[2 s, 6 H, CH_3(Pz)], 3.80 and 3.83 [2 s, 4 H, (Pz)CCH_2C(Tz)], 3.70 [br s, 6 H, N-CH_3(Tz)], 5.03 and 5.10 [2 s, 4 H, (Pz)NCH_2C(Tz)], 5.86 and 5.93 [2 s, 2 H, CH(Pz)]; MS m/z 378. Anal. Calcd for $C_{18}H_{22}N_{10}$: C, 57.20; H, 5.87; N, 37.05. Found: C, 57.29; H, 5.90; N, 36.88.

Macrocycle 3cc. The same method described for **3bb** was used for condensation of **7c** and **12c**. The residue obtained was purified by chromatography on alumina (eluant: CH_2Cl_2/C_2H_5OH, 96/4) (25% yield): mp 110-112 °C; ^{1}H NMR ($CDCl_3$) δ 2.00 and 2.13 [2 s, 6 H, CH_3(Pz)], 3.66 and 3.70 [2 s, 4 H, (Pz)CCH_2C(Tz)], 4.90 and 5.00 [2 s, 4 H, (Pz)NCH_2C(Tz)], 5.16 and 5.21 (2 s, 4 H, CH_2Ph), 5.73 and 5.83 [2 s, 2 H, CH(Pz)], 7.15 (br, 10 H, Ph); MS m/z 530. Anal. Calcd for $C_{30}H_{30}N_{10}$: C, 67.99; H, 5.71; N, 26.43. Found: C, 67.82; H, 5.80; N, 26.32.

Macrocycle 3bc. This macrocycle was obtained as described for **3bb** or **3cc** by condensation of **7b** and **12c**. Purification of the crude product was done by chromatography on alumina (eluant: CH_2Cl_2/C_2H_5OH, 96/4) (25% yield): mp 152-154 °C; ^{1}H NMR ($CDCl_3$) δ 2.08 and 2.25 [2 s, 6 H, CH_3(Pz)], 3.70 [s, 3 H, CH_3(Tz)], 3.76 and 3.80 [2 s, 4 H, (Pz)CCH_2C(Tz)], 4.93 and 5.03 [2 s, 4 H, (Pz)NCH_2C(Tz)], 5.30 (s, 2 H, CH_2Ph), 5.88 [br s, 2 H, CH(Pz)], 7.26 (br, 5 H, Ph); MS m/z 454. Anal. Calcd for $C_{24}H_{26}N_{10}$: C, 63.50; H, 5.77; N, 30.85. Found: C, 63.71; H, 5.68; N, 30.78.

Macrocycle 3ac. Macrocycle **3cc** (0.33 mmol) was added to a suspension of 10% Pd/C (186 mg) in anhydrous methanol under nitrogen. The ammonium formate was added portionwise. The mixture was refluxed for 72 h. After total disappearance of macrocycle **3cc**, the mixture was filtered on Celite, and the methanol was evaporated to give an oil (23% yield), which is the monobenzylated macrocycle **3ac** or **3ca**: ^{1}H NMR ($CDCl_3$) δ 2.20 [s, 6 H, CH_3(Pz)], 4.07 [br, 4 H, (Pz)CCH_2C(Tz)], 5.30 [br, 6 H, (Pz)NCH_2C(Tz) and CH_2Ph], 5.93 [br s, 2 H, CH(Pz)], 7.26 (br, 5 H, Ph); MS m/z 440. Anal. Calcd for $C_{23}H_{24}N_{10}$: C, 62.79; H, 5.50; N, 31.83. Found: C, 62.88; H, 5.48; N, 31.72.

Macrocycle 3aa. Macrocycle **3cc** (0.1 mmol) was added to liquid ammonia. Small pieces of Na (0.44 mmol) were added until the blue color did not disappear anymore. Ammonium chloride (0.72 mmol) was added, and the ammonia was allowed to evaporate. The residue obtained was totally insoluble in organic solvents.

2,5-Bis(chloromethyl)furan. A solution of $SOCl_2$ (6.1 mL) in $CHCl_3$ (4 mL) was added to a mixture of 2,5-(hydroxymethyl)furan (0.04 mol) and pyridine (7.7 mL) in $CHCl_3$ (12 mL) between -10 and 0 °C under nitrogen. The solution was stirred for 2 h at -10 °C and poured into a mixture HCl/H_2O (1/10) at 0 °C. The solution was decanted, the chloroform phase was washed twice with an aqueous solution of HCl (1/10) and once with a solution of 3% NaOH on cooling with ice. The organic phase was dried over KOH and evaporated to dryness without heating in order to avoid any oxidation of the furan derivative. An oil was obtained (lit. mp 63-67 °C)[21] (45% yield): ^{1}H NMR ($CDCl_3$) δ 4.26 (s, 4 H, CH_2Cl), 6.06 [s, 2 H, H(Fur)].

Macrocycles 4. Macrocycles **4b** and **4c** were obtained by condensation of 2,5-bis(chloromethyl)furan with the triheterocycles **7b** and **7c**, respectively, following the same procedure as for the synthesis of macrocycles **2** in heterogeneous phase under nitrogen. The products were purified by chromatography on alumina (eluant CH_2Cl_2/C_2H_5OH, 95/5).

