The combined organic phases were dried over $Na_2SO_4$, the solvent was stripped off, and the residue was Kugelrohr distilled to provide compounds **3** (Table I).

**Geminal Dimethylation of Ketones 7 (Method B).** $TiCl_4$ (4.6 mL, 42 mmol) in 80 mL of $CH_2Cl_2$ was treated with 14 mL of a 3 M solution of $(CH_3)_2Zn$[10] in $CH_2Cl_2$ at −40 °C under nitrogen, and the mixture was stirred for 10 min. At that temperature 20 mmol of ketone **7** was slowly added and the mixture stirred for 2 h while the temperature was slowly allowed to come to −10 °C. The reaction mixture was then worked up as above (for yields of **3**, see Table I).

**Spectroscopic and Analytic Data. 5-(1,1-Dimethylpropyl)resorcinol Dimethyl Ether (3a):** Kugelrohr distillation at an 80 °C oven temperature and 0.1 torr; $^1H$ NMR ($CCl_4$) $\delta$ 0.7 (s, 3), 1.25 (s, 6), 1.63 (q, 2), 3.9 (s, 6), 6.05 (d, 1), 6.2 (d, 2); IR (neat) 2985, 1600, 1205, 1155, 695 $cm^{-1}$. Anal. Calcd for $C_{13}H_{20}O_2$: C, 75.02; H, 9.61. Found: C, 75.20; H, 9.75.

**5-(5-Methylnon-5-yl)resorcinol Dimethyl Ether (3d):** Kugelrohr distillation at a 130 °C oven temperature and 0.1 torr; $^1H$ NMR ($CCl_4$) $\delta$ 0.82 (t, 6), 1.2 (s, 3), 1–1.7 (m, 12), 3.7 (s, 6), 6.2 (br s, 1), 6.35 (br s, 2); IR (neat) 2980, 2940, 1595, 1460, 1205, 1160, 705 $cm^{-1}$. Anal. Calcd for $C_{18}H_{30}O_2$: C, 77.71; H, 10.78. Found: C, 78.01; H, 10.90.

Data for compounds **3b** and **3c** correspond to literature values.[2]

**Acknowledgment.** This work was supported by the Deutsche Forschungsgemeinschaft und the Fonds der Chemischen Industrie.

**Registry No.** **3a**, 83816-35-7; **3b**, 22930-08-1; **3c**, 60526-81-0; **3d**, 83816-36-8; **5**, 2747-38-8; **6**, 35739-70-9; **7** ($R^1$ = $CH_3$), 39151-19-4; **7** ($R^1$ = $CH_3(CH_2)_3$), 5333-29-9; **7** ($R^1$ = $CH_3(CH_2)_5$), 39192-51-3; **8a**, 83816-37-9; **8b**, 83816-38-0; **8c**, 83816-39-1; **8d**, 83816-40-4; $CH_3CH_2Li$, 811-49-4; $CH_3(CH_2)_3Li$, 109-72-8; $CH_3(CH_2)_5Li$, 21369-64-2.

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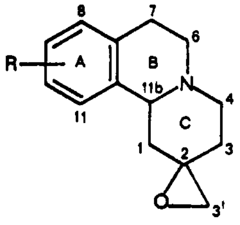
# Synthesis of Spiro[1,3,4,6,7,11b-hexahydro-2*H*-benzo[*a*]quinolizine-2,2′-oxiranes] and Spiro[1,3,4,6,7,11b-hexahydro-2*H*-benzo[*a*]quinolizine-2,5′-oxazolidin-2′-ones] and the Use of Carbon-13 Nuclear Magnetic Resonance Spectroscopy in the Assignment of Stereochemistry to Epoxides[1]

Roman Davis, Arthur F. Kluge,* Michael L. Maddox, and Mark L. Sparacino

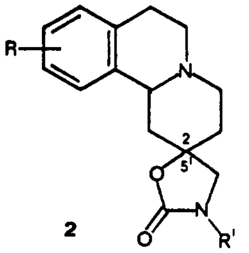
*Institute of Organic Chemistry, Syntex Research, Palo Alto, California 94304*

*Received February 2, 1982*

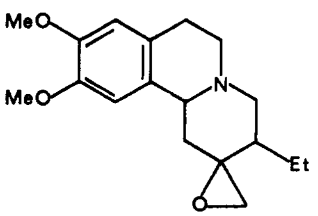
We required substituted spiro epoxides **1** as intermediates for making derivatives of the spiro[1,3,4,6,7,11b-hexahydro-2*H*-benzo[*a*]quinolizine-2,5′-oxazolidin-2′-one] system **2**.[2] The preparation of epoxide **3** had been reported by Popp;[3,4] however, there was no assignment given to the relative stereochemistry of the three asymmetric centers in this compound. Since we required methodology for making compounds such as **2** with defined stereochemistry at the spiro fusion point, we have examined the precursor system **1** in greater detail. We now report stereoselective methods for the preparation of both diastereoisomers of epoxide **1**, the subsequent transformation of these epoxides into the separate isomers of spiro compounds **2**, and the application of $^{13}C$ NMR spectroscopy to the assignment of stereochemistry to epoxides such as **1**.



