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

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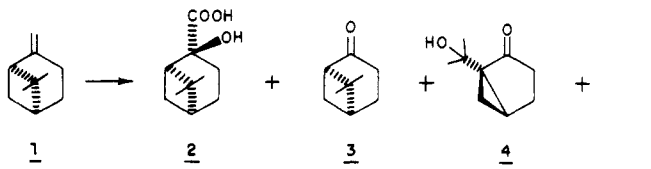
Summary: Two novel rearrangement products were isolated from the oxidation reaction of β-pinene with permanganate which should find wide applicability in the synthesis of *o*-menthanes and thujanes.

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**.



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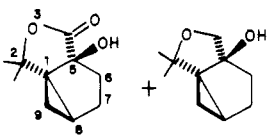

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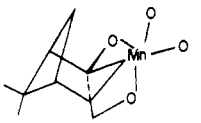

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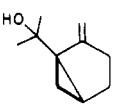

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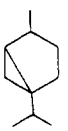

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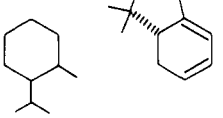


10 11

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 ν_{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 ν_{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:

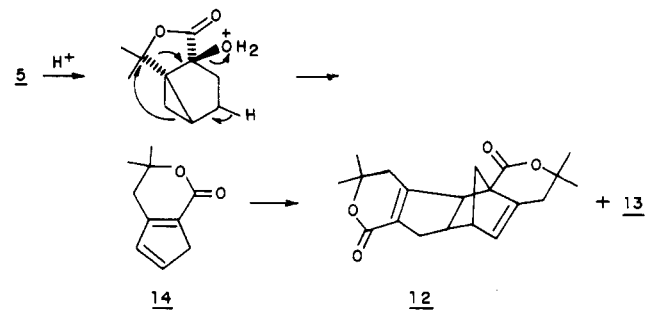
	5	**12**
number of ind. reflections	1687	2705
number of reflections with $I > 3\sigma(I)$ included in refinement	1306	1888
maximum 2θ value	25°	25°
number of refined parameters	218	218
R factor	0.045	0.047
weighted *R* factor	0.051	0.057
$S = \sum w(\|F_o\| - \|F_c\|)^2/(m - n)$	0.96	0.93

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

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

to the bicyclo[3.1.0]hexane system **9** and *o*-menthane skeleton **10** is concerned.

A first attempt to transform **5** into lactone **11**, an *o*-menthane isolated from the urine of koala bear,[7] treating **5** with perchloric acid, led to the formation of two dimers **12** (36%) and **13** (18%). Spectroscopic data[8] and X-ray diffraction[5] revealed structure **12** for the major product, indicating that a Diels-Alder cycloaddition had occurred between two diene molecules possessing structure **14**. We are currently investigating the application of these rearrangement compounds in natural product synthesis.



(7) Southwell, I. A. *Tetrahedron Lett.* **1975**, 1885.

(8) Spectral data of **12**: mp 162.6–163.6 °C; IR ν_{max}^{KBr} (cm^{-1}) 1720 (C=O); ^1H NMR (270 MHz, $CDCl_3$) δ 1.31, 1.36, 1.46 and 1.52 (4 s, 3 H each), 1.95 (d, 2 H), 3.18 (m, 2 H), 3.93 (dm, J = 9.2 Hz, 1 H), 5.80 (m, 1 H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 173.6 (s), 163.5 (s), 153.6 (s), 140.2 (s), 131.0 (s), 128.7 (d), 82.2 (s), 80.9 (s), 64.2 (d), 56.3 (t), 55.7 (s), 46.6 (d), 42.0 (d), 37.9 (t), 37.1 (t), 32.2 (t), 29.7 (q), 29.5 (q), 27.5 (q), 27.1 (q).

Acknowledgment. We wish to thank FAPESP and FINEP for financial support and CAPES for scholarships to V.N. and M.H.S.

Registry No. 1, 18172-67-3; 2, 471-83-0; 3, 38651-65-9; 4, 123482-50-8; 5, 123380-83-6; 6, 123380-84-7; 12, 123380-85-8.