4b (20% yield): mp 178-180 °C; ^{1}H NMR ($CDCl_3$) δ 2.20 [s, 6 H, CH_3(Pz)], 3.86 [s, 3 H, CH_3(Tz)], 3.90 (s, 4 H, $PzCH_2Tz$), 5.03 and 5.06 (2 s, 4 H, $PzCH_2$Fur), 5.90 [s, 2 H, CH(Pz)], 6.16 [s, 2 H, H(Fur)]; MS m/z 363. Anal. Calcd for $C_{19}H_{21}N_7O$: C, 62.87; H, 5.83; N, 27.01. Found: C, 62.73; H, 5.91; N, 27.19.

4c (22% yield): mp 143-145 °C; ^{1}H NMR ($CDCl_3$) δ 2.06 [s, 6 H, CH_3(Pz)], 3.73 and 3.83 (2 s, 4 H, $PzCH_2Tz$), 4.90 and 4.95 (2 s, 4 H, $PzCH_2$Fur), 5.26 (s, 2 H, CH_2Ph), 5.66 and 5.76 [2 s, 2 H, CH(Pz)], 6.03 [s, 2 H, CH(Fur)], 7.15 (br s, 5 H, Ph); MS m/z 439. Anal. Calcd for $C_{25}H_{25}N_7O$: C, 68.40; H, 5.74; N, 22.39. Found: C, 68.62; H, 5.79; N, 22.18.

^{17}O NMR Studies on Alkyl-Substituted 1-Tetralones: Effect of Torsion Angle Change and Repulsive van der Waals Interactions

David W. Boykin*

Department of Chemistry, Georgia State University, Atlanta, Georgia 30303

Brahmadeo Dewprashad and Edmund J. Eisenbraun*

Department of Chemistry, Oklahoma State University, Stillwater, Oklahoma 74078

Received July 28, 1989

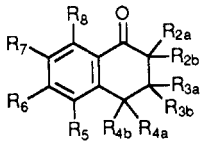
Natural abundance ^{17}O NMR spectroscopic data, in acetonitrile at 75 °C, were obtained for 24 substituted 1-tetralones. Substituent effect additivity was observed for the ^{17}O NMR chemical shifts for these compounds. Substituents ortho to the carbonyl group produced large (~40 ppm) downfield shifts. The downfield shifts could be quantitatively predicted based upon a combination of molecular mechanics estimated torsion angle twist of the carbonyl group and repulsive van der Waals interactions. A general method of analysis of carbonyl ^{17}O NMR chemical shifts in semiflexible systems is presented and applied to previously published chromanone results.

^{17}O NMR spectroscopy continues to be exploited as a probe for a range of structural problems of interest to organic chemistry.[1] Recent investigations have demonstrated a relationship between downfield shift of ^{17}O NMR data and torsion angles for a variety of function groups[1] including aryl ketones.[2,3] In these systems torsion angle rotation results in local repulsive van der Waals energies being near zero. Large downfield shifts of ^{17}O NMR data have also been observed for aromatic carbonyl groups, located near bulky groups in rigid planar systems, for which torsion angle change is not thought to be possible.[1,4-6] In these rigid planar systems, bond angle defor-

(1) Boykin, D. W.; Baumstark, A. L. *Tetrahedron* **1989**, *45*, 3613.
(2) Baumstark, A. L.; Balakrishnan, P.; Dotrong, M.; McCloskey, C. J.; Oakley, M. G.; Boykin, D. W. *J. Am. Chem. Soc.* **1987**, *109*, 1059.
(3) Oakley, M. G.; Boykin, D. W. *J. Chem. Soc., Chem. Commun.* **1986**, 439.
(4) Baumstark, A. L.; Balakrishnan, P.; Boykin, D. W. *Tetrahedron Lett.* **1986**, 3079.
(5) (a) Baumstark, A. L.; Dotrong, M.; Oakley, M. G.; Stark, R. R.; Boykin, D. W. *J. Org. Chem.* **1987**, *52*, 3640. (b) Baumstark, A. L.; Dotrong, M.; Stark, R. R.; Boykin, D. W. *Tetrahedron Lett.* **1988**, 2143.

0022-3263/90/1955-0425$02.50/0

Table I. ^{17}O Chemical Shifts of Alkyl-Substituted 1-Tetralones[a]



compd no.	R_{2a}	R_{2b}	R_{3a}	R_{3b}	R_{4a}	R_{4b}	R_5	R_6	R_7	R_8	δ(C=O)	Δ(δ)[b]
1	H	H	H	H	H	H	H	H	H	H	527.2	0
2	CH_3	H	H	H	H	H	H	H	H	H	521.0	-6.2
3	H	H	CH_3	H	H	H	H	H	H	H	528.3	1.1
4	H	H	tBu	H	H	H	H	H	H	H	527.3	0.1
5	H	H	H	H	CH_3	H	H	H	H	H	527.0	-0.2
6	H	H	H	H	H	H	H	H	CH_3	H	525.8	-1.4
7	H	H	H	H	H	H	H	H	C_2H_5	H	526.2	-1.0
8	H	H	H	H	H	H	CH_3	H	H	CH_3	556.5	29.3
9	H	H	H	H	H	H	CH_3	H	CH_3	H	525.0	-2.2
10	H	H	H	H	H	H	H	CH_3	CH_3	H	520.0	-7.2
11	CH_3	H	H	H	H	H	CH_3	H	H	CH_3	550.0	22.8
12	CH_3	H	H	H	H	H	CH_3	H	H	iPr	552.5	25.3
13	H	H	CH_3	H	H	H	CH_3	H	H	CH_3	557.8	30.6
14	H	H	H	H	CH_3	H	CH_3	H	CH_3	H	527.1	-0.1
15	H	H	H	H	CH_3	H	CH_3	H	H	CH_3	558.1	30.9
16	H	H	CH_3	CH_3	H	H	H	CH_3	H	CH_3	556.0	28.8