**1**



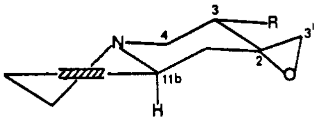
**2**



**3**

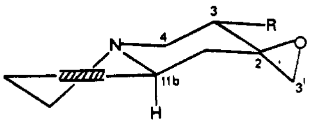
The preparation of epoxides was achieved according to Scheme I. Reaction of ketone **4**[5] with oxosulfonium ylide **5** gave the crystalline epoxide **6** in 45% yield. Sulfonium ylide **7** combined with **4** to give a ca. 1:4 mixture of **6** and isomer **8** in 69% yield. The crystalline isomer **8** was isolated in 27% yield by trituration of the mixture with hot hexane. In our hands the ylide **5** reacted with ketone **9**[6] to give a 93% yield of **3a** as compared to 67% reported in the literature.[3] Reaction of **9** with **7** gave a ca. 6:1 mixture of **3a** and **3b** in 82% yield. We were not able to isolate pure **3b** from this mixture.

The stereochemical assignments given to **6**, **8**, and **3a**,**b** are founded on the stereoselective preferences of ylides **5** and **7** as originally determined by a study of the products obtained from their reaction with 4-*tert*-butylcyclohexanone.[7] The argument used to assign stereochemistry to **6** and **8** states that the stabilized oxosulfonium ylide **5** gives the product of thermodynamic control, one which contains a pseudoequatorial methylene. The more reactive sulfonium ylide **7** gives the product mixture of kinetic control, since its addition to a carbonyl is less reversible than is the case with ylide **5**.[8] The reactivity of **7** leads to two products (**3a** and **3b**) from reaction with **9**, whereas the less reactive, and thus more selective, ylide **5** reacts with α-ethyl-substituted ketone **9** to give a single product, which is assigned structure **3a** (Popp's epoxide **3**) on the basis of the assumption that it is the product of thermodynamic control and that it therefore contains the ethyl



**6** : R = H

**3a** : R = Et



**8** : R = H

**3b** : R = Et

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(1) Contribution No. 620 from the Institute of Organic Chemistry.

(2) A substituted example of heterocyclic system **2** has been reported in the literature: Maillard, J.; Langlois, M.; DeLaunay, P.; Vo Van, T.; Chenu, J.; Morin, R.; Benharkate, M.; Manuel, C.; Montoso, F. *J. Med. Chem.* **1972**, *15*, 1123.

(3) Popp, F. D.; Watts, R. F. *J. Pharm. Sci.* **1978**, *67*, 871.

(4) Popp, F. D.; Watts, R. F. *J. Heterocycl. Chem.* **1978**, *15*, 675.

(5) Beke, D.; Szantay, C. *Chem. Ber.* **1962**, *65*, 2132.

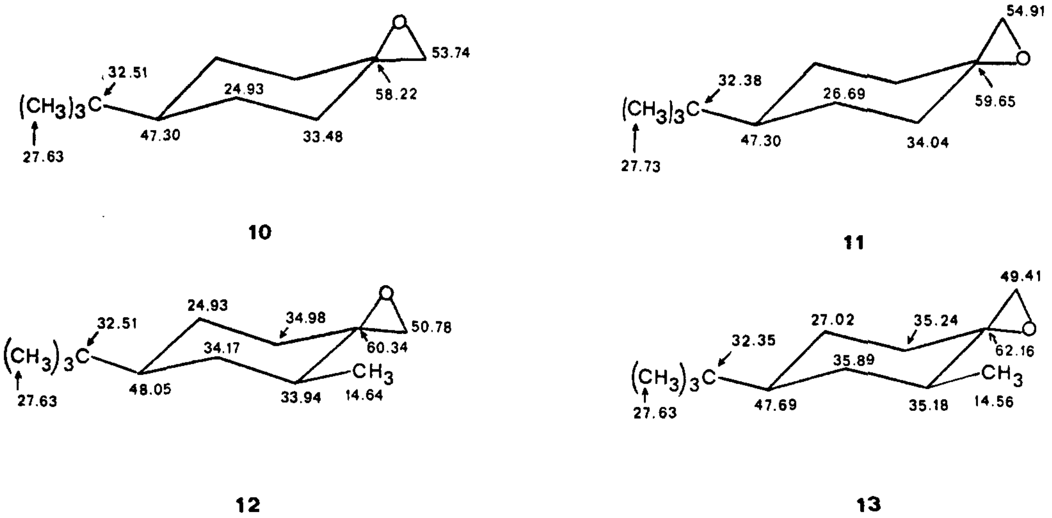
(6) Oppenshaw, H. T.; Whittaker, N. *J. Chem. Soc.* **1963**, 1449.

(7) Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1353.

(8) House, H. O. "Modern Synthetic Reactons", 2nd ed.; W. A. Benjamin: Menlo Park, CA, 1972, p 718.

