4.35 (s, 2 H, CH_2Ph), 5.4–5.6 (m, 2 H, CH=), 7.15 (s, 5 H, Ph); IR (neat) 3400 (OH), 2960, 2920, 2860, 1455, 1370, 1100, 975, 740, 700 cm^{-1}. Anal. Calcd for $C_{17}H_{26}O_2$: C, 77.82; H, 9.99. Found: C, 77.66; H, 9.74. In a similar manner, **5b**[8] was obtained in 95% yield.

(3*S*)-7-Methoxy-3,7-dimethyloct-5-enyl benzyl ether (5c): bp 78–80 °C (0.025 mmHg); $[\alpha]^{24}_{D}$ −2.57° (*c* 1.44, EtOH); ^{1}H NMR (CCl_4) δ 0.90 (d, *J* = 5 Hz, 3 H, CH_3), 1.15 (s, 6 H, CH_3), 1.3–2.2 (m, 5 H, CH_2, CH), 3.02 (s, 3 H, CH_3O), 3.42 (t, *J* = 6 Hz, 2 H, CH_2O), 4.40 (s, 2 H, CH_2Ph), 5.3–5.6 (m, 2 H, CH=), 7.20 (br s, 5 H, Ph); IR (neat) 2965, 2920, 2860, 1450, 1375, 1360, 1100, 1075, 730, 690 cm^{-1}. Anal. Calcd for $C_{18}H_{28}O_2$: C, 78.21; H, 10.21. Found: C, 78.38; H, 10.28. In a similar manner, **5d**[8] was obtained in 84% yield.

(3*S*)-3,7-Dimethyl-4,6-octadienyl Benzyl Ether (6a). To a solution of **5a** (500 mg, 1.9 mmol) in THF (16 mL) was added 60% $HClO_4$ aqueous solution (1.6 mL, 14.3 mmol) and the mixture was stirred for 1 h at 60–65 °C. After addition of water, the reaction mixture was extracted with ether and the organic layer was worked up in the usual manner to give **6a** as a colorless oil (445 mg, 89%): bp 74–76 °C (0.05 mmHg); $[\alpha]^{20}_{D}$ −49.60° (*c* 8.45, EtOH); ^{1}H NMR ($CDCl_3$) δ 1.02 (d, *J* = 6.6 Hz, 3 H, CH_3), 1.50–1.65 (m, 2 H, CH_2), 1.76 (s, 6 H, CH_3), 2.10–2.60 (m, 1 H, CH), 3.52 (t, *J* = 6.6 Hz, 2 H, CH_2O), 4.45 (s, 2 H, CH_2Ph), 5.46 (dd, J_1 = 14.8 Hz, J_2 = 7.6 Hz, 1 H, CH=), 5.82 (d, *J* = 10.7 Hz, 1 H, CH=), 6.26 (dd, J_1 = 14.8 Hz, J_2 = 10.7 Hz, 1 H, CH=), 7.40 (s, 5 H, Ph); IR (neat) 2960, 2920, 2860, 1660, 1455, 1365, 1100, 730, 700 cm^{-1}. Anal. Calcd for $C_{17}H_{24}O$: C, 83.61; H, 9.83. Found: C, 83.36; H, 9.80. The reaction of **5b** and **5d** in the similar conditions provided **6b**[9] in 72% yield.

Electrochemical Dehydration of 5a. A mixture of **4b** (60 mg, 0.24 mmol) and $LiClO_4$ (125 mg, 1.18 mmol) in dry THF (8 mL) was electrolyzed at room temperature under a constant current (3.3 mA/cm^2 for 3 min, 0.08 F/mol) using platinum foils as electrodes in a breaker-type undivided cell. After addition of saturated $NaHCO_3$ and evaporation of solvents under reduced pressure, the usual workup and chromatography (SiO_2) provided **6a** as a regioisomeric mixture (59 mg, 98%; 4,6-diene:5,7-diene = 40:60 by VPC).