[a] Chemical shift values (±1 ppm) obtained at natural abundance in acetonitrile at 75 °C. The $^1/_2$ height widths of signals were 250 ± 50 Hz for monomethyl-substituted compounds and 350 ± 100 Hz for the multisubstituted compounds. [b] Chemical shift difference between 1 and the compound listed.

mation reduces but does not eliminate repulsive van der Waals interactions, and ther "residual" van der Waals energy is correlated with ^{17}O NMR chemical shift.[1,4-7] Thus, it has been clearly demonstrated that downfield ^{17}O NMR chemical shift changes in hindered aryl carbonyl systems can arise from two different phenomena: torsion angle rotation and repulsive van der Waals interactions. To date this method of analysis has been applied to systems in which only one of the two phenomena was dominant. It is the purpose of this investigation to examine semiflexible systems in which steric crowding near a carbonyl group can potentially be relieved by both torsion angle change and by bond angle deformation. The latter could result in retention of significant repulsive van der Waals interactions. Our approach is to study substituted 1-tetralones which due to the conformational flexibility of the saturated ring may be expected to experience some torsion angle rotation in order to relieve steric interactions; the geometric constraints of this ring are such that it is also reasonable to expect that in highly hindered cases torsion angle rotation sufficient to relieve all steric interactions will not be possible. If the latter is true, then the ^{17}O chemical shift for such cases will be dependent upon both torsion angle changes and repulsive van der Waals interactions which remain as a consequence of the proximity of the carbonyl group to a crowding group. Earlier results demonstrating the dependence of ^{17}O chemical shifts on ring size for indanone, tetralone, and benzosuberone suggest that this is a reasonable hypothesis.[8] Torsion angles and repulsive van der Waals energies will be estimated by MM2 methodology using approaches we have previously described.[1]

Results and Discussion

Table I contains the ^{17}O NMR chemical shift data for 15 substituted 1-tetralones (**2–16**) obtained at natural abundance from acetonitrile solutions at 75 °C. Significant downfield changes in chemical shift are noted on introduction of alkyl groups proximate to the carbonyl group (**8**, **11**, **12**, **13**, **15**, and **16**). Introduction of a methyl group into the cyclohexane ring gives results analogous to those noted for similarly substituted alkylindanones[6] and alkylcyclohexanones.[9] Introduction of alkyl groups in nonhindering locations on the aromatic ring causes shifts similar to those observed for acetophenones[10] and indanones[6] which are explained by conventional electronic effects.

It is apparent from Table I that the 1-tetralones with alkyl groups substituted at C-8 near the carbonyl group exhibit large downfield shifts compared to their unhindered isomers; compare, for example, **8** to **9** and **14** to **15**. Potentially, these downfield shifts for the hindered isomers can originate from a combination of torsion angle twist and repulsive van der Waals interactions between the carbonyl group and the methyl group. Molecular mechanics calculations[11] predict a modest torsion angle twist of 5° between the carbonyl group and the aromatic ring of **8**. Employing the torsion angle–^{17}O chemical shift relationship of 0.84 δ/degree developed for aryl ketones,[2] it is estimated that 4 ppm of the downfield shift arises from torsion angle twist. As noted earlier, the ^{17}O chemical shift data, doubtlessly, reflect the weighted average for rapid equilibration between several conformations, and the ^{17}O NMR data torsion angle correlations with a single structure predicted by molecular mechanics may be fortuitous.[2] Comparison of the MM2 estimated van der Waals energies for **8** and **9** yields a difference of 1.69 kcal [9.62 - 7.93]. Use of the previously developed relationship[5,6] between van der Waals energies and ^{17}O chemical shifts predicts a 22

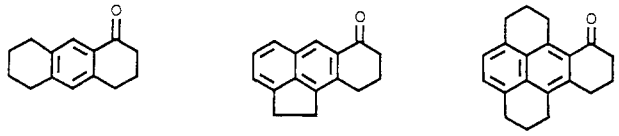
(6) Boykin, D. W.; Hertzler, R. L.; Delphon, J. K.; Eisenbraun, E. J. *J. Org. Chem.* **1989**, *54*, 1418.
(7) (a) Li, S.; Chesnut, D. B. *Org. Magn. Reson.* **1985**, *23*, 625. (b) Li, S.; Chesnut, D. B. *Org. Magn. Reson.* **1986**, *24*, 93. (c) Li, S.; Allinger, N. L. *Tetrahedron* **1988**, *44*, 1339.
(8) Boykin, D. W.; Balakrishnan, P.; Baumstark, A. L. *Magn. Reson. Chem.* **1987**, *25*, 248.
(9) Crandall, J. K.; Centeno, M.; Borresen, S. *J. Org. Chem.* **1979**, *44*, 1184.
(10) Brownlee, R. T. C.; Sadek, M.; Craik, D. J. *Org. Magn. Reson.* **1983**, *21*, 616.
(11) (a) Burket, U.; Allinger, N. L. *Molecular Mechanics*; American Chemical Society: Washington, DC, 1982. (b) Osawa, E.; Musso, H., Applications of Molecular Mechanics Calculations in Organic Chemistry. In *Topics in Stereochemistry*; Allinger, N. L., Eliel, E. L., Wilen, S. H., Eds.; Wiley: New York, 1982.
(12) Duddeck, H.; Jaszberenyi, J. C.; Levai, A.; Timar, T.; Elgamal, M. H. A. *Magn. Reson. Chem.* **1989**, *27*, 170.

