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Optically active cyclobutanones and γ-butyrolactones from asymmetric alkylidenecyclopropanes

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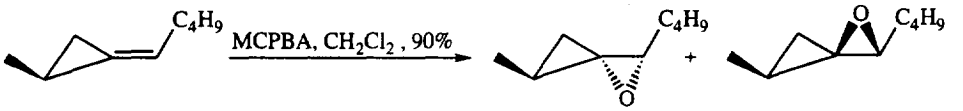
Abstract: Epoxidation of (E)-(2*S*)-pentylidene(2-methylcyclopropane) **1** by MCPBA gave a 70:30 mixture of diastereomeric oxaspiropentanes **2** and **3**, which underwent lithium iodide induced ring expansion and Baeyer Villiger oxidation to produce the Quercus lactone a (>92% ee). © 1997 Elsevier Science Ltd

Alkylidenecyclopropane epoxidation by peracetic,[1] peroxybenzimidic,[2] *p*-nitroperbenzoic[3] or *m*-chloroperbenzoic[4] acids produced oxaspiropentanes in high yields (70–90%). Otherwise, these strained spiro compounds have been also prepared through the nucleophilic addition of 1-lithio-1-bromocyclopropane to ketones at low temperature;[5] their intermediary formation has been observed in the addition of 1,3-bis diazopropane to ketones[2] and in the reaction of dimethyloxosulfonium methylide with α-haloketones.[6] They have been also obtained from the reaction of sulfur cyclopropylides with ketones.[7] But as far as we know, optically active oxaspiropentanes have not been prepared from epoxidation of chiral alkylidenecyclopropanes. We report now a convenient route to these strained compounds and their diastereoselective ring expansions into chiral cyclobutanones and γ-butyrolactones.[8,9]



(2*S*)-**1** (2*R*,3*S*,4*S*)-**2** (70%) (2*S*,3*R*,4*S*)-**3** (30%)

Thus for instance, epoxidation by *m*-chloroperbenzoic acid (MCPBA)[4] of the (E)-(2*S*)-pentylidene(2-methylcyclopropane) **1**, readily available diastereochemically pure from palladium(0) catalyzed hydrogenolysis by sodium formate of (1*R*,2*S*)-2-methyl-1-(1-pentenyl)cyclopropyl mesylate,[10] gave in 65% yield a mixture of the expected epoxides **2** and **3**, besides aromatic by-products, likely arising from competitive *m*-chlorobenzoic acid addition.[4] On the other hand, epoxidation of (2*S*)-**1** by a preformed insoluble (2.4 equiv.) MCPBA–KF complex (from addition of 100% molar excess of potassium fluoride referred to MCPBA in dichloromethane)[11] for 5 h at room temperature, as monitored by t.l.c., produced in higher yield (90%) a 70:30 mixture of (2*R*,3*S*,4*S*)-2-butyl-4-methyl-1-oxaspiro[2+2] pentane **2** and of its diastereomer (2*S*,3*R*,4*S*)-**3**,[12] as determined from their ^{1}H and ^{13}C NMR data.

Upon treatment with a catalytic amount (1%) of lithium iodide in dichloromethane at reflux for 5 h, as monitored by g.c.,[13] this unseparable 70/30 mixture of oxaspiropentanes (2*R*,3*S*,4*S*)-**2** and (2*S*,3*R*,4*S*)-**3** underwent quantitative C_3–C_4 ring expansion,[8] to provide a 55:17:28 mixture of diastereomeric (2*R*,3*S*)-**4** and (2*S*,3*S*)-2-butyl-3-methylcyclobutanone **5**, besides the regioisomeric 2-butyl-4-methyl cyclobutanone **6**. The *cis* four-membered ring (2*S*,3*S*)-**5** was isolated by preparative gas chromatography (SE 30, 100°C, N_2, 1 bar) and its structure was determined by comparison of its IR, ^{1}H NMR, mass-spectra, specific rotation with the published data.[9,14] The structure of the