(2*R*)-4-(Benzyloxy)-2-methyl-1-butanal (3c). Ozonolysis was carried out by bubbling ozone through the ether (50 mL) solution of **6a** (500 mg, 2.05 mmol) at −50 to −60 °C for 8 h. After bubbling N_2 gas for 20 min, water (5 mL) and AcOH (1.5 mL) were added to the mixture to which was added zinc powder (100 mg) and AcOH (1 mL). Under vigorous stirring at room temperature for 15 min, another 100 mg of zinc and AcOH (1 mL) were added and the stirring was continued for 10 min. This procedure was repeated 5 times in every 10 min. After final addition of zinc (200 mg), the mixture was stirred at room temperature for 3 h. The mixture was filtered and the filtrate was concentrated under reduced pressure. The usual workup of the residual mixture gave the crude aldehyde which was reduced with $NaBH_4$ without further purification. An analytical sample of **3c** was obtained by chromatography and distillation: bp 73–75 °C (0.025 mmHg); $[\alpha]^{24}_{D}$ −11.61° (*c* 3.28, hexane); ^{1}H NMR (CCl_4) δ 1.00 (d, *J* = 7 Hz, 3 H, CH_3), 1.25–2.10 (m, 2 H, CH_2), 2.10–2.60 (m, 1 H, CH), 3.38 (t, *J* = 6 Hz, 2 H, CH_2O), 4.33 (s, 2 H, CH_2Ph), 7.12 (s, 5 H, Ph), 9.40 (d, *J* = 2 Hz, 1 H, CHO); IR (neat) 3020, 2920, 2860, 2710, 1725 (C=O), 1455, 1370, 1100, 740, 700 cm^{-1}. Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 75.16; H, 8.25.

(2*R*)-4-(Benzyloxy)-2-methyl-1-butanol (3a). A solution of **3c** (250 mg, 1.3 mmol) in EtOH (5 mL) was added dropwise to a solution of $NaBH_4$ (49 mg, 1.3 mmol) in EtOH (5 mL) in an ice bath and the mixture was stirred for 1 h at room temperature. The usual workup and chromatography (SiO_2) provided **3a** as a colorless oil (230 mg, 92% from **6a**): bp 68–70 °C (0.03 mmHg); $[\alpha]^{18}_{D}$ +9.39° (*c* 6.02, EtOH); ^{1}H NMR ($CDCl_3$) δ 0.94 (d, *J* = 6.6 Hz, 3 H, CH_3), 1.4–2.0 (m, 3 H, CH_2, CH), 2.6 (br s, 1 H, OH), 3.3–3.7 (m, 4 H, CH_2O), 4.56 (s, 2 H, CH_2Ph), 7.23 (s, 5 H, Ph); IR (neat) 3360 (OH), 2920, 2860, 1455, 1365, 1100, 1040, 740, 695 cm^{-1}. Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.10; H, 9.19.

Registry No. **1** (*n* = 14), 89363-37-1; **1** (*n* = 15), 89363-38-2; **1** (*n* = 16), 89363-39-3; **3a**, 73408-07-8; **3c**, 91550-14-0; **4a**, 7540-51-4; **4b**, 84237-05-8; **4c**, 67601-05-2; **5a**, 92142-15-9; **5b**, 90359-34-5; **5c**, 92078-51-8; **5d**, 92056-72-9; (*E*)-**6a**, 92056-73-0; (*Z*)-**6a**, 92056-74-1; **6b**, 92142-16-0; (3*S*)-3,7-dimethyl-5,7-octadienyl benzyl ether, 92056-75-2.

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^{17}O NMR Spectroscopic Study of Substituted Benzoyl Cations[1]

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The structure of benzoyl and acylium cations has been well studied in our laboratory as well as others by a variety of methods.[2] Ample evidence suggests that the benzoyl cations **1** may be adequately described in terms of resonance hybrids shown in Scheme I with a substantial contribution from the "ketene-like" mesomer **1C**.

On the other hand, the acylium ion structure **2** is predominantly dominated by the contributions from resonance hybrids of the oxocarbenium ion **2A** and the oxonium ion **2B**. Such interpretations were further reinforced during our recent study of one-bond ^{13}C–^{13}C coupling constants in a series of substituted benzoyl cations.[3] Interested in probing the substituent-induced electronic effects at the terminal oxygen center of carbocationic carbonyl moiety, we analysed these systems by ^{17}O NMR spectroscopy.

Results and Discussion

The ^{17}O NMR chemical shifts of all the substituted benzoyl cations were measured in natural abundance samples (~0.037%) and are listed in Table I. A remarkably constant value around 320 ppm is obtained for the cationic carbonyl oxyen with the entire range of substituents (i.e., from the most electron donating 4-OCH_3 to the most electron withdrawing 4-CF_3).