0022-3263/83/1948-0255$01.50/0

Chart I[a]



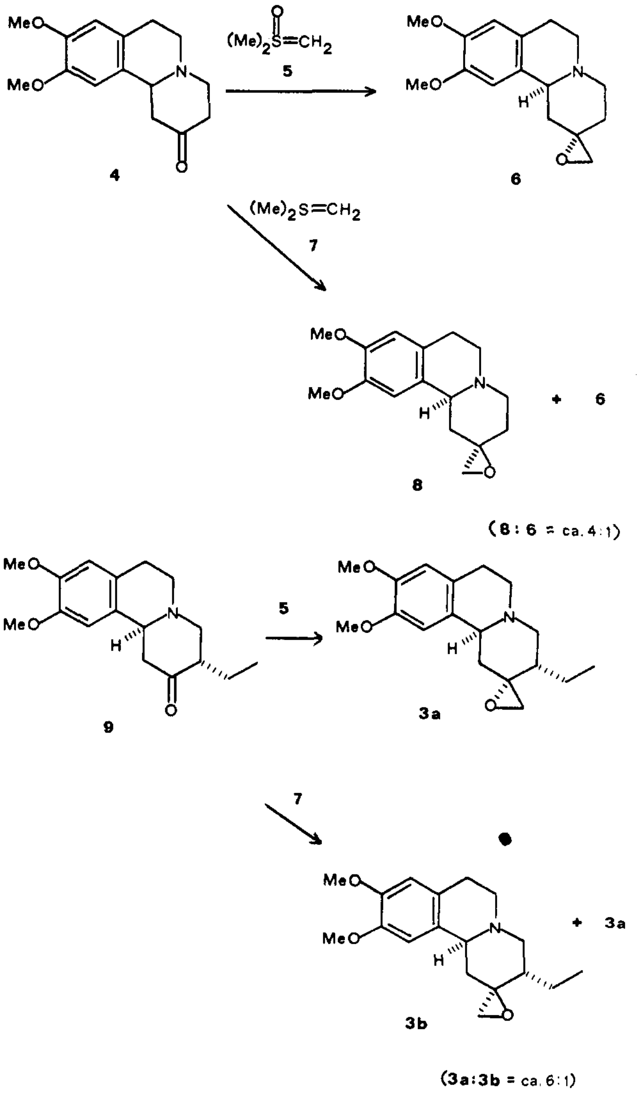
[a] Chemical shifts in parts per million are given for solutions of the compounds in deuteriochloroform.

substituent in an equatorial position and the epoxide methylene in a pseudoequatorial position.

Compounds **6**, **8**, and **3a,b** were examined by $^{13}$C NMR spectroscopy, and the individual assignments are given in Table I. The assignments were made on the basis of off-resonance decoupling and by analogy to literature assignments for 1,3,4,6,7,11b-hexahydro-2*H*-benzo[*a*]quinolizin-2-ones.[9,10] Comparison of assignments for **6** and **8** showed the surprising result that C-3′ in **6** was upfield from its position in **8** by 1.92 ppm. Given a chair conformation for the C ring, one expects C-3′ to occupy a pseudoequatorial position in **6** and a pseudoaxial position in **8**. Thus one would have expected on the basis of the well-documented steric compression effect in carbon-13 nuclear magnetic resonance spectroscopy[11] that C-3 in **8** would be found at 2.3–3.5 ppm higher field than C-3 in **6**. Since the reverse order of chemical shifts was found to be the case, we searched for some rationale that would explain the anomaly. We suspected at first that this reversal of chemical shifts was due to the existence of major conformational differences between the two isomers; however, this explanation seemed not to hold since we observed in the infrared spectra of both **6** and **8** the presence of strong Bohlmann bands[12] at 2760, 2820, and 2835 cm$^{-1}$, which indicated that both **6** and **8** existed predominantly with a B/C-trans junction.[13]

The isomeric epoxides **10**[7] and **11**[7] (Chart I) and their methyl-substituted analogues **12** and **13** were evaluated as model compounds for $^{13}$C NMR spectroscopy (see structures for chemical shifts in deuteriochloroform).[14] The pseudoequatorial epoxide methylene in **10** absorbed at 1.17 ppm upfield of the corresponding pseudoaxial methylene in **11**, whereas in diastereoisomers **12** and **13** the pseudoaxial epoxide methylene of **13** was 1.37 ppm upfield of the pseudoequatorial methylene in **12** (vide infra). This relative positioning of the epoxide methylenes was also found between the heterocyclic pairs **6**/**8** and **3a**/**3b**. Another correlation that was found between the heterocycles and the carbocyclic models was the relative shift for the spiro fusion carbon, which was always upfield in the isomer with

Scheme I



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(9) Buzas, A.; Cavier, R.; Cossais, F., Finet, J. P. Jacquet, J. P.; Lavielle, G.; Platzer, N. *Helv. Chem. Acta* **1977**, *60*, 2122.

(10) Szabo, L.; Nogradi, K.; Toth, I; Szantay, G.; Radics, L.; Virag, S.; Kanyo, E. *Acta Chim. Acad. Sci. Hung.* **1979**, *100*, 19.

(11) Stothers, J. B. "Carbon-13 NMR Spectroscopy"; Academic Press: New York, 1972; p 163 ff.

(12) Bohlmann, F. *Chem. Ber.* **1958**, *91*, 2157.

(13) A referee has noted that the $^{13}$C NMR data exclude a B/C-cis arrangement in one diastereoisomer of each pair. If the B/C ring were cis, C-4 and C-7 would experience a reciprocal $\gamma$ effect, and C-7 would therefore appear at significantly higher field in the cis isomer than in the trans. In fact, each pair of diastereoisomers exhibit very close C-7 resonances.

(14) The assignments given to C-3 and C-6 in **12** and **13** are ambiguous and may be interchanged.