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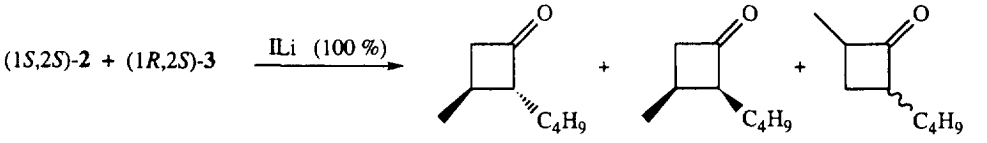
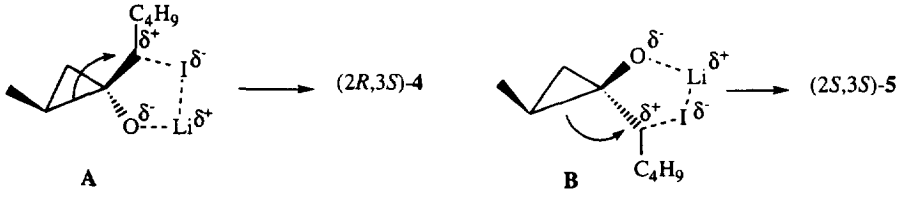
major ring expansion product (2*R*,3*S*)-**4**, unseparable from the regioisomeric compound **6**, was easily elucidated from the ^{1}H NMR (250 MHz) spectrum of a 72:28 mixture of these regioisomeric α,β- and α,α′-disubstituted cyclobutanones, which exhibits three characteristic cyclobutanone α,α′,α′-carbonyl protons at δ (ppm) 2.60 (ddd, J=17.3, 7.5 and 3.1 Hz, 1H), 2.78 (m, 1H) and 3.04 (ddd, J=17.3, 8.5 and 2.3 Hz, 1H) respectively, besides a cyclobutanone β-carbonyl methyne proton at 2.11 ppm (h, J=6.9 Hz, 1H) and the methyl signal at δ 1.20 ppm (J=7.3 Hz, 3H); the *trans* stereochemistry and the enantiomeric excess of (2*R*,3*S*)-**4** have been confirmed from its further transformation into a natural γ-lactone (*vide infra*). The formation of the 2-butyl-4-methylcyclobutanone **6**, was deduced from the occurrence of two cyclobutanone α,α′-carbonyl methyne protons at δ 3.23 ppm (m, 2H) and of cyclobutanone β-carbonyl methylene protons at δ 1.90 ppm (m, 2H).[15]



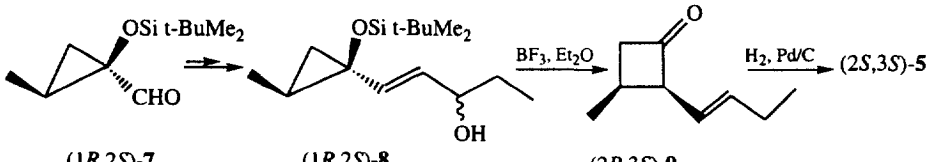
(2*R*,3*S*)-**4** (55 %) (2*S*,3*S*)-**5** (17 %) **6** (28 %)

In general, acid catalyzed opening of epoxides leads to products resulting from the cleavage of the carbon–oxygen bond entailing formation of the more stable carbonium ion;[16] however oxaspiropentanes underwent ring opening at the primary center with lithium iodide, hydrogen chloride, perchloric and sulfuric acids.[3,4,17] In particular, ring expansion of 3,3-dimethyl-1-oxaspiro[2.2]pentane provided quantitatively a mixture of regioisomeric 3,3- and 2,2-dimethylcyclobutanones, with product ratios (7.5, 10 and 15) depending on the nature of the catalysts (lithium iodide, perchlorate and tosylate, respectively).[4] In fact the amount by which tertiary migration was favoured over primary migration depended on the degree of positive charge development at the migrating centre;[18] the lower regioselectivity observed for the rearrangement of the substituted 2-butyl-4-methyloxaspiropentanes **2** and **3**, likely results from a lower reactivity due to the formation of a secondary cyclopropylcarbinyl cation, requiring then comparatively harsher conditions to lead the ring expansion to completion.



A B

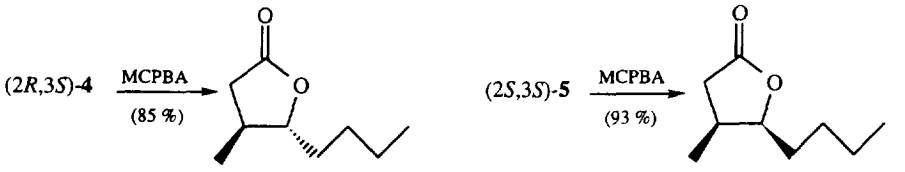
Lithio halohydrin-type intermediates have been proposed for this ring expansion.[18] Thus, on addition of lithium iodide (2*R*,3*S*,4*S*)-oxaspiropentane **2** underwent ring opening into the intermediate A, which then rearranged to (2*R*,3*S*)-**4**, while under the same conditions, (2*S*,3*R*,4*S*)-oxaspiropentane **3** underwent ring opening to the intermediate B, which rearranged to (2*S*,3*S*)-**5**. As the cyclobutanones (2*R*,3*S*)-**4**/(2*S*,3*S*)-**5** ratio (76/24) is very similar to the oxaspiropentanes (2*R*,3*S*,4*S*)/(2*S*,3*R*,4*S*) ratio (70/30), it could be considered that this C_3–C_4 ring expansion was also diastereoselective.[9]