We have previously reported the δ ^{17}O of acetyl and propionyl cations to be ~300 ppm.[4] Since the acyl cations may be primarily described by the resonance hybrid of mesomers **2A** and **2B** (Scheme I), the ~20 ppm relative deshielding observed in the benzoyl cations **1** may well reflect the greater contribution from the "ketene-like" mesomer **1C**. A closer look at the mesomers **1A** and **1B** (Scheme I), however, shows that a simple qualitative analysis of ^{17}O may not be easy, since the oxygen atom changes its hydridisation from sp^2 to sp, respectively. Since an sp-hybridized oxygen has a chemical shift value (δ^{17}O of model carbon monoxide being 350)[5] intermediate to a sp^2 (δ ^{17}O 600) and sp^3 (δ^{17}O 0–50) hybridized oxygen, a triple bond may be assumed to cause a diamagnetic

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0022-3263/84/1949-4317$01.50/0

Scheme I

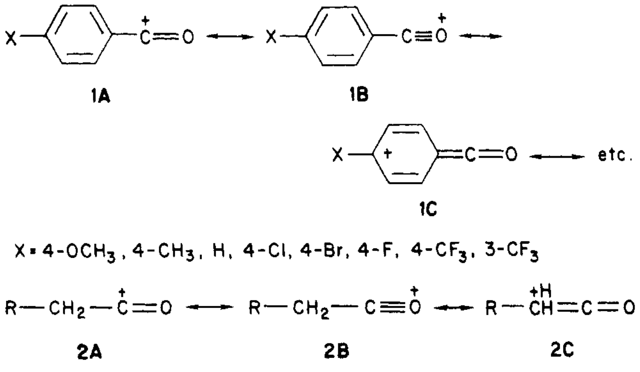

Table I. ^{17}O NMR Chemical Shifts[a] of Substituted Benzoyl Cations[b] 1

X	δ_{CO^+}	line width, Hz
4-OCH$_3$	321	327
4-CH$_3$	319	142
H	318	185
4-Cl	320	62
4-Br	321	87
4-F	320	223
4-CF$_3$	322	165
3-CF$_3$	320	175

[a] Referenced internally to SO$_2$ (δ 505). [b] 30% solution in FSO$_3$H:SbF$_5$ (1:1)/SO$_2$ at -65 °C).

shielding in the screening constant for δ^{17}O similar to its analogue in δ^{13}C. Based on this premise, it may be noted that in mesomer **2B**, the shielding effect of the triple bond, and the deshielding effect of the positive charge now resident on the oxygen should be expected to have opposing influences on the δ^{17}O.

The apparent insensitivity of ^{17}O chemical shifts to substituent effect seems to suggest that either (i) δ^{17}O is inherently insensitive or (ii) a combination of factors (as previously discussed) exists which seemingly nullify each others effects to give a near constant value.

This apparent insensitivity might seem surprising considering the wide spread of ^{17}O chemical shifts (range of ~600 ppm for organic compounds) and its known extreme sensitivity to π-bond order changes.[6] A recent study[7] reported a total change of approximately 50 ppm in the δ^{17}O values in going from 4-aminoacetophenone to 4-nitroacetophenone, an effect argued to be primarily dominated by local π-electron densities with lesser contributions from changes in the average excitation energy $\Delta E_{n-\pi^*}$. Recent ab initio studies[8] do show large substituent induced changes in the π-electron densities at the oxygen center of the benzoyl cations. Furthermore, the ^{15}N chemical shifts of the corresponding isoelectronic benzonitrile series[9] span a range of ~12 ppm, with donors inducing upfield shifts (e.g., -2.7 ppm for 4-OCH$_3$) and acceptors inducing downfield shifts (e.g., +8.8 ppm for 4-NO$_2$ derivative). The good correlation (r = 0.97) obtained in the plot of C$_1$ chemical shifts of benzonitrile vs. benzol cations (see Figure 1) and similarly between the C$_\alpha$ chemical shifts (see Figure 2) between these two systems (r = 0.89) seem to suggest that such a comparison may not be unreasonable.

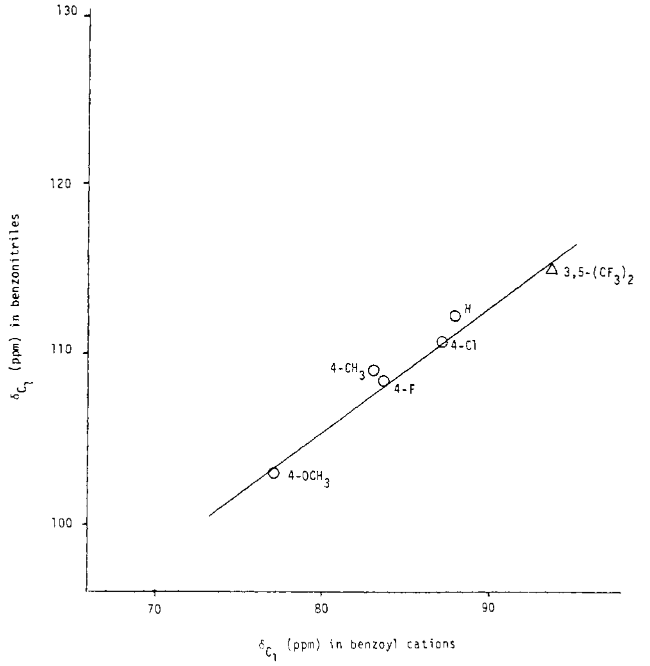

Figure 1. Plot of C$_1$ chemical shift in benzoyl cations vs. those in benzonitriles: (○) ref 2a and 14; (△) present study.

