is facing a bulky neohexyl substituent of **1b**. This is very similar to the stereostructure of the corresponding osmate ester–diamine complex reported by Tomioka and Koga et al.[1d] The study of the structure of the complex of **1b** and $OsO_4$ is currently underway. The detailed mechanisms for the asymmetric osmylation will be discussed in due course.

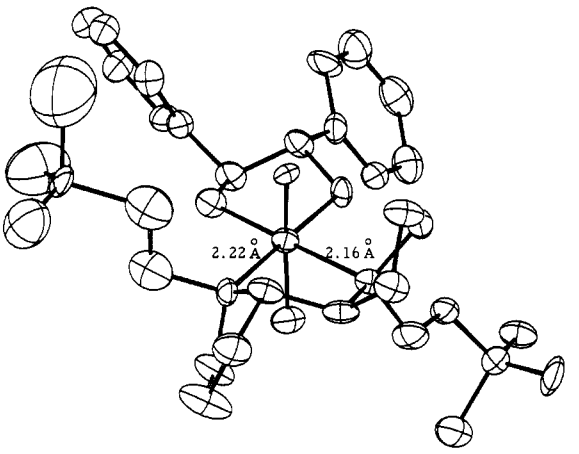



**Figure 1.** ORTEP drawing of **2**.

(8) After the 1:1:1 mixture was stirred at −78 °C for 12 h, the volatiles were removed in vacuo and the resultant dark brown slurry was purified on silica, recrystallized from hexane–$CH_2Cl_2$ to give **2** as brown needles: mp 180 °C dec. Crystal data: orthorhombic crystals, $P2_12_12_1$, with $a$ = 25.92 Å, $b$ = 12.16 Å, $c$ = 10.57 Å, $\alpha = \beta = \gamma = 90.0°$, $Z = 4$, $V$ = 3328 Å$^3$, $D_{calcd}$ = 1.49 g cm$^{-3}$, final $R$ value = 0.066 for 2879 reflections (Rigaku AFC5-R, Mo-K$\alpha$).

(9) Oxidative hydrolysis of the isolated **2** with *N*-methylmorpholine *N*-oxide in aqueous acetone turned out to be too slow in accordance with Sharpless' findings for chelating ligands.[3a]

(10) Conn, J. F.; Kim, J. J.; Suddath, F. L.; Blattmann, P.; Rich, A. *J. Am. Chem. Soc.* **1974**, *96*, 7152.

(11) Cartwright, B. A.; Griffith, W. P.; Schroder, M.; Skapski, A. C. *J. Chem. Soc., Chem. Commun.* **1978**, 853.

## Chiral Recognition in Clefts and Cyclophane Cavities Shaped by the 1,1′-Binaphthyl Major Groove

Peter P. Castro, Taxiarchis M. Georgiadis, and François Diederich*

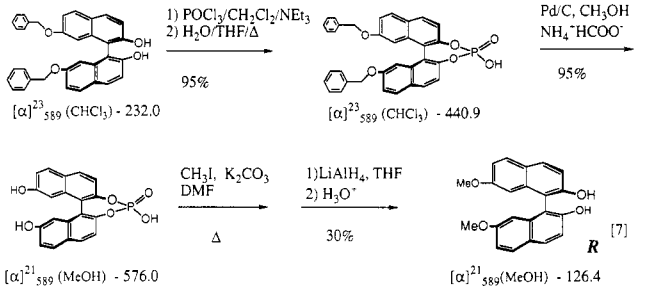
*Department of Chemistry and Biochemistry, University of California, Los Angeles, California 90024-1569*

*Received September 19, 1989*

*Summary:* The optical resolution of 7,7′-bis(benzyloxy)-2,2′-dihydroxy-1,1′-binaphthyl through clathrate formation with quinine is described. Optically active cyclophanes incorporating this spacer bind enantioselectively naproxen derivatives. Hydrogen bonding and $\pi$–$\pi$ interactions lead to a high degree of chiral recognition in the binding of cinchona alkaloids at the major groove of 1,1′-binaphthyls.