ppm shift attributable to repulsive van der Waals interactions. Thus, based upon these two factors, a chemical shift of 555.2 ppm [527.2 + 4.0 + 22.0] is predicted for **8** compared to the observed value of 556.5 ppm. It is interesting that the interaction of the methyl groups at positions 4 and 5 of **14** and **15** gives rise to significant conformation changes in the saturated ring as reflected in the torsion angle twist of the carbonyl group; MM2 calculations predict a carbonyl group–aryl ring twist angle of 16° for **14** and 30° for **15**. The combination of 4–5-methyl–methyl and 8-methyl–carbonyl van der Waals interactions for **15** yields the larger carbonyl twist angle. In a manner similar to that described above, the chemical shift value predicted for **15** is 559.4 [527.2 + 25.2 + 7 ppm] and the observed value is 558.1. Consequently, it is seen that an analysis using a combination of torsion angle change and repulsive van der Waals interactions allows the reasonably accurate prediction of ^{17}O chemical shifts in these semiflexible systems.

The chemical shift values for **11**, **12**, **13**, and **16**, all of which have a hindering group at the C-8 position, are consistent with those of **8** and **15** which have been shown to be a consequence of the combination of a small torsion angle twist and repulsive van der Waals interactions. The MM2 predicted twist angle for **11**, **13**, and **16** is 2 ± 1°. For **12**, the minimized structure has the isopropyl methyl groups rotated away from the carbonyl group such that the torsion angle twist of **12** is 12°, only moderately larger than that for **11** its methyl homologue. However, predicted repulsive van der Waals interactions are also greater for **12** than for methyl-substituted analogues; thus the combination methodology predicts a chemical shift for **12** of ca. 562 ppm, significantly larger than observed. The origin of the deviation between the observed value and the predicted one is not clear (vide infra).

To further examine the applicability of this approach, we have investigated the ^{17}O NMR chemical shifts of some linear fused-ring 1-tetralones **17**–**19** as well as some related angular fused-ring 1-tetralones **20**–**25**.

519.5 PPM 530.0 PPM 565.3 PPM

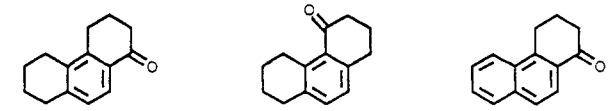


17 18 19

The fusion of a distal saturated six-membered ring to tetralone as in **17** results in an upfield shift consistent with the electronic effect of a meta and para alkyl group. The value of 519.5 ppm for **17** is in good agreement with the value of 520.0 ppm for 6,7-dimethyl-1-tetralone (**10**). The addition of another aromatic ring to the 1-tetralone system as in **18** results in a small downfield shift (ca. 3 ppm) of the carbonyl signal relative to that of 1-tetralone. Introduction of peri type alkyl groups in **19** produces a large downfield shift analogous to those noted for **8** and **15**. MM2 calculations predict a torsion angle of 28° for **19** which accounts for approximately half of the downfield shift observed. The remainder of the downfield shift is very likely due to repulsive van der Waals interactions; we were not able to estimate the repulsive van der Waals energies for this system due to the lack of a suitable unhindered isomer to use as a model.

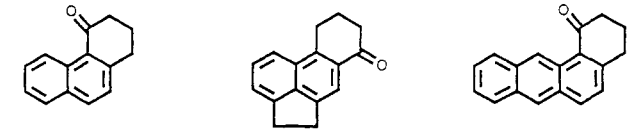
The angular fused-ring systems **20**–**25** provide further opportunity to explore the results of combined torsion angle twist and repulsive van der Waals interactions on ^{17}O NMR chemical shift. The isomeric pair **20** and **21**

519.8 PPM 560.6 PPM 529.6 PPM



20 21 22

551.6 PPM 529.3 PPM 550.0 PPM

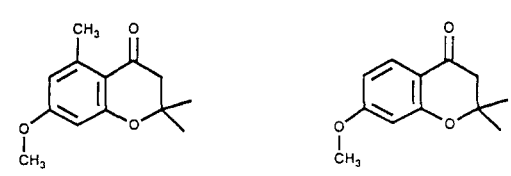


23 24 25

exhibit a large chemical shift difference. The ^{17}O NMR chemical shift for the unhindered isomer **20** is consistent with that of **10** and **17** and reflects normal alkyl electronic effects. A large downfield shift for **21** is expected as a result of a combination of torsion angle rotation and repulsive van der Waals interactions. The estimated torsion angle twist for **21** is 17°, which corresponds to a 14 ppm shift. The shift estimated from residual repulsive van der Waals interactions (Δ = 0.8 kcal/m) is 10 ppm. Thus this method only accounts for 25 ppm of the 40 ppm difference between **20** and **21**. This case represents the largest deviation encountered in predicting ^{17}O NMR chemical shifts using the combination methodology; it is not clear whether this reflects an inherent problem with the MM2 calculations for this system or an unrecognized influence on the ^{17}O NMR chemical shift. The isomeric pair **22** and **23** differ by 22 ppm with the downfield signal corresponding to the hindered isomer. A torsion angle twist of 22° is predicted for **23** which corresponds to an 18.5 ppm shift, whereas a twist angle of only 2° is predicted for **22**. The van der Waals energy difference between **22** and **23** is 0.56 kcal, which corresponds to a 7 ppm shift. Thus a total 25.5 ppm shift is predicted, and a 22 ppm shift is observed. The distal five-membered ring of **24** is expected to have only a very small effect and the data for **24**, which is very similar to that of **22**, is consistent with expectation. The chemical shift of **25**, consistent with that of **23**, can be predicted in terms of a combination of torsion angle twist and repulsive van der Waals interactions: a 23° twist angle is predicted by MM2, which corresponds to a 19 ppm downfield shift, and the van der Waals term is equivalent to a 6 ppm shift; hence, a 25 ppm downfield shift is predicted relative to 1-tetralone and a 22.5 ppm shift is noted.