Table I. Carbon-13 Chemical Shifts[a,b]

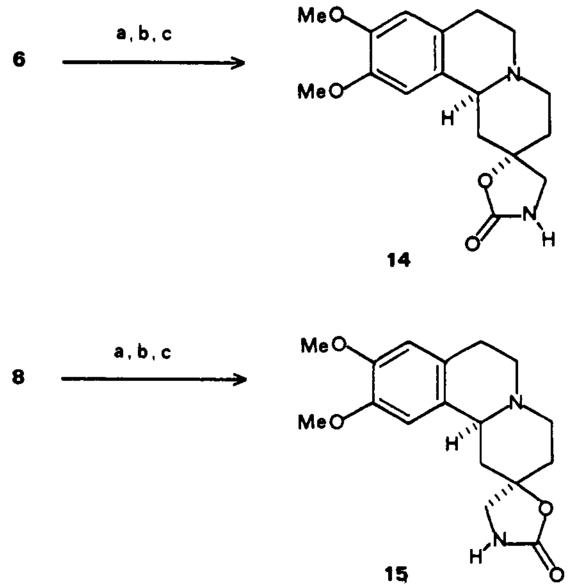
| assignment | chemical shift, ppm | | | | | |
|---|---|---|---|---|---|---|
| | 6 | 8 | 3a | 3b[c] | 14 | 15 |
| C-1 | 39.24 | 39.27 | 39.43 | 40.44 | 40.99 | 41.35 |
| C-2 | 57.38 | 58.55 | 59.25 | 60.74 | 79.75 | 80.66 |
| C-3 | 32.48 | 32.93 | 40.63 | 41.14 | 35.14 | 35.34 |
| C-4 | 53.80 | 55.07 | 58.80 | 60.45 | 51.10 | 50.62 |
| C-6 | 52.05 | 51.79 | 51.98 | 51.80 | 51.33 | 51.49 |
| C-7 | 29.32 | 29.36 | 29.19 | 29.26 | 28.77 | 28.80 |
| C-7a | 126.82 | 126.59 | 126.54 | 126.46 | 126.53 | 126.40 |
| C-8 | 111.64 | 111.64 | 111.29 | 111.63 | 111.99 | 111.90 |
| C-9[d] | 147.40 | 147.43 | 147.06 | 147.38 | 147.11 | 147.10 |
| C-10[d] | 147.63 | 147.79 | 147.33 | 147.73 | 147.27 | 147.30 |
| C-11 | 108.91 | 108.00 | 107.85 | 108.02 | 108.65 | 108.94 |
| C-11a | 129.68 | 129.22 | 129.37 | 129.04 | 129.45 | 129.06 |
| C-11b | 60.30 | 61.67 | 60.21 | 61.97 | 57.77 | 58.13 |
| C-3′ | 53.15 | 55.07 | 50.23 | 49.96 | | |
| C-2′ | | | | | 158.00 | 158.00 |
| C-4′ | | | | | 51.27 | 48.67 |
| $OCH_3$ | 55.85 | 55.88 | 55.73 | 55.91 | 55.88 | 55.92 |
| $OCH_3$ | 56.01 | 56.01 | 55.88 | 56.04 | 56.18 | 56.21 |
| $CH_2$ | | | 18.24 | 18.75 | | |
| $CH_3$ | | | 11.98 | 11.94 | | |

[a] Chemical shifts in parts per million downfield from internal $Me_4Si$. [b] Compounds **6**, **8**, **3a**, and **3b** were dissolved in deuteriochloroform. Compounds **12** and **13** were dissolved in deuteriodimethyl sulfoxide. [c] The spectrum of 3b was obtained from a ca. 4:1 mixture of 3b and ketone **9**. [d] The assignments given to C-9 and C-10 are interchangeable.

the pseudoequatorial epoxide methylene. These correlations strengthened the structural assignments given to **6**, **8**, and **3a**,**b**, and they also allowed us to rule out the possibility that the nitrogen atom in **6** and **8** was the source of the reversal of the normal $^{13}C$ NMR chemical shift pattern, which has an axial carbon 2.3–3.5 ppm upfield of an equatorial carbon.

Any explanation of the γ upfield shift seen with the pseudoequatorial epoxide methylenes in this series of compounds would be a matter of considerable conjecture since the origin of the γ upfield shift in the general case is known to be a multifactoral expression of steric[15] and electronic[16] effects. Our epoxides provide a further complication since they contain several simultaneous γ interactions. For example, the γ ring carbons (C-3 and C-5 of **10**/**11** and **12**/**13** and C-4 and C-11b of **6**/**8** and **3a**/**3b**) are situated γ to both an epoxide methylene and an epoxide oxygen. In pairs **12**/**13** and **3a**/**3b** the epoxide methylene is also situated γ to an alkyl substituent, and in these compounds one also finds an upfield shift of the pseudoaxial epoxide methylene, which represents a reversal of the pattern seen with the unsubstituted epoxide pairs **10**/**11** and **6**/**8**. This reversal is due to the superimposition of an additional γ upfield shift arising from the alkyl substituent ($CH_3$ in **13** and $CH_3CH_2$ in **3b**), which is closer to the epoxide methylene in the pseudoaxial isomer (**13** and **3b**) than in the pseudoequatorial isomer (**12** and **3a**). In the alkyl-substituted cases 12/13 and 3a/3b a reciprocal γ shift effect is not seen with the alkyl substituent since its shift is also determined by a countervailing γ effect residing in the epoxide oxygen. When one considers the relative shifts of the ring carbons that are γ to the epoxide methylene, one sees that the upfield shifts found in **10**, **13**, **6**, and **3a** are reciprocal with the upfield shifts of the corresponding pseudoequatorial epoxide methylene, which reciprocity would suggest that the two shifts are related through some interaction between the epoxide methylene and the γ-situated ring carbons. However, the situation is ambiguous, and one may not conclude with certainty that the two shifts are mechanistically linked in tandem since the γ ring carbons are also subject to an upfield shift caused by the γ-situated pseudoaxial epoxide oxygen.[17] The involvement of multiple contributors to the γ shift effect (hybridization and steric interactions) and the simultaneous presence of two γ substituents (epoxide methylene and epoxide oxygen) combine to prevent us from assigning a single explanation to the relative shifts found with these epoxide pairs. However, we have provided sufficient examples to make the point that these shifts, whatever their source, are general.