*Sir:* Chiral recognition of neutral organic substrates in designed molecular complexes has attracted increasing interest in recent years.[1] Successful developments in this research area promise to provide new approaches to enantiomer separation in chromatographic, crystallographic, or transport experiments as well as new chiral environments and reagents for asymmetric synthesis and catalysis.[2] In our exploration of optically active cyclophanes for the resolution of naproxen derivatives, e.g. **1a–f**, we recently prepared racemic cyclophane **3**.[3] We showed that the major groove of the 1,1′-binaphthyl unit is ideal for shaping cyclophane binding sites for aromatic guests like naproxen. In this paper, we report on the optical resolution of the binaphthyl spacer **4a** and on the preparation and chiral recognition properties of the optically active cyclophane **3** and chiral molecular clefts readily assembled from resolved **4a**.

**Scheme I**




Recently, quinine has been described as a useful chiral solvating agent for the determination of the enantiomeric composition of binaphthyl derivatives by $^1$H NMR spectroscopy.[4] We found that quinine can also be used as a chiral resolving agent for these compounds, and the large-scale (0.1 mol) optical resolution of **4a** was readily

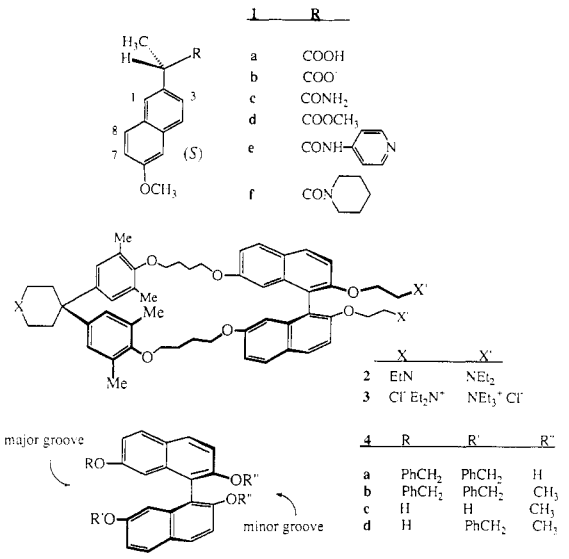
(1) For recent work, see: (a) Canceill, J.; Lacombe, L.; Collet, A. *J. Am. Chem. Soc.* **1985**, *107*, 6993–6996. (b) Rebek, J., Jr.; Askew, B.; Ballester, P.; Doa, M. *J. Am. Chem. Soc.* **1987**, *109*, 4119–4120. (c) Pirkle, W. H.; Reno, D. S. *J. Am. Chem. Soc.* **1987**, *109*, 7189–7190. (d) Dharanipragada, R.; Ferguson, S. B.; Diederich, F. *J. Am. Chem. Soc.* **1988**, *110*, 1679–1690. (e) Petti, M. A.; Shepodd, T. J.; Barrans, R. E., Jr.; Dougherty, D. A. *J. Am. Chem. Soc.* **1988**, *110*, 6825–6840. (f) Echavarren, A.; Galán, A.; Lehn, J.-M.; De Mendoza, J. *J. Am. Chem. Soc.* **1989**, *111*, 4994–4995. (g) Lightner, D. A.; Gawronski, J. K.; Wijekoon, W. M. D. *J. Am. Chem. Soc.* **1987**, *109*, 6354–6362.

(2) (a) For chiral stationary phases, see: Pirkle, W. H.; Pochapsky, T. C. *Chem. Rev.* **1989**, *89*, 347–362. (b) For enantioselective transport, see: Pirkle, W. H.; Doherty, E. M. *J. Am. Chem. Soc.* **1989**, *111*, 4113–4114. (c) For ligand-accelerated asymmetric synthesis, see: Jacobsen, E. N.; Marko, I.; France, M. B.; Svendsen, J. S.; Sharpless, K. B. *J. Am. Chem. Soc.* **1989**, *111*, 737–739.

(3) (a) Diederich, F.; Hester, M. R.; Uyeki, M. A. *Angew. Chem.* **1988**, *100*, 1775–1777; *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1705–1707. (b) The full experimental details for the preparation of racemic **4a** and **3** are described in: Hester, M. R.; Uyeki, M. A.; Diederich, F. *Isr. J. Chem.*, in press.

(4) Rosini, C.; Uccello-Barretta, G.; Pini, D.; Abete, C.; Salvadori, P. *J. Org. Chem.* **1988**, *53*, 4579–4581.