A recent report[11] describes ^{17}O NMR data for a series of substituted 2,2-dimethylchromanones, in chloroform solution, including data for 5-methyl-7-methoxy-2,2-dimethylchromanone (**26**) which exhibited a downfield shift of 25 ppm compared to 7-methoxy-2,2-dimethylchromanone **27**. This downfield shift was attributed to

525 PPM 500 PPM



26 27

a δ effect and the loss of coplanarity between the carbonyl group and the aromatic ring. However, molecular mechanics calculations predict the torsion angle for **26** to be only 3° (which should result in a 2.5 ppm shift). Consequently, the major contribution to the downfield shift must be due to repulsive van der Waals interactions. In fact,

using our approach for estimation of repulsive van der Waals interactions, a downfield shift of 18 ppm is predicted for **26**; consequently, a total downfield shift of 20.5 ppm is predicted by this approach. Our expressions are based upon data collected in acetonitrile solution, and the data reported for the chromanones were from chloroform solutions. Consequently, predictions by our methodology are in reasonable agreement with the reported results and point to the importance of repulsive van der Waals interactions in accounting for ^{17}O NMR chemical shifts of the 5-substituted chromanones.

The methodology described in this report demonstrates that in semiflexible carbonyl group containing systems the ^{17}O NMR chemical shifts can be generally accounted for by a combination of chemical shift terms deducible from functional group torsion angle change and from residual repulsive van der Waals interactions. ^{17}O NMR spectroscopy can be expected to be employed as a valuable tool in assessment of molecular structure and conformational analysis of semiflexible systems.

Experimental Section

^1H and ^{13}C NMR were obtained, in $CDCl_3$ with TMS (δ in ppm) as internal standard, using a Varian XL 300 NMR instrument operating at 300 and 75 MHz respectively. All ketones were characterized by NMR (^1H and ^{13}C) analyses.

3,4-Dihydro-1(2*H*)-naphthalenone (1):[13] ^1H NMR 2.06 (quin, 2), 2.59 (t, 2), 2.90 (t, 2), 7.22 (m, 2), 7.42 (m, 1), 7.98 (d, 1); ^{13}C NMR 23.2, 29.6, 39.1, 126.5, 127.0, 128.8, 132.5, 133.3, 144.4, 198.0.

2-Methyl-3,4-dihydro-1(2*H*)-naphthalenone (2):[13,14] ^1H NMR 1.21 (d, 3), 1.75 (m, 1), 2.08 (m, 1), 2.45 (7, 1), 2.88 (m, 2), 7.13 (d, 1), 7.21 (t, 1), 7.35 (t, 1), 7.97 (d, 1); ^{13}C NMR 14.9, 28.2, 30.8, 42.0, 125.9, 126.6, 128.2, 131.7, 132.4, 143.6, 199.7.

3-Methyl-3,4-dihydro-1(2*H*)-naphthalenone (3):[14] ^1H NMR 1.05 (d, 3), 2.19 (m, 2), 2.65 (m, 2), 2.88 (d, 1), 7.18 (m, 2), 7.37 (t, 1), 7.95 (d, 1); ^{13}C NMR 20.7, 29.8, 37.2, 46.4, 125.9, 126.2, 128.2, 131.5, 132.8, 143.0, 197.3.

3-*tert*-Butyl-3,4-dihydro-1(2*H*)-naphthalenone (4):[14,15] ^1H NMR 0.99 (s, 9), 1.95 (m, 1), 2.32 (m, 1), 2.87 (m, 2), 2.95 (m, 1), 7.29 (m, 2), 7.47 (m, 1), 8.02 (d, 1); ^{13}C NMR 27.1, 31.6, 32.5, 41.2, 45.7, 126.5, 126.9, 129.0, 132.3, 133.4, 144.4, 199.2.

4-Methyl-3,4-dihydro-1(2*H*)-naphthalenone (5):[13] ^1H NMR 1.35 (d, 3), 1.82 (m, 1), 2.14 (m, 1), 2.17 (m, 1), 2.56 (m, 1), 2.70 (m, 1), 3.02 (m, 1), 7.24 (m, 2), 7.45 (t, 1), 8.00 (d, 1); ^{13}C NMR 20.2, 30.1, 32.2, 35.8, 125.9, 126.6, 126.9, 131.3, 133.1, 148.3, 197.5.

7-Methyl-3,4-dihydro-1(2*H*)-naphthalenone (6):[16] ^1H NMR 2.09 (m, 2), 2.33 (s, 3), 2.61 (t, 2), 2.89 (t, 2), 7.11 (d, 1), 7.24 (d, 1), 7.82 (s, 1); ^{13}C NMR 20.7, 23.2, 29.1, 39.0, 127.0, 128.5, 132.1, 134.1, 136.0, 141.4, 198.3.