Scheme II[a]



[a] (a) $NH_3$, MeOH, 100 °C, 8 h; (b) *N*,*N*′-carbonyldiimidazole, THF, reflux, 2 h; (c) KO-*t*-Bu, ca. 25 °C, 15 min.

The epoxides **6** and **8** were transformed into the spiro[quinolizine-2,5′-oxazolidinones] **14** and **15** in two steps consisting of epoxide opening with ammonia followed by ring closure with *N*,*N*′-carbonyldiimidazole (Scheme II). The $^{13}C$ NMR chemical shifts for these compounds are found in Table I. Carbon 4′ is found at 2.6 ppm higher field in **15** than in isomer **14**. This relative positioning of chemical shifts for C-4′ shows that in **15** C-4′ occupies a pseudoaxial, sterically compressed position relative to C-4′ in **14**, which is pseudoequatorial. The model compounds **16** and **17** also show these correlations in their $^{13}C$ NMR spectra. Thus the stereochemical assignments of **6**, **8**, and **3a**,**b**, while initially based on the argument of relative reactivities of ylides **5** and **7** and the $^{13}C$ NMR correlation with **10**-**13**, were substantiated by the $^{13}C$ NMR analysis of **14** and **15**.

## Experimental Section

Melting points (corrected) were obtained by using a Fisher-Johns apparatus. Infrared spectra were obtained with a Perkin-Elmer grating spectrophotometer. For $^1H$ and $^{13}C$ NMR tetramethylsilane was used as an internal standard, and samples were measured as ca. 10% (v/v) solutions in deuteriochloroform

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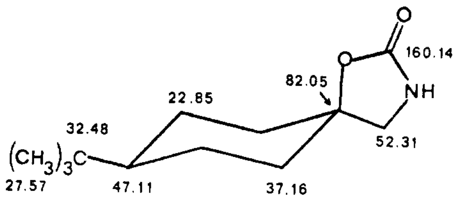
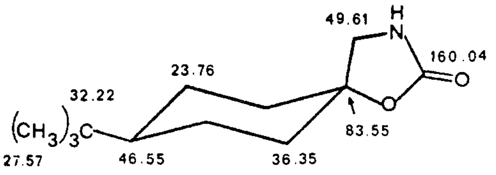
[15] Lambert, J. B.; Vagenas, A. R. *Org. Magn. Reson.* **1981**, *17*, 265.

[16] Lambert, J. B.; Vagenas, A. R. *Org. Magn. Reson.* **1981**, *17*, 270.

(17) The upfield shift of the γ ring carbon in the pseudoequatorial epoxide methylene isomers correlates with the C–C(β)–C(α)–O dihedral angle in the same direction, but not the same magnitude, as was observed with a hydroxy substituent as reported in ref 16. From Dreiding models the approximate dihedral angles formed between the epoxide oxygen and the γ ring carbon are ca. 90° for the pseudoaxial oxygen and ca. 170° for the pseudoequatorial oxygen.



**16**



**17**

or deuteriodimethyl sulfoxide. Proton spectra were obtained on a Varian HA-100 spectrometer, and carbon spectra were obtained with either a Bruker WH-90 or a Bruker WM-300 spectrometer. Elemental analyses were performed by the Syntex Analytical Services group.

**(2*S**,11b*S**)-Spiro[1,3,4,6,7,11b-hexahydro-2*H*-benzo[*a*]quinolizine-2,2′-oxirane] (6).** To a 500-mL flask equipped with a magnetic stirrer was added 5.35 g (0.111 mol) of 50% sodium hydride in mineral oil. The flask was repeatedly evacuated and recharged with argon. The sodium hydride was washed with three 100-mL portions of hexane while an argon atmosphere was maintained in the flask. To the washed sodium hydride was added 150 mL of dimethyl sulfoxide and 24.54 g (0.111 mol) of trimethyloxosulfonium iodide. This mixture was stirred for 20 min, and then a slurry of 22.7 g (0.087 mol) of ketone **4** in a mixture of 20 mL of THF and 60 mL of dimethyl sulfoxide was added at once. After being stirred 15 min at 25 °C and 1 h at 50 °C, the mixture was poured onto 1000 mL of ice–water. This mixture was extracted with five 150-mL portions of 75% ethyl acetate–hexane. The combined organic extract was extracted twice with 200-mL portions of water. After the mixture was dried over sodium sulfate, the extract was evaporated to give an oil, which was layered with 300 mL of hexane and left at 5 °C for 48 h. The product was collected by filtration: 10.75 g (45%); mp 93–94 °C; mass spectrum, *m/e* 275 ($M^+$). Anal. Calcd for $C_{16}H_{21}NO_3$: C, 69.79; H, 7.69; N, 5.09. Found: C, 69.85; H, 7.65; N, 5.10.