0022-3263/89/1954-5835$01.50/0 




accomplished through simple clathrate formation[5] with this cinchona alkaloid.[6] When racemic **4a** together with 1 equiv of quinine was recrystallized twice from ethanol, one crystalline diastereomeric complex was obtained. Its optical purity (>99% ee) was demonstrated by its $^1$H NMR spectrum in $CDCl_3$, which is distinctively different from the spectrum of the other diastereomeric complex. Acidic aqueous workup of the preferentially crystallized complex yielded enantiomerically pure **4a** ($[\alpha]^{23}_{589}$ ($CHCl_3$) = −232.0°) in 76% yield. Following the synthetic sequence shown in Scheme I, the absolute configuration of this enantiomer was assigned as (*R*)-(−)-**4a**.[7] Multiple recrystallizations (3–5 times) from 90% ethanol of the residue, obtained upon evaporation of the mother liquors, afforded the second diastereomeric quinine clathrate, and acidic workup led to pure (*S*)-(+)-**4a** in 65% yield ($[\alpha]^{23}_{589}$ ($CHCl_3$) = +229.2°).[8]

Starting from (*R*)- and (*S*)-**4a**, the optically pure cyclophanes (*R*)-**2** ($[\alpha]^{21}_{589}$ ($CHCl_3$) = +170.6°)[9] and (*S*)-**2** ($[\alpha]^{21}_{589}$ ($CHCl_3$) = −170.8°) and subsequently the quaternary hosts (*R*)-**3** ($[\alpha]^{21}_{589}$ (MeOH) = +150.5°) and (*S*)-**3** ($[\alpha]^{21}_{589}$ (MeOH) = −148.9°) were prepared following procedures previously published for the synthesis of racemic **3**.[3] The $^1$H NMR chiral recognition studies (500 MHz) with optically pure naproxen derivatives described below provided unambiguous evidence for the enantiomeric purity (>99% ee) of (*R*)- and (*S*)-**3**.

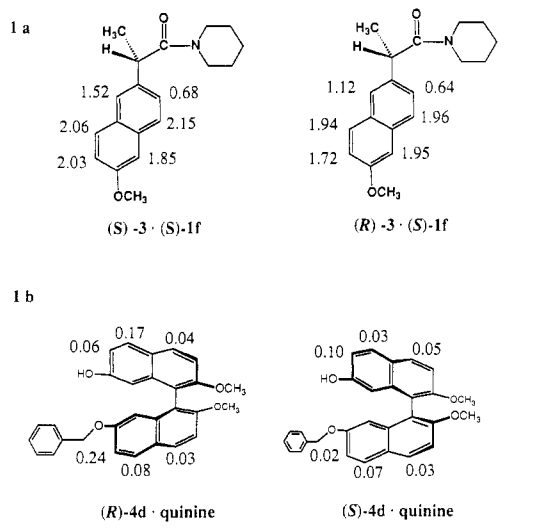



**Figure 1.** Upfield $^1$H NMR complexation shifts (ppm) calculated for saturation binding (a) of (*S*)-**1f** by (*R*,*S*)-**3** in $D_2O$/MeOH-$d_4$ (60:40 v/v) and (b) of (*R*,*S*)-**4d** by quinine in $CDCl_3$. The experimentally observed degrees of saturation binding were ≈ 80–90%; $T$ = 293 K.

**Table I. Association Constants, $K_a$, and Free Energies of Formation, $-\Delta G°$, of the Diastereomeric Complexes between (*R*,*S*)-3 and (*S*)-1a–f in $D_2O$/MeOH-$d_4$ (60:40, $T$ = 293 K)[a] (The Calculated Differences in Stability between Diastereomeric Complexes $\Delta(\Delta G°)$ Are Given)**

| | (*R*)-3 | | (*S*)-3 | | |
|---|---|---|---|---|---|
| naproxen derivative | $K_a$, L mol$^{-1}$ | $-\Delta G°$, kcal mol$^{-1}$ | $K_a$, L mol$^{-1}$ | $-\Delta G°$, kcal mol$^{-1}$ | $\Delta(\Delta G°)$, kcal mol$^{-1}$ |
| **1a**[b] | 2105 | 4.45 | 2540 | 4.56 | 0.16 |
| **1b**[c] | 1040 | 4.04 | 1335 | 4.19 | 0.15 |
| **1c** | 775 | 3.87 | 1010 | 4.02 | 0.15 |
| **1d** | 2075 | 4.45 | 3110 | 4.68 | 0.23 |
| **1e** | 1760 | 4.35 | 2840 | 4.63 | 0.28 |
| **1f** | 1405 | 4.22 | 2490 | 4.55 | 0.33 |