7-Ethyl-3,4-dihydro-1(2*H*)-naphthalenone (7):[16] ^1H NMR 1.22 (t, 3), 2.08 (q, 2), 2.61 (m, 4), 2.89 (t, 2), 7.14 (d, 1), 7.28 (d, 1), 7.86 (s, 1); ^{13}C NMR 15.5, 23.4, 28.4, 29.3, 39.2, 126.0, 128.8, 132.4, 133.3, 141.9, 142.6, 198.6.

5,8-Dimethyl-3,4-dihydro-1(2*H*)-naphthalenone (8):[13] ^1H NMR 2.08 (q, 2), 2.25 (s, 3), 2.60 (m, 5), 2.81 (t, 2), 6.97 (d, 1), 7.18 (d, 1); ^{13}C NMR 19.7, 22.4, 23.3, 27.4, 40.6, 129.8, 131.4, 133.7, 138.7, 138.7, 143.6, 200.8.

5,7-Dimethyl-3,4-dihydro-1(2*H*)-naphthalenone (9):[13] ^1H NMR 2.09 (m, 2), 2.25 (s, 3), 2.32 (s, 3), 2.58 (t, 2), 2.78 (t, 2), 7.16 (s, 1), 7.22 (s, 1); ^{13}C NMR 19.4, 20.8, 22.7, 26.1, 38.7, 125.1, 132.6, 135.5, 135.8, 136.2, 139.9, 199.0.

6,7-Dimethyl-3,4-dihydro-1(2*H*)-naphthalenone (10):[13] ^1H NMR 2.09 (quin, 2), 2.27 (s, 3), 2.28 (s, 3), 2.61 (t, 2), 2.87 (t, 2), 7.02 (s, 1), 7.79 (s, 1); ^{13}C NMR 19.4, 20.2, 23.6, 29.3, 39.2, 127.9, 129.9, 130.6, 135.2, 142.3, 143.3, 198.6.

2,5,8-Trimethyl-3,4-dihydro-1(2*H*)-naphthalenone (11):[17] ^1H NMR 1.21 (s, 3), 1.80 (m, 1), 2.16 (m, 1), 2.57 (m, 4), 2.80 (m, 1), 2.90 (m, 1), 6.97 (d, 1), 7.16 (d, 1); ^{13}C NMR 15.3, 19.5, 23.1, 26.8, 30.4, 42.6, 129.7, 131.4, 133.3, 133.8, 138.2, 142.9, 204.3.

2,5-Dimethyl-8-isopropyl-3,4-dihydro-1(2*H*)-naphthalenone (12):[18] ^1H NMR 1.20 (d, 6), 1.26 (d, 3), 1.80 (m, 1), 2.23 (m, 4), 2.65 (m, 1), 2.84 (m, 2), 3.90 (m, 1), 7.23 (s, 2); ^{13}C NMR 15.5, 19.6, 23.9, 24.7, 26.9, 28.7, 30.9, 43.5, 124.1, 131.7, 133.3, 133.5, 142.4, 148.8, 204.4.

3,5,8-Trimethyl-3,4-dihydro-1(2*H*)-naphthalenone (13):[17] ^1H NMR 1.14 (d, 3), 2.26 (m, 6), 2.60 (s, 4), 2.69 (m, 1), 6.98 (d, 1), 7.19 (d, 1); ^{13}C NMR 19.6, 21.6, 23.1, 29.3, 35.8, 48.5, 129.7, 130.8, 133.7, 138.4, 142.8, 200.9.

4,5,7-Trimethyl-3,4-dihydro-1(2*H*)-naphthalenone (14):[17] ^1H NMR 1.29 (d, 3), 2.03 (m, 1), 2.24 (m, 1), 2.31 (s, 3), 2.35 (s, 3), 2.59 (m, 1), 2.78 (m, 1), 3.26 (m, 1), 7.18 (s, 1), 7.73 (s, 1); ^{13}C NMR 18.5, 18.7, 20.8, 28.7, 29.1, 33.1, 125.6, 131.6, 135.4, 135.7, 136.6, 136.6, 144.9, 200.0.

4,5,8-Trimethyl-3,4-dihydro-1(2*H*)-naphthalenone (15):[17] ^1H NMR 1.23 (d, 3), 1.95 (m, 1), 2.18 (m, 1), 2.31 (s, 3), 2.57 (m, 4), 2.85 (m, 1), 3.28 (m, 1), 6.95 (m, 1), 7.15 (m, 1). ^{13}C NMR 18.4, 18.7, 22.9, 27.9, 29.3, 34.5, 129.7, 130.3, 132.4, 134.1, 138.5, 148.3, 200.0.

3,3,6,8-Tetramethyl-3,4-dihydro-1(2*H*)-naphthalenone (16):[14] ^1H NMR 1.04 (s, 6), 2.30 (s, 3), 2.44 (s, 2), 2.61 (s, 3), 2.78 (s, 2), 6.87 (s, 1), 6.88 (s, 1); ^{13}C NMR 21.4, 23.2, 28.0, 33.1, 44.7, 54.4, 127.9, 131.3, 141.2, 143.0, 144.0, 199.8.

3,4,5,6,7,8-Hexahydro-1(2*H*)-anthracenone (17):[19] ^1H NMR 1.76 (m, 4), 2.01 (m, 2), 2.59 (t, 2), 2.64 (m, 4), 2.85 (t, 2), 6.92 (s, 1), 7.73 (s, 1); ^{13}C NMR 22.9, 23.1, 23.5, 28.9, 29.3, 29.7, 39.2, 127.5, 129.1, 130.2, 135.7, 141.4, 143.7, 195.5.