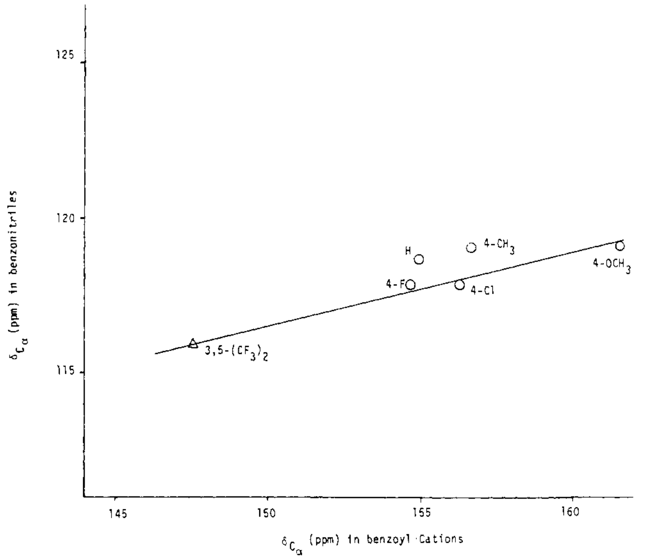

Figure 2. Plot of C$_\alpha$ chemical shift in benzoyl cations vs. those in benzonitriles: (○) ref 2a and 14; (△) present study.

Though no conclusive argument can be made at this juncture, it is, however, interesting to compare the δ^{17}O values obtained with the δ^{13}C of the C$_\beta$ carbons of similarly substituted phenyl acetylene series.[10] The total range observed in δ^{13}C is about 4 ppm when the substituent is varied from 4-OCH$_3$ to 4-CF$_3$. Though such empirical correlations between δ^{17}O and δ^{13}C have in the past proved successful in a number of systems,[11-13] an explanation for the near constancy observed for the δ^{17}O values in substituted benzoyl cations is elusive. Although at this point we are unable to offer a definite explanation for the near constancy of observed ^{17}O chemical shift values in substituted benzoyl cations, these somewhat unexpected observations are of interest and reporting them may help

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focus further studies in this area.

Experimental Section

Natural abundance ^{17}O NMR chemical shifts measurements were made in ~30% solutions of cations in FSO$_3$H:SbF$_5$ (1:1)/SO$_2$ systems at -65 °C. Typical spectral parameters include 1.25 K data points, a 25–kHz spectral width, and acquisition time of 25 ms. Alfa delays of 30 μs were used to prevent pulse break through. A reasonable quality spectrum was obtained in ~500 000 scans. In view of the small number of data points and rolling baseline, errors in δ^{17}O measurements are estimated to be ±2 ppm.

Acknowledgment. Support of our work by the National Institutes of Health is gratefully acknowledged.

Registry No. 1 (X = 4-OMe), 41868-76-2; 1 (X = 4-Me), 20122-40-1; 1 (X = H), 19270-10-1; 1 (X = 4-Cl), 20122-41-2; 1 (X = 4-Br), 45709-42-0; 1 (X = 4-F), 39981-36-7; 1 (X = 4-CF$_3$), 46061-29-4; 1 (X = 3-CF$_3$), 46060-47-3; ^{17}O, 13968-48-4.

Communications

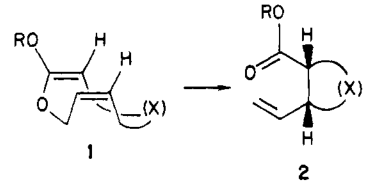
A New Approach to Heterocycles: Synthesis of (±)-*N*-Benzoylmeroquinene Methyl Ester

Summary: A new approach to the total synthesis of *N*-benzoylmeroquinene methyl ester is described and features the stereospecific Claisen rearrangement of the (*E*)-silyl ketene acetal derived from azalactone **7** as the key step in the construction of the disubstituted piperidine ring.