[a] Errors in $K_a$: ±10%. [b] In 0.1 M DCl/MeOH-$d_4$ (60:40). [c] In 0.01 M $K_2CO_3$/MeOH-$d_4$ (60:40).

$^1$H NMR complexation studies in $D_2O$/methanol-$d_4$ (60:40 v/v, $T$ = 293 K) showed that the naproxen derivatives (*S*)-**1a–f** form diastereomeric 1:1 complexes of differential geometry and stability with the host enantiomers (*R*)- and (*S*)-**3**. The large differential complexation shifts of the resonances of (*S*)-**1f** in the two diastereomeric, axial-type inclusion complexes (Figure 1a) exemplify that (*R*)- and (*S*)-**3** are efficient chiral solvating agents.

Table I gives the association constants, $K_a$, and the free energies of formation, $-\Delta G°$, at 293 K for the diastereomeric complexes formed between (*R*)- and (*S*)-**3** and the naproxen derivatives (*S*)-**1a–f**. Corresponding data are obtained in $^1$H NMR titrations with the (*R*)-naproxen derivatives.[10] For all (*S*)-naproxen derivatives, the *S*–*S* complexes are more stable, and the difference in stability between diastereomeric complexes, $\Delta(\Delta G°)$, varies between 0.15 and 0.33 kcal mol$^{-1}$. The stability difference is most pronounced for the complexes of the naproxen derivatives **1e** and **1f** with bulky amide groups which indicates that

(5) (a) Worsch, D.; Vögtle, F. *Top. Curr. Chem.* **1987**, *140*, 21–41. (b) Toda, F. *Top. Curr. Chem.* **1987**, *140*, 43–69.

(6) For a conformational analysis of the cinchona alkaloids, see: Dijkstra, G. D. H.; Kellogg, R. M.; Wynberg, H. *Recl. Trav. Chim. Pays-Bas* **1989**, *108*, 195–204.

(7) The *R* configuration was assigned to (−)-2,2′-dihydroxy-7,7′-dimethoxy-1,1′-binaphthyl based on the elution sequence on the chiral stationary phase CSP 2; Pirkle, W. H.; Schreiner, J. L. *J. Org. Chem.* **1981**, *46*, 4988–4991.

(8) The optical resolution of **4a** was also accomplished using the longer route described for 2,2′-dihydroxy-1,1′-binaphthyl. This route involves the formation of the cyclic phosphate at the minor groove of **4a**, resolution with cinchonine and cinchonidine, respectively, and dephosphorylation with lithium aluminum hydride. See: (a) Cram, D. J.; Helgeson, R. C.; Peacock, S. C.; Kaplan, L. J.; Domeier, L. A.; Moreau, P.; Koga, K.; Mayer, J. M.; Chao, Y.; Siegel, M. G.; Hoffman, D. H.; Sogah, G. D. Y. *J. Org. Chem.* **1978**, *43*, 1930–1946. (b) Jacques, J.; Fouquey, C. *Org. Synth.* **1988**, *67*, 1–12. The complete resolution of (*R*)- and (*S*)-**4a** was also confirmed by the 500-MHz $^1$H NMR spectra of the diastereomeric esters formed upon conversion with the Mosher reagent [(*R*)-(+)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride]; Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512–519.

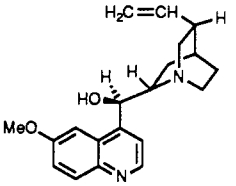
(9) For the observation of a similar change in the sign of the optical rotation accompanying the transition from cyclization component to macrocycle, see ref 1e.