3,4,5,6,7,8-Hexahydro-1(2*H*)-phenanthrenone (20):[15] ^1H NMR 1.82 (m, 4), 2.12 (q, 2), 2.60 (m, 4), 2.77 (m, 4), 7.3 (d, 1), 7.84 (d, 1); ^{13}C NMR 22.3, 22.6, 23.1, 26.0, 26.4, 30.7, 38.5, 124.1, 124.2, 127.5, 127.6, 130.6, 135.0, 143.1, 143.4, 198.8.

1,2,5,6,7,8-Hexahydro-4(3*H*)-phenanthrenone (21):[15] ^1H NMR 1.72 (m, 4), 2.03 (quin, 2), 2.61 (t, 2), 2.76 (t, 2), 2.87 (t, 2), 3.12 (t, 2), 6.98 (d, 1), 7.13 (d, 1); ^{13}C NMR 22.3, 23.1, 23.4, 29.0, 30.3, 31.0, 41.3, 125.9, 131.2, 133.9, 136.4, 140.4, 143.5, 200.6.

Compounds **22** and **23** were gifts from Dr. K. W. Bair of Burroughs-Wellcome. Compounds **24** and **25** were commercially available (Aldrich).

The ^{17}O NMR spectra were recorded on a JEOL GX-270 or on a Varian VXR-400 spectrometer equipped with a 10-mm broad-band probe. All spectra were acquired at natural abundance at 75 °C (±1 °C) in acetonitrile (Aldrich, anhydrous gold label under nitrogen) containing 1% of 2-butanone as an internal standard. The concentration of the ketones employed in these experiments was 0.5 M, except for **19** and **25** which were saturated solutions. The signals were referenced to external deionized water at 75 °C. The 2-butanone resonance (558 ± 1 ppm) was used as an internal check on the chemical shift measurements for these compounds. The instrumental settings for the GX-270 at 36.5 MHz were as follows: spectral width 25 kHz, 2K data points, 90° pulse angle (28-ms pulse width), 200-ms acquisition delay, 40-ms acquisition time, and 40 000–100 000 scans were required. The instrumental settings for the VXR-400 at 54.22 MHz were as follows: spectra width 35 kHz, 2K data points, 90° pulse angle (40-ms pulse width), 200-ms acquisition delay, 29-ms acquisition time, and 30 000–60 000 scans. The spectra were recorded with sample spinning and without lock. The signal-to-noise ratio was improved by applying a 25-Hz exponential broadening factor to the FID prior to Fourier transformation. The data point resolution was improved to ±0.1 ppm on the VXR-400 and ±0.2 ppm on the GX-270 by zero filling to 8K data points. The reproducibility of the chemical shift data is estimated to be better than ±1.0 ppm.

Molecular mechanics calculations were carried out by use of the program MODEL Version KS2.93, available from Professor

(13) Purified commercial sample.
(14) Burnham, J. W.; Duncan, W. P.; Eisenbraun, E. J.; Keen, G. W.; Hamming, M. C. *J. Org. Chem.* **1974**, *39*, 1416.
(15) Rangarajan, R.; Eisenbraun, E. J. *J. Org. Chem.* **1985**, *50*, 2435.
(16) Prepared by cyclization of 4-(4-alkylphenyl)butanoic acid with hot PPA as per ref 17.
(17) Eisenbraun, E. J.; Hinman, C. W.; Springer, J. M.; Burnham, J. W.; Chou, T. S.; Flanagan, P. W.; Hamming, M. C. *J. Org. Chem.* **1971**, *36*, 2480.
(18) Prepared by cyclization of 4-(3-isopropyl-6-methylphenyl)-2-methylbutanoic acid as per ref 17.
(19) Prepared by chromic acid oxidation of 1,2,3,4,5,6,7,8-octahydrophenanthrene as per ref 15.

K. Steliou, University of Montreal.

Acknowledgment (D.W.B.) is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research, to the NSF Instrumentation Program (CHEM-8409599), and to the Georgia State University Research Fund. The OSU authors thank the American Petroleum Institute and the National Institute for Petroleum and Energy Research for earlier financial support, which made materials available for this study and the NSF Instrumentation Program (CHEM-DMB8603864).

Registry No. 1, 530-93-8; 2, 1590-08-5; 3, 14944-23-1; 4, 42981-74-8; 5, 19832-98-5; 6, 22009-37-6; 7, 22531-06-2; 8, 5037-63-8; 9, 13621-25-5; 10, 19550-57-3; 11, 10468-59-4; 12, 6897-77-4; 13, 10468-60-7; 14, 27410-97-5; 15, 10468-61-8; 16, 5409-55-2; 17, 5440-71-1; 18, 22516-44-5; 19, 68151-08-6; 20, 75490-06-1; 21, 13250-73-2; 22, 573-22-8; 23, 778-48-3; 24, 7467-80-3; 25, 57652-74-1; 26, 20052-62-4; 27, 20321-73-7.