**(2*R**,11b*S**)-Spiro[1,3,4,6,7,11b-hexahydro-2*H*-benzo[*a*]quinolizine-2,2′-oxirane] (8).** A solution of dimsyl sodium was prepared according to the method of Corey and Chaykovsky[7] by using 3.68 g (0.077 mol) of 50% mineral oil suspension of sodium hydride and 55 mL of diemthyl sulfoxide. This mixture was cooled to −10 °C after addition of 55 mL of THF. A solution of 15.61 g (0.077 mol) of trimethyl sulfonium iodide in 60 mL of dimethyl sulfoxide was added over a 3-min period. After the mixture was stirred at −10 °C for an additional minute, a slurry of 20 g (0.077 mol) of ketone **4** in 150 mL of THF was added at once. This mixture was stirred for 10 min at −10 °C and then for 3 h at 25 °C. The mixture was poured into 600 mL of ice–water, and the resulting mixture was extracted with four 100-mL portions of 85% ethyl acetate–hexane. The combined organic extract was washed with 100 mL of water, and it was dried over sodium sulfate. Evaporation gave 14.53 g of a mixture of **8** and **6** in a ratio of ca. 4:1 as shown by TLC with 5% methanol–dichloromethane (69%). This mixture was triturated with two 150-mL portions of boiling hexane. The combined hexane washings were evaporated, and the residue was recrystallized from 2-propanol to give 5.65 g of white, crystalline, **8**, mp 117–118 °C. Anal. Calcd for $C_{16}H_{21}NO_3$: C, 69.79; H, 7.69; N, 5.09. Found: C, 69.80; H, 7.71; N, 5.08.

**(2*R**,3*S**,11b*S**)-Spiro[3-ethyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2*H*-benzo[*a*]quinolizine-2,2′-oxirane] (3a).** By use of the procedure specified for **6** with 0.7 g (0.0146 mol) of 50% sodium hydride, 3.5 g (0.0159 mol) of trimethyloxosulfonium iodide, and 4 g (0.0138 mol) of ketone **9** there was obtained 3.9 g of **3a** (93%) as light yellow crystals, mp 107–110 °C. Recrystallization from ethanol gave off-white crystals, mp 111–112 °C (lit.[3] mp 111–112 °C).

**(2*R**,3*S**,11b*S**)-Spiro[3-ethyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2*H*-benzo[*a*]quinolizine-2,2′-oxirane] (3a) and (2*S**,3*S**,11b*S*)-Spiro[3-ethyl-9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2*H*-benzo[*a*]quinolizine-2,2′-oxirane] (3b).** A solution of dimsyl sodium was prepared by using 0.91 g (0.019 mol) of 50% sodium hydride and 15 mL of dimethyl sulfoxide.[7] To this solution was added 15 mL of THF, and the resulting mixture was cooled to −10 °C. A solution of 3.88 g (0.019 mol) of trimethylsulfonium iodide in 15 mL of dimethyl sulfoxide was added over 3 min. The mixture was stirred for 1 min, at which time a solution of 5.5 g (0.019 mol) of **9** in 200 mL of THF was added at once. This mixture was stirred for 10 min at −10 °C and then for 3 h at 25 °C. The mixture was poured into 200 mL of ice–water, and it was extracted with three 100-mL portions of 75% ethyl acetate–hexane. The combined extract was washed with two 50-mL portions of water. This solution was concentrated by evaporation to give an oil, which was then taken up in 200 mL of boiling hexane. Crystals deposited upon cooling of the hexane, and after filtration there was obtained 3.39 g (59%) of a ca. 6:1 mixture (by silica gel TLC with 60:40:1 ethyl acetate–hexane–concentrated $NH_4OH$ and visualizing the plate with molybdate reagent) of **3a** and **3b**, mp 106–115 °C. Anal. Calcd for $C_{18}H_{25}NO_3$: C, 71.26; H, 8.30; N, 4.62. Found: C, 71.41; H, 8.19; N, 4.59.

The above filtrate was evaporated to give 1.51 g of a thick oil, which was estimated by TLC to be about 90% **3a** and **3b** along with the starting ketone **9** as the third identified component. The ratio of **3a** to **3b** in this oil was estimated to be about 4:1 by TLC. The total yield of **3a** and **3b** was 4.71 g (82%). A partially purified sample of **3b** was prepared by chromatography from 80–230-mesh silica gel (100:1 loading) with a gradient of 20% ethyl acetate–hexane plus 0.5% triethylamine to 50% ethyl acetate–hexane plus 0.5% triethylamine. The best fraction from this column was concentrated and was further purified by preparative TLC with 70% ethyl acetate–hexane plus 0.5% triethylamine. This procedure gave a 4:1 mixture of **3b** and **9**, which was used for $^{13}C$ NMR study.