(10) The 500-MHz $^1$H NMR titrations at constant total guest concentration were evaluated by a nonlinear least-squares curve fitting procedure. The host concentration ranges were chosen to provide approximately 15–90% complexation of the guest. At $K_a$ values around 1000–2000 L mol$^{-1}$, the guest concentration was normally chosen as ≈ 1 × 10$^{-3}$ M, and the host concentration was varied between 3 × 10$^{-4}$ and 7 × 10$^{3}$ M. In most titrations, all six naproxen protons were evaluated, and the binding data in Table I are averaged data. For sample preparations, the molecular weight of the trihydrate of **3**, supported by elemental analysis,[3b] was taken.

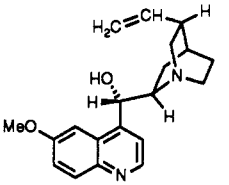
**Table II. Association Constants, $K_a$, and Free Energies of Formation, $-\Delta G°$, of the Diastereomeric Complexes between (*R*,*S*)-4a–d and Cinchona Alkaloids in $CDCl_3$, $T$ = 293 K[a] (The Calculated Differences in Stability between Diastereomeric Complexes $\Delta(\Delta G°)$ Are Given)**

| alkaloid[b] | $K_a$, L mol$^{-1}$ | $-\Delta G°$, kcal mol$^{-1}$ | $K_a$, L mol$^{-1}$ | $-\Delta G°$, kcal mol$^{-1}$ | $\Delta(\Delta G°)$, kcal mol$^{-1}$ |
|---|---|---|---|---|---|
| | (*R*)-**4a** | | (*S*)-**4a** | | |
| quinine | 95 | 2.65 | 60 | 2.38 | 0.27 |
| quinidine | 20 | 1.77 | 75 | 2.51 | 0.74 |
| | (*R*)-**4b** | | (*S*)-**4b** | | |
| | no measurable complexation | | | | |
| | (*R*)-**4c** | | (*S*)-**4c** | | |
| quinine | 1270 | 4.16 | 650 | 3.77 | 0.39 |
| quinidine | 625 | 3.75 | 850 | 3.93 | 0.18 |
| | (*R*)-**4d** | | (*S*)-**4d** | | |
| quinine | 775 | 3.87 | 140 | 2.88 | 0.99 |
| quinidine | 105 | 2.72 | 550 | 3.67 | 0.95 |

[a] Errors in $K_a$: ±20%. [b] The alkaloid structures are



quinine



quinidine

differential steric interactions are most probably at the origin of the observed chiral recognition. The degree of enantioselectivity is quite considerable since the binding sites of (*R*,*S*)-**3** are partially shaped by an achiral diphenylmethane unit. A much higher enantioselectivity in the binding of naproxen derivatives is therefore expected for optically active cyclophane hosts shaped by two 1,1′-binaphthyl major grooves that are currently under construction.

Surprising results were obtained in $^1$H NMR studies of the interactions between the optically active cinchona alkaloids quinine and quinidine and the enantiomerically pure 2,2′,7,7′-tetrahydroxy-1,1′-binaphthyl derivatives (*R*)- and (*S*)-**4a–d** in $CDCl_3$ (Table II).[11] The formation of complexes with 1:1 stoichiometry is demonstrated in binding titrations at 293 K in which the resonances of the binaphthyl derivative, chosen at constant concentration, are monitored as a function of increasing alkaloid concentration.[12] With **4a**, moderately strong complexation of the two alkaloids as well as significant differential stabilities of the diastereomeric complexes are observed. The (*R*)-**4a**–quinine complex that precipitated first in the optical resolution process described above is also the most stable one. Alkylation of all binaphthyl hydroxy groups in **4b** leads to the complete disappearance of measurable binding interactions. This is clear evidence for the relevance of hydrogen bonding for the recognition process.[13]

The complexes formed by **4c** and **4d** through hydrogen bonding at the major groove have considerably higher overall stability than the complexes formed by **4a** at the minor groove. In addition, the degree of chiral recognition can be very large (Table II). With **4d**, lacking any $C_2$ symmetry,[14] differential stabilities between diastereomeric complexes are as high as $\Delta(\Delta G°) \approx 1$ kcal mol$^{-1}$. The $^1$H NMR data in Figure 1b suggest that the more stable (*R*)-**4d**–quinine complex presumably is stabilized by $\pi$–$\pi$ interactions between the aromatic rings of the binding partners whereas such interactions seem much less effective in the less stable complex formed by (*S*)-**4d**. The resonances of 5-H and 6′-H (Figure 1b) at the binaphthyl major groove show considerably larger upfield complexation shifts (0.17 and 0.24 ppm at saturation binding, respectively) in the more stable complex of (*R*)-**4d** than in the less stable complex of (*S*)-**4d** (0.03 and 0.02 ppm, respectively).