(1*R*,2*S*)-**7** (1*R*,2*S*)-**8** (2*R*,3*S*)-**9**

Effectively, we had previously reported that the E (1*R*,2*S*)-1-(1-t-butyldimethylsiloxy-2-methylcyclopropyl)-pent-1-en-3-ol **8**, prepared from the cyclopropanecarbaldehyde (1*R*,2*S*)-**7** (>95% ee), underwent regio- and diastereoselective trifluoroboron–etherate (BF_3–Et_2O) catalyzed ring

expansion into the optically active (E) 2-(but-1-enyl)-3-methyl cyclobutanone (2*R*,3*S*)-**9**, with total preservation of the configuration of the stereocenter.[9]



(3*S*,4*R*)-**10** *Quercus lactone a* (3*S*,4*S*)-**11** *Quercus lactone b*

The 72:28 mixture of regioisomeric cyclobutanones (2*R*,3*S*)-**4** and **6** was treated with MCPBA in dichloromethane at 0°C, to produce in 68% yield, after purification by flash chromatography (silica gel, pentane/ether, 85/15) the (3*S*,4*R*) 4-butyl-3-methyl butanolide **10** (*Quercus lactone a*),[19,20] with >92% enantiomeric excess.[21] Likewise the pure cyclobutanone (2*S*,3*S*)-**5** underwent Baeyer–Villiger oxidation upon treatment with MCPBA under the same conditions, to provide in 93% yield the (3*S*,4*S*)-4-butyl-3-methyl butanolide **11** (*Quercus lactone b*),[9,19] with >89% enantiomeric excess.[22]

Quercus lactone a and *b* have been isolated from white oak wood and are found in wines and spirits kept in oak barrels for maturing.[23] We had reported the first asymmetric synthesis of *Quercus lactone b*, from reduction (Pd/C, H_2, AcOEt) of the 2-vinylcyclobutanone (2*R*,3*S*)-**9**, followed by Baeyer–Villiger oxidation;[9] now from the (2*R*,3*S*,4*S*) oxaspiropentane **2**, resulting from asymmetric alkylidenecyclopropane epoxidation, in two steps, lithium iodide catalyzed ring expansion and oxidation (MCPBA), we have performed the total asymmetric synthesis of the diastereomeric *Quercus lactone a*. It must be underlined that all these compounds have a common precursor, *i.e.* the (2*S*)-dimethyl 2-methylsuccinate, readily available as its (*R*)-enantiomer, from enzymatic hydrolysis of the racemate[10] and that such asymmetric cyclobutanones, from low-cost preparation, can lead not only to γ-butyrolactones (MCPBA), but also to cyclopentanones (CH_2N_2) and to γ-butyrolactams ($ArSO_2ONH_2$).[24]

As the (2*S*)-pentylidene(2-methylcyclopropane) **1**, was prepared from (2*S*)-dimethyl-2-methylsuccinate (>91.5% ee),[10] the formation of the *Quercus lactone b* (>92% ee) proves that the configuration of the former stereogenic center, *i.e.* of the (2*S*) 2-methylsuccinate, was totally retained during the whole synthetic sequence involving sodium induced acyloin cyclization, base induced C_4–C_3 ring contraction,[9] palladium(0) catalyzed hydrogenolysis,[10b] lithium iodide induced C_3–C_4 ring expansion and Baeyer–Villiger oxidation, also known to occur with complete retention of configuration.[25]

Acknowledgements

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References

1. Crandall, J. K.; Paulson, D. R. *J. Org. Chem.* **1968**, *33*, 991 and 3291.
2. Wiseaman, J. R.; Chan, H. F. *J. Am. Chem. Soc.* **1970**, *92*, 4749.
3. Salaün, J.; Conia, J. M. *J. Chem. Soc. Chem. Commun.* **1971**, 1579; Salaün, J.; Garnier, B.; Conia, J. M. *Tetrahedron* **1974**, *30*, 1413; Salaün, J.; Champion, J.; Conia, J. M. *Org. Synth.* **1977**, *57*, 36.
4. Aue, D. H.; Meshishnek, M. J.; Shellhamer, D. F. *Tetrahedron Lett.* **1973**, 4799.
5. Braun, M.; Seebach, D. *Angew. Chem.* **1974**, 279; *Angew. Chem. Int. Ed.* **1974**, *13*, 277; Braun, M.; Dammann, R.; Seebach, D. *Chem. Ber.* **1975**, *108*, 2368; Dammann, R.; Braun, M.; Seebach, D. *Helv. Chim. Acta* **1976**, *59*, 2821; Hiyama, T.; Takehara, S.; Kitatani, K.; Nozaki, H. *Tetrahedron Lett.* **1974**, 3295.
6. Wiechert, R. *Angew. Chem.* **1970**, *82*, 219; *Angew. Chem. Int. Ed. Engl.* **1970**, *9*, 237.