**(2*S**,11b*S**)-Spiro[9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2*H*-benzo[*a*]quinolizine-2,5′-oxazolidin-2′-one] (14) and (2*R**,11b*S**)-Spiro[9,10-dimethoxy-1,3,4,6,7,11b-hexahydro-2*H*-benzo[*a*]quinolizine-2,5′-oxazolidin-2′-one] (15).** To a stainless steel bomb was added a solution of 7.5 g (0.027 mol) of **6** in 30 mL of methanol followed by 66 mL of ca. 30% solution of ammonia in methanol. The bomb was sealed, and the mixture was heated at 100 °C for 8 h. After cooling to 0 °C, the bomb was opened, and the contents were transferred to an evaporation flask. The solvent was removed by evaporation to give 7.7 g of an oil. This oil was dissolved in 200 mL of THF, 6.6 g (0.041 mol) of *N*,*N*′-carbonyldiimidazole was added, and the mixture was heated at reflux for 2 h. The mixture was evaporated, and the residue was taken up in 300 mL of dichloromethane. This solution was washed with 100 mL of water and was then dried over sodium sulfate. After filtration and evaporation a residue was obtained, which was then dissolved in 100 mL of THF and treated with 5 g of potassium *tert*-butoxide. After 15 min the solvent was removed by evaporation, and the residue was layered with 300 mL of dichloromethane and 100 mL of water. The dichloromethane layer was separated, was washed with 100 mL of water, and was dried over sodium sulfate. After evaporation a residue was obtained, which yielded 3.41 g (40% from **6**) of **14** as white crystals after trituration with ethyl acetate–diethyl ether: mp 223–224 °C dec; IR (KBr) 2750, 2800, 1735 $cm^{-1}$; NMR ($Me_2SO$-$d_6$) $\delta$ 1.5–3.6 (m, 13 H), 3.68 (s, 3 H), 3.70 (s, 3 H), 6.64 (s, 1 H), 3.74 (s, 1 H), 7.49 (s, 1 H, NH). Anal. Calcd for $C_{17}H_{22}N_2O_4$: C, 64.13; H, 6.97; N, 8.80. Found: C, 64.17, H, 7.04; N, 8.75.

Compound **15** was prepared in the same way as **14**. With 2 g of epoxide **8** there was obtained 0.97 g of **15**: mp 222–230 °C dec; NMR ($Me_2SO$-$d_6$) $\delta$ 1–3.6 (m, 13 H), 3.67 (s, 3 H), 3.69 (s, 3 H), 6.60 (s, 1 H, 6.77 (s, 1 H), 7.5 (s, 1 H, NH); mass spectrum, *m/e* 318 ($M^+$). Anal. Calcd for $C_{17}H_{22}N_2O_4$: C, 64.13; H, 6.97; N, 8.80. Found: C 63.93; H, 7.03 N, 8.74.

**Preparation of Epoxides 10 and 11.** Compound **10** was prepared by using dimethylsulfoxonium methylide **5**.[7] Compounds **10** and **11** were obtained as a mixture from the reaction of 4-*tert*-butylcyclohexanone with dimethylsulfonium methylide **7**.[7] A 55:45 mixture of **11** and **10** was obtained by HPLC (10-$\mu$m silica gel, 10% ethyl acetate–hexane, 1400 psi, 60 × 13 mm column), and this mixture was used to obtain the $^{13}C$ NMR of **11**.

**Preparation of Epoxides 12 and 13.** Compound **12**, an oil, was prepared from the reaction of 2-methyl-4-*tert*-butylcyclohexanone[18] and **5**[7] in 35% yield after flash chromatography[19] with 1% ethyl acetate–hexane. Anal. Calcd for $C_{12}H_{22}O$: 76.06; H, 12.16. Found: C, 78.82; H, 12.30. Compounds **12** and **13** were obtained as a mixture in 85% yield from the reaction of 2-methyl-4-*tert*-butylcyclohexanone with **7**.[7] A ca. 2:1 mixture of **13** and **12** was obtained by flash chromatography with 0.75% ethyl acetate–hexane. Anal. Calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.16. Found: C, 78.97; H, 12.07.

**Preparation of Oxazolidinones 16 and 17.** Compound **16** (mp 207–208 °C) was prepared in 50% yield starting with **10** and using the same procedure as outlined for **14**. Anal. Calcd for $C_{12}H_{21}NO_2$: C, 68.21; H, 10.02; N, 6.63. Found: C, 68.42; H, 10.12; N, 6.44. Compounds **16** and **17** were obtained in 24% yield by starting with epoxide mixture **10**/**11** and using the same procedure outlined for **14**. The mixture (mp 138–145 °C) resisted attempted separation by preparative chromatography, and it was judged to be a ca. 3:1 ratio of **17**/**16** by proton NMR ($CDCl_3$), which showed $CH_2N$ at $\delta$ 3.27 for **16** and at $\delta$ 3.37 for **17**. Anal. Calcd for $C_{12}H_{21}NO_2$: C, 68.21; H, 10.02; N, 6.63 Found: C, 67.98; H, 10.28; N, 6.65.

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**Registry No.** **3a**, 83946-21-8; **3b**, 83946-22-9; **4**, 841-95-2; **6**, 83917-83-3; **8**, 83917-84-4; **9**, 47136-76-5; **10**, 7787-78-2; **11**, 18881-26-0; **12**, 53730-20-4; **13**, 53698-73-0; **14**, 83917-85-5; **15**, 83917-86-6; **16**, 83917-87-7; **17**, 83917-88-8; trimethyloxosulfonium iodide, 1774-47-6; trimethylsulfonium iodide, 2181-42-2; *N,N'*-carbonyldiimidazole, 530-62-1; 4-*tert*-butylcyclohexanone, 98-53-3; 2-methyl-4-*tert*-butylcyclohexanone, 5064-52-8.