Our preliminary studies clearly demonstrate the potential for chiral recognition at the binaphthyl major groove as a result of hydrogen bonding, $\pi$–$\pi$, and steric interactions. In studies with a variety of additional chiral guests and with other suitably functionalized 1,1′-binaphthyl derivatives, the structural and electronic characteristics for this promising mode of enantioselective complexation provided by readily available molecular clefts are now being explored in great detail.

**Acknowledgment.** We thank the National Science Foundation and the National Institutes of Health (NIH) for supporting this work. P.P.C. thanks the NIH for a

(11) (*R*)- and (*S*)-**4b–d** were prepared from optically pure **4a**. Alkylation ($K_2CO_3$/MeI/DMF) gave **4b** (89%). Catalytic transfer hydrogenation of **4b** (Pd/C, $NH_4^+HCOO^-$) afforded **4c** (62%) or, if interrupted early, **4d** (31%). The structures of all new binaphthyl derivatives in this paper were fully supported by spectral and analytical data. An X-ray crystal analysis confirms the structure assigned to (*R*)-**4c**: Knobler, C. B.; Castro, P. P.; Diederich, F., unpublished results.

(12) For the evaluation of the NMR titrations in which the binaphthyl derivative is taken at constant total concentration, see ref 10. To assure ca. 10–80% saturation binding at $K_a \approx 100$ L mol$^{-1}$, the binaphthyl concentration was chosen as $\approx 1 \times 10^{-2}$ M, and the alkaloid concentration was varied between $\approx 3 \times 10^{-3}$ and $7 \times 10^{-2}$ M. For quantitative evaluation of the titrations, only binaphthyl resonances with complexation shifts at saturation binding, $\Delta\delta_{sat}$, ≥0.1 ppm were considered. Presumably due to the smaller complexation shifts at saturation binding (0.1–0.4 ppm versus 1.0–2.5 ppm), the uncertainty of the association constants for 1:1 major groove complexation is twice as large (±20%) as for 1:1 cyclophane complexation (±10%). All data in Table II are confirmed in duplicate or triplicate titrations.

(13) For recent examples of hydrogen-bonding receptors, see: (a) Askew, B.; Ballester, P.; Buhr, C.; Jeong, K. S.; Jones, S.; Parris, K.; Rebek, J., Jr. *J. Am. Chem. Soc.* **1989**, *111*, 1082–1090. (b) Kelly, T. R.; Bilodeau, M. T.; Bridger, G. J.; Zhao, C. *Tetrahedron Lett.* **1989**, *30*, 2485–2488. (c) Goswami, S.; Hamilton, A. D.; Van Engen, D. *J. Am. Chem. Soc.* **1989**, *111*, 3425–3426. (d) Chapman, K. T.; Still, W. C. *J. Am. Chem. Soc.* **1989**, *111*, 3075–3077. (e) Sheridan, R. E.; Whitlock, H. W., Jr. *J. Am. Chem. Soc.* **1986**, *108*, 7120–7121. (f) Bell, T. W.; Liu, J. *J. Am. Chem. Soc.* **1988**, *110*, 3673–3674. (g) Aarts, V. M. L. J.; van Staveren, C. J.; Grootenhuis, P. D. J.; van Eerden, J.; Kruise, L.; Harkema, S.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1986**, *108*, 5035–5036.

(14) We thank Professor Julius Rebek, Jr., for enjoyable discussions with regard to the (ir)relevance of $C_2$ symmetry for enantioselective complexation.

MARC-Fellowship. We thank Syntex Corp., Palo Alto, CA, for a generous gift of (*R*)-naproxen.