A New MODEL Parameter Set for β-Lactams

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Summary: The original parameters in the MM-2 force field of MODEL gave poor structural data for β-lactams. A new atom type was defined for the β-lactam nitrogen, and new parameters, giving substantially better minimized structures, were derived using X-ray and AMPAC data.

Sir: β-Lactams have long been of interest to scientists because of their antibiotic activity.[1] In particular, it is known that their antibacterial activity, on a molecular level, involves inhibition of the transpeptidase normally responsible for cross-linking proteins in the formation of bacterial cell walls.[2] A thorough understanding of this process necessitates good structural information about the β-lactam in question. We undertook a structural study of these materials using molecular mechanics calculations and found that the predicted geometries of these molecules differed substantially from experimentally determined geometries. Other workers have obtained similar poor results for penicillin analogues and developed new modeling parameters to overcome their difficulties.[3] Using X-ray data[4,5] and semiempirical calculations (AMPAC),[6] we have developed a new set of parameters for β-lactams that provides much better structural information than the original parameters in the MM-2/MODEL force field.[7,8]

Results

As an initial test case, we examined the geometry of **1** using the MM-2 force field available in MODEL.[9] Overlay of the calculated geometry with the X-ray structure showed a root mean square (rms) deviation of 0.092 Å when the seven ring atoms were compared. While this degree of deviation initially appeared satisfactory, detailed examination of the differences between the two structures indicated that there were substantial errors in the calculated bond lengths and angles around the β-lactam nitrogen. We found that the sum of the angles around the β-lactam nitrogen in the calculated structure differed from the X-ray structure by as much as 30°. Since this sum has been used as an indicator of activity, this was particularly disturbing.[10,11] Realizng that the character of the nitrogen in the β-lactam might best be viewed as having an intermediate hybridization (i.e., ~$sp^{2.5}$), we decided to examine the geometry of the β-lactam using a transition state type nitrogen (atom type 55) already parameterized in the MODEL force field. Use of this atom type in the structure minimization gave improved results in the bond lengths but poorer overall results with an rms deviation of 0.110 Å in the ring atoms. In particular, while the X-ray structure showed the four-membered ring to be almost completely planar, there was a substantial degree of puckering of this ring in the calculated structure. This lack of planarity introduced a significant degree of error in all of the bond angles. It was evident that the available parameters were inappropriate for the purpose of predicting β-lactam structures.

In our development of new parameters, we defined a new atom type for the β-lactam nitrogen. In many molecular mechanics programs, there is an option to specify new atoms as wild card types for which parameters are easily

(1) *β-Lactam Antibiotics*; Salton, M. R. J., Shockman, G. D., Eds.; Academic Press: New York, 1981.

(2) Knowles, J. *Acc. Chem. Res.* **1985**, *18*, 97.

(3) Wolfe, S.; Khalil, M.; Weaver, D. F. *Can. J. Chem.* **1988**, *66*, 2715.

(4) Allen, F. H.; et al. *Acta. Crystallogr. B.* **1979**, *35*, 2331.

(5) We wish to thank Drs. Dennis Keith and Kin-Chun Luk of Hoffman-LaRoche for providing us with X-ray coordinates for five of our structures.

(6) Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902.

(7) These new parameters are currently being incorporated into MODEL and will be available in newer versions of the program.

(8) The difficulties we found in the MODEL treatment of β-lactams were unrelated to the now resolved problems of MODEL treatment of any four-membered ring.

(9) All molecular modeling calculations were done on version 2.94 of MODEL developed by K. Steliou and W. C. Still. This program is available from Kosta Steliou at the University of Montreal. We wish to thank Kosta Stelio for his helpful comments in the preparation of this manuscript.

(10) Baldwin, J. E.; Greengrass, C. W.; et al. *Tetrahedron* **1986**, *42*, 4879

(11) Woodward, R. B. *Philos. Trans. R. Soc. London, Ser. B* **1980**, 239.

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