7. Johnson, C. R.; Katekar, G. F.; Huxol, R. F.; Janiga, E. R. *J. Am. Chem. Soc.* **1971**, *93*, 371. Bogadanowicz, M. J.; Trost, B. M. *Tetrahedron Lett.* **1972**, 887; Trost, B. M.; Bogdanowicz, M. J. *J. Am. Chem. Soc.* **1973**, *95*, 289, 5311.
8. Salaün, J. *Top. Curr. Chem.* **1988**, *144*, 1.
9. Salaün, J.; Karkour, B. *Tetrahedron Lett.* **1988**, 1537; Salaün, J.; Karkour, B.; Ollivier, J. *Tetrahedron* **1989**, *45*, 3151.
10. a) Chevtchouk, T.; Ollivier, J.; Salaün, J.; Merlet, D.; Courtieu, J. *Tetrahedron: Asymmetry* **1997**, *8*, 999; b) Chevtchouk, T.; Ollivier, J.; Salaün, J. *Tetrahedron: Asymmetry* **1997**, *8*, 1005.
11. Camps, F.; Coll, J.; Messeguer, A.; Pericàs, M.A. *Tetrahedron Lett.* **1981**, *22*, 3895.
12. Use of MCPBA-KF complex made also the work-up easier, simple filtration afforded a *m*-chlorobenzoic acid free solution of epoxides **2** and **3**.
13. Comparatively, addition of a catalytic amount of lithium iodide to the parent oxaspiropentane in dichloromethane, produced an exothermic C_3–C_4 ring expansion into cyclobutanone, instantaneously (see ref. 3).
14. IR, ^{1}H NMR, mass spectra and optical rotation of (2S,3S)-**5** are identical to reported data; ^{13}C NMR ($CDCl_3$, 50 MHz) δ ppm: 13.90, 15.51, 21.90, 22.63, 23.90, 30.07, 51.97, 62.03, 212.03.
15. The stereochemistry of the regioisomer **6** was not determined.
16. Chapman, N. B.; Wray, V. J. *Chem. Soc. (B)* **1971**, 71; Guest, I. G.; Marples, B. A. *J. Chem. Soc. (C)* **1970**, 1626; Blackett, B. N.; Coxon, J. M.; Hartshorn, M. P.; Prichards, K. E. *Tetrahedron* **1969**, 25, 4999.
17. Erickson, K. L.; Kim, K. *J. Org. Chem.* **1971**, *36*, 2915.
18. Salaün, J. 'Rearrangements involving the cyclopropyl group' in Rappoport, Z., Ed. *The Chemistry of the Cyclopropyl Group*, Wiley, New York **1987**, p. 809.
19. Masuda, M.; Nishimura, K. *Chemistry Lett.* **1981**, 1333.
20. Ortuno, R. M.; Merce, R.; Font, J. *Tetrahedron* **1987**, *43*, 4497; Bloch, R.; Gilbert, L. *J. Org. Chem.* **1987**, *52*, 4603;
21. Enantiomeric excess of γ-butyrolactone (3*S*,4*R*)-**10** was established by comparison of its specific rotation ($[\alpha]_D$=+72.9, c1, MeOH) with literature data ($[\alpha]_D$=+79, c1, MeOH).[19]
22. Enantiomeric excess of γ-butyrolactone (3*S*,4*S*)-**11** was established by comparison of its specific rotation ($[\alpha]_D$=−77.5, c1, MeOH) with literature data ($[\alpha]_D$=−87, c1, MeOH).
23. Günther, C.; Mosandl, A. *Liebigs Ann. Chem.* **1986**, 212 and references cited therein.
24. Delair, Ph.; Kanazawa, A. M.; de Azevedo, M. B. M.; Greene, A. E. *Tetrahedron: Asymmetry* **1996**, *7*, 2707.
25. Trost, B. M.; Bogdanowciz, M. J. *J. Am. Chem. Soc.* **1973**, *95*, 5321.

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