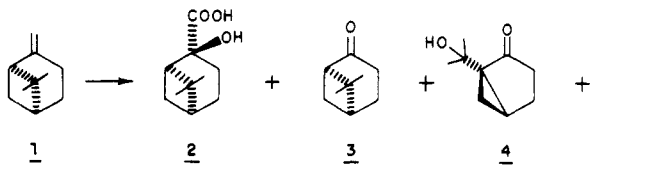
**Supplementary Material Available:** Optical rotations of the resolved intermediates on the way from the enantiomers of **4a** to the two cyclophanes (*R*)- and (*S*)-**3**, $^1$H NMR spectra of a complete binding titration, and titration data to illustrate the determination of the stabilities of diastereomeric complexes (4 pages). Ordering information is given on any current masthead page.

## Envisaging an Old Reaction from a New Point of View

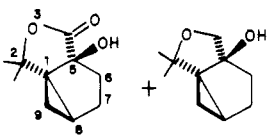
Anita J. Marsaioli,*,† Vilma Nurnberg,† Maria Helena Sarragiotto,† and E. E. Castellano‡
*Instituto de Química, Universidade Estadual de Campinas, 13081, Campinas, SP, Brazil, and Instituto de Física e Química de São Carlos, CP 369, 13560, S. Carlos, SP, Brazil*
*Received September 18, 1989*

*Summary:* Two novel rearrangement products were isolated from the oxidation reaction of β-pinene with permanganate which should find wide applicability in the synthesis of *o*-menthanes and thujanes.

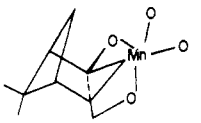
*Sir:* Oxidation of β-pinene **1** with potassium permanganate is a classical method to obtain nopinic acid **2** and nopinone **3** as a secondary product.[1] Although in some conditions a major compound was obtained, in most reactions eight products could be detected by GC and TLC. In some instances the undesirable compounds were produced in considerable amounts.[2] From the isolation and spectroscopic analysis of the reaction products it was clear that they could be divided in two categories: those with the bicyclic [3.1.1]heptane skeleton (**2**, 21% and **3**, 2%) and those that showed high-field absorptions in PMR (ca. 0.5–1.0 ppm) and $^{13}$C NMR (ca. 8.00 ppm, t) which could be assigned to the presence of a cyclopropane ring (**4**, 1%; **5**, 63%; **6**, 13%). A search in the literature revealed that compound **4** was identical with the ketol reported by Jefford et al.[3] as an anomalous oxidation of β-pinene using von Rudloff reagent. Structures **5**[4] and **6**[4] were suggested based on spectral data evidences, and final proof was obtained from the X-ray diffraction of **6** which also confirmed the presence of only one enantiomer in the crystal under observation.[5] The question on how the formation of **5** and **6** occurs still remains to be answered. Based on the isolation of **5** and **6** we suggest that the reaction pathway has first to involve the complexation and formation of a five-membered cyclic manganate(V) diester **7**.[6] This intermediate would then either follow the normal double bond oxidation mechanism leading to the formation of **2** and **3** or rearrange giving rise to **4**, **5**, and **6**. The close proximity of the oxygen atom of the manganate(V) of **7** to the bridgehead hydrogen atom could favor this rearrangement. Consequently, no rearrangement product with terminal double bond as **8** would be expected from this reaction. We are presently trying to prove that **6** (and not **8**) is the first rearrangement product, by monitoring the reaction from the beginning using authentic samples of **6** and **8**.



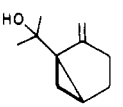

1 2 3 4



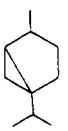

5 6



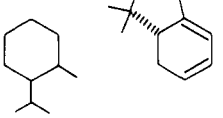

7




8



9




10 11

We consider the isolation of these two novel rearrangements **5** and **6** to be a breakthrough so far as access

(1) Wallach, O.; Bulmann, A. *Chem. Abstr.* **1908**, *2*, 277. Winstein, S.; Holness, N. J. *J. Am. Chem. Soc.* **1955**, *77*, 3054.

(2) β-Pinene and potassium permanganate in pyridine and water are allowed to react during 4 h at 10 °C. Acidification of the solution followed by continuous liquid–liquid extraction with diethyl ether for 48 h.

(3) Jefford, C. W.; Roussel, A.; Evans, S. M. *Helv. Chim. Acta* **1975**, *58*, 2151.