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[18] Conia, J.-M.; Briet, P. *Bull. Soc. Chim. Fr.* **1966**, 3881.

[19] Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

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# Reaction of Alkyl Peroxides and Hydroperoxides with Iron Pentacarbonyl and Dicobalt Octacarbonyl[1]

Kang-Wook Lee and Joseph San Filippo, Jr.*

*Rutgers University, Department of Chemistry,*
*New Brunswick, New Jersey 08903*

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Many substrates that contain simple homonuclear bonds undergo facile oxidative addition reaction with low- or zero-valent transition-metal complexes. Such reactions

$$Fe(CO)_5 + X_2 \rightarrow Fe(CO)_4X_2 + CO$$

$$Co_2(CO)_8 + X_2 \rightarrow 2XCo(CO)_4$$

are generally cited for simple diatomic systems, e.g., the halogens, oxygen, and hydrogen.[2] In an effort to determine if such activity is extendible to simple homonuclear bonds in general, we have examined the reactions of several organic peroxides with iron pentacarbonyl and dicobalt octacarbonyl. Here we report the results of this study and describe the products of several representative reactions.

## Results and Discussion

Di-*tert*-butyl peroxide exhibits no apparent reaction with either iron pentacarbonyl or dicobalt octacarbonyl in benzene after 1 week at ambient temperature. Similar treatment of di-*sec*-butyl peroxide results in a slow but steady reaction with a half-life of ca. 3 days. By comparison, the corresponding reaction with di-*n*-hexyl peroxide shows a half-life of ca. 3 h, leading to a reactivity order of primary > secondary > tertiary. These results are summarized in Table I.

In contrast to alkyl peroxides, alkyl hydroperoxides exhibit a much enhanced reactivity toward both iron pentacarbonyl and dicobalt octacarbonyl. Reaction with these substrates is accompanied by the immediate, vigorous evolution of carbon monoxide. The resulting product mixtures are presented in Table II. Briefly summarized, they reveal the following. First, essentially equivalent product ratios are obtained with either $Fe(CO)_5$ or $Co_2(CO)_8$. Thus, the 1:5 reaction of $Fe(CO)_5$ or $Co_2(CO)_8$ with *tert*-butyl hydroperoxide produces an ~76–90% yield of *tert*-butyl alcohol, an ~3% yield of di-*tert*-butyl peroxide, and <1% acetone. The equivalent reactions with *sec*-butyl hydroperoxide results in an ~65% yield of *sec*-butyl alcohol, an ~20% yield of 2-butanone, and <1% di-*sec*-butyl peroxide while the reaction with *n*-hexyl hydroperoxide leads to the following product mixture: ~50% *n*-hexanol, ~30% *n*-hexanal, and <1% di-*n*-hexyl peroxide. Second, these product ratios remain largely unaffected by gross variations (1:1, 5:1, 10:1, 50:1) in reactant ratios.

A detailed examination of the mechanisms leading to these products has not been carried out. However, a comparison between these products and those observed from the cobalt(II)- and iron(II)-catalyzed homolytic decomposition of hydroperoxides (Table III) is informative. Indeed, the strong similarity in product distributions suggests that similar processes are involved. Thus, the variety of products formed in these reactions can be rationalized in terms of a scheme (eq 1–6) first proposed by

$$RO_2H + M(II) \rightarrow RO\cdot + M(III) + {}^{-}OH \qquad (1)$$

$$RO_2H + M(III) + {}^{-}OH \rightarrow RO_2\cdot + M(II) + H_2O \qquad (2)$$

$$RO\cdot + RO_2H \rightarrow ROH + RO_2\cdot \qquad (3)$$

$$\text{for R = primary:}\ 2RCH_2O_2\cdot \rightarrow RCH_2OH + RCHO + O_2 \qquad (4)$$

$$\text{for R = secondary:}\ 2R_2CHO_2\cdot \rightarrow R_2CHOH + R_2C(O) + O_2 \qquad (5)$$

$$\text{for R = tertiary:}\ R_3CO_2\cdot \rightarrow R_3COH + [R_3CO]_2 + O_2 \qquad (6)$$

Hiatt.[3] This conclusion is sustained by the coproduction of several solvent-derived products. Thus, reaction of *tert*-butyl hydroperoxide with dicobalt octacarbonyl in *n*-heptane yields small amounts (~1–3%) of each of the following solvent-derived products: 4-heptanol and 2-, 3-, and 4-heptanones, as well as the unsymmetrical peroxide $t\text{-}C_4H_9OOC_7H_{15}$.

In summary, the reaction of iron pentacarbonyl and dicobalt octacarbonyl with organic peroxides falls into two distinct classes: the limited reactivity characteristic of dialkyl peroxides and the very substantial reactivity exhibited by alkyl hydroperoxides. Since the O–O bond strength is essentially the same in either substrate, the dramatic difference in their reactivities suggests that different rate-determining steps are involved. Although an oxidative addition is clearly indicated, its nature is not readily apparent and may, in fact, be a relatively minor

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[2] Cotton, F. A.; Wilkinson, G. "Advanced Inorganic Chemistry", 3rd ed.; Wiley-Interscience: New York, 1972; Chapter 24.

[3] Hiatt, R.; Irwin, K. C.; Gould, C. W. *J. Org. Chem.* **1968**, *33*, 1430.

0022-3263/83/1948-0259$01.50/0