Ring-Closure Reactions Initiated by the Peroxydisulfate Ion Oxidation of Diphenyl Diselenide

M. Tiecco,* L. Testaferri, M. Tingoli,* D. Bartoli, and R. Balducci

Istituto di Chimica Organica, Facoltà di Farmacia, Università di Perugia, 06100-Perugia, Italy

Received May 1, 1989

The oxidation of diphenyl diselenide with ammonium peroxydisulfate proceeded cleanly to afford phenylselenium cations and sulfate anions. This is a very simple and efficient method to produce phenylselenium cations in the absence of nucleophilic counterions. This reaction was employed to effect selenium-induced ring closure reactions starting from alkenes containing internal nucleophiles. Thus, unsaturated alcohols and amides, β-diketones and β-keto esters gave the products of phenylselenoetherification. The same process occurred with dienes and unsaturated ketones when the reaction was carried out in the presence of water or methanol, respectively. Unsaturated acids, esters, and imides afforded the phenylselenolactonization products.

The facile addition of phenylselenium cations to unsaturated compounds has been largely used as a crucial step of many important synthetic transformations. The phenylseleno group is, in fact, a very useful and versatile functionality. It can be employed to direct further selective transformations of the molecule, and it can then be easily removed either by oxidation or by reduction.[1,2] The most common reagent employed to effect addition reactions to unsaturated compounds is the commercially available phenylselenenyl chloride. However, the presence of the nucleophilic halide anions is sometimes responsible for some undesirable processes such as addition of the halide ion and decrease in stereoselectivity. Moreover, the addition of PhSeCl to an alkene is sometimes complicated by further reaction of the formed alkyl phenyl selenides with PhSeCl, which affords the deselenenylation products; the two processes often proceed with comparable rates, and mixtures of products can thus be obtained.[3,4] The production of the electrophilic phenylselenium cations can also be effected by electrochemical oxidation of diphenyl diselenide, but this usually requires the use of halide anions as mediators.[5-7] Other selenenylating agents which do not suffer from these complications have been reported in the literature. The stable *N*-phenylselenophthalimide (NPSP) was employed to effect several types of selenenylation reactions.[8,9] Phenylselenenylating agents which have a nonnucleophilic counterion, such as SbF_6^-, PF_6^-,[10] or $CF_3SO_3^-$,[11,12] can be generated in situ and were introduced to effect conversions which did not take place with PhSeCl or NPSP. We have recently reported that electrophilic selenium species which act as phenylselenium cation equivalents can be easily produced from the oxidation of diphenyl diselenide with ammonium peroxydisulfate in several solvents.[13] This simple, unexpensive, and efficient method was employed to effect the methoxy- and hydroxyselenenylation of alkenes;[13] it also gives good results in the amido- and sulfonamidoselenenylation of the same substrates.[14] We report in this paper several examples of ring-closure reactions of alkenes, containing internal nucleophiles, initiated by the peroxydisulfate ion oxidation

(1) (a) Paulmier, C. *Selenium Reagents and Intermediates in Organic Synthesis*; Pergamon Press: Oxford, 1986. (b) Liotta, D. *Organoselenium Chemistry*; Wiley Interscience: New York, 1987.
(2) (a) Nicolaou, K. C.; Petasis, N. A. *Selenium in Natural Products Synthesis*; CIS Inc.: Philadelphia, 1984; p 207. (b) Ley S. V. *Chem. Ind. (London)* **1985**, 101.
(3) Tiecco, M.; Testaferri, L.; Tingoli, M.; Chianelli, D.; Bartoli, D. *Tetrahedron* **1988**, *44*, 2261.
(4) Tiecco, M.; Testaferri, L.; Tingoli, M.; Chianelli, D.; Bartoli, D. *Tetrahedron* **1988**, *44*, 2273.
(5) (a) Torii, S.; Uneyama, K.; Ono, M.; Bannou, T. *J. Am. Chem. Soc.* **1981**, *103*, 4606. (b) Uneyama, K.; Ono, M.; Torii, S. *Phosphorus Sulphur* **1983**, *16*, 35. (c) Torii, S.; Uneyama, K.; Ono, M. *Tetrahedron Lett.* **1980**, *21*, 2653, 2741.
(6) Mihailovic, M. Lj.; Konstantinovic, S.; Vukicevic, R. *Tetrahedron Lett.* **1987**, *28*, 4343.
(7) Konstantinovic, S.; Vukicevic, R.; Mihailovic, M. Lj.; *Tetrahedron Lett.* **1987**, *28*, 6511.
(8) (a) Nicolaou, K. C.; Claremon, D. A.; Barnette, W. E.; Seitz, S. P. *J. Am. Chem. Soc.* **1979**, *101*, 3704. (b) Nicolaou, K. C.; Petasis, N. A.; Claremon, D. A. *Tetrahedron* **1985**, *41*, 4835.
(9) Jackson, W. P.; Ley, S. V.; Morton, J. A. *J. Chem. Soc., Chem. Commun.* **1980**, 1028.
(10) (a) Schmid, G. H.; Garratt, D. G. *Tetrahedron Lett.* **1975**, 3991. (b) Remion, J.; Krief, A. *Tetrahedron Lett.* **1976**, 3743. (c) Jackson, W. P.; Ley, S. V.; Whittle, A. J. *J. Chem. Soc., Chem. Commun.* **1980**, 1173.
(11) Murata, S.; Suzuki, T. *Chem. Lett.* **1987**, 849.
(12) Murata, S.; Suzuki, T. *Tetrahedron Lett.* **1987**, *28*, 4297, 4415.
(13) Tiecco, M.; Testaferri, L.; Tingoli, M.; Chianelli, D.; Bartoli, D. *Tetrahedron Lett.* **1989**, *30*, 1417.
(14) Unpublished results from this laboratory.

0022-3263/90/1955-0429$02.50/0