(4) The spectral data of **5** and **6** are consistent with the assigned structures, and selected data are cited. Compound **5**: IR $\nu_{max}^{neat}$ (cm$^{-1}$) 3440 (OH), 3060–3030 (cyclopropane ring), 1760 (C=O); $^1$H NMR (100 MHz, $CDCl_3$) δ 0.50–1.00 (m, 2 H), 1.20 and 1.64 (2 s, 3 H each), 4.50 (m, 1 H); $^{13}$C NMR (25.2 MHz, $CHCl_3$) δ 177.2 (s, C-4), 85.2 (s, C-5), 84.7 (s, C-2), 43.7 (d, C-1), 33.8 (t, C-6), 26.5 and 24.3 (2 q, 2 Me on C-2), 25.0 (t, C-7), 23.5 (d, C-8), 9.4 (t, C-9); MS *m/z* 182 ($M^{+\cdot}$, 15%). Compound **6**: mp 69–71 °C; $[\alpha]^{25}_D$ +11.0° (*c* 1.9, $CHCl_3$); IR $\nu_{max}^{KBr}$ (cm$^{-1}$) 3400 (OH), 3060 and 3015 (cyclopropane ring); $^1$H NMR (80 MHz, $CDCl_3$) δ 0.50–1.00 (m, 2 H), 1.00 and 1.44 (2 s, 3 H each), 3.77 (d, 1 H, *J* = 7.2 Hz), 4.00 (d, 1 H, *J* = 7.2 Hz); $^{13}$C NMR (25.2, $CHCl_3$) δ 89.5 (s, C-2), 79.8 (s, C-5), 75.0 (t, C-4), 46.6 (s, C-1), 28.0 and 25.5 (2 q, 2 $CH_3$ on C-2), 25.5 (t, C-7), 21.8 (d, C-8), 9.4 (t, C-9); MS *m/z* 168 ($M^{+\cdot}$, 1%).

(5) X-ray Analysis of Compounds. **5**: X-ray quality crystals were obtained (by slow evaporation) from hexane–diethyl acetate mixture. Crystal data: $C_{10}H_{16}O_2$, *M* = 168.24, monoclinic, space group $P_{2_1}$, *a* = 8.390 (2) Å, *b* = 10.052 (3) Å, *c* = 12.163 (2) Å, β = 108.65 (2)°, *U* = 971.9 (7) Å$^3$, *Z* = 4, $D_c$ = 1.150 g cm$^{-3}$, λ = 0.710 73 Å, μ (Mo Kα) = 0.073 mm$^{-1}$, *F*(000) = 368. **12**: X-ray quality crystals were obtained by slow evaporation from diethyl acetate. Crystal data: $C_{20}H_{24}O_4$, *M* = 328.41, monoclinic, space group $P_{2_1/n}$, *a* = 10.546 (5) Å, *b* = 8.774 (2) Å, *c* = 18.931 (9) Å, β = 101.88 (4)°, *U* = 1714 (1) Å$^3$, *Z* = 4, $D_c$ = 1.272 g cm$^{-3}$, λ = 0.710 73, μ (Mo Kα) = 0.082 mm$^{-1}$, *F*(000) = 704. Intensities from both compounds were collected on an Enraf Nonius CAD-4 diffractometer, at room temperature, using specimens of 0.5 × 0.5 × 0.3 mm for **5** and 0.3 × 0.5 × 0.6 for **12**. Anisotropic least-squares refinement of all non-hydrogen atoms, H atoms fixed with common refined isotropic are summarized in Table below:

| | **5** | **12** |
|---|---|---|
| number of ind. reflections | 1687 | 2705 |
| number of reflections with $I > 3\sigma(I)$ included in refinement | 1306 | 1888 |
| maximum 2θ value | 25° | 25° |
| number of refined parameters | 218 | 218 |
| *R* factor | 0.045 | 0.047 |
| weighted *R* factor | 0.051 | 0.057 |
| $S = \sum w(\|F_o\| - \|F_c\|)^2/(m - n)$ | 0.96 | 0.93 |

(6) Freeeman, F.; Kappos, J. C. *J. Am. Chem. Soc.* **1985**, *107*, 6628.

0022-3263/89/1954-5838$01.50/0 