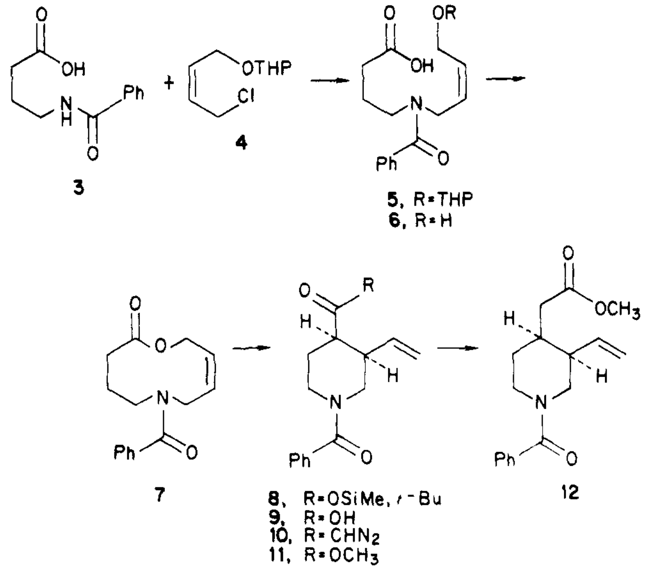
Sir: We have recently reported a general, stereospecific synthesis of *cis*-2-alkenylcycloalkanecarboxylic acids **2** by way of a Claisen-rearrangement-mediated-four-atom ring contraction of macrocyclic ketene acetals **1**.[1] Ketene acetals **1** (X = (CH$_2$)$_n$, n = 1, 3, 4, 5, 6) proceed through a boat-like transition state to yield exclusively the cis-disubstituted carbocycles **2** (Scheme I). The potential for extending this methodology to the synthesis of heterocycles clearly exists. Substitution of a heteroatom for one of the carbon atoms not participating in the sigmatropic rearrangement of **1** should allow access to heterocycle **2**. In principle, one could synthesize a wide variety of heterocycles using this approach, provided the heteroatom is suitably positioned and can withstand the necessary conditions to effect the Claisen rearrangement. An attractive target for exploring this synthetic approach is the alkaloid derivative *N*-benzoylmeroquinene methyl ester **12**,[2] a key intermediate in several recent total syntheses of *Cinchona* alkaloids, e.g., quinine.[3]

Previous syntheses[2] of **12** established the cis stereorelationship of the two side chains on the piperidine ring by catalytic hydrogenation followed by the subsequent unraveling of a latent vinyl group. In our approach, we anticipated that the Claisen rearrangement of the (*E*)-silyl ketene acetal derived from azalactone **7** should afford the disubstituted piperidine ring with concomitant introduction of the *cis*-3-vinyl moiety. Homologation of the carboxylic acid **9** would then complete the synthesis of **12**. Therefore, the synthesis of **7** became our immediate synthetic goal (Scheme II).

Scheme I



Scheme II



To this end, the dianion of *N*-benzoyl-4-aminobutyric acid (**3**,[5] 2 equiv of NaH, DMF, 0 °C) was treated with *cis*-1-chloro-2-butene 4-tetrahydropyranyl ether (**4**,[6] 1.2 equiv, DMF, 0 → 25 °C, 16 h) to give **5** as an oil in 67% yield. Removal of the tetrahydropyranyl ether[7] (PPTs, methanol, reflux 4 h) gave hydroxy acid **6** in 92% yield. Lactonization of **6** by the procedure of Mukaiyama[8] (2-chloro-1-methylpyridinium iodide, Et$_3$N, 0.005 M in ace-

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(1) Abelman, M. M.; Funk, R. L.; Munger, J. D., Jr. *J. Am. Chem. Soc.* **1982**, *104*, 4030. We have coined the term "Alicyclic Claisen Rearrangement" to describe this methodology.

(2) For the synthesis of 12, see the elegant work of the Hoffmann-La Roche group: Uskoković, M. R.; Henderson, T.; Reese, C.; Lee, H. L.; Grethe, G.; Gutzwiller, J. *J. Am. Chem. Soc.* **1978**, *100*, 571. Prior to this work, compound 12 was available only from meroquinene, a degradation product of cinchonine.[4] Also see: Imanishi, T.; Inoue, M.; Wada, Y.; Hanaoka, M. *Chem. Pharm. Bull.* **1982**, *30*, 1925.

(3) For syntheses of *Cinchona* alkaloids based on utilization of 12, see: (a) Gutzwiller, J.; Uskoković, M. R. *J. Am. Chem. Soc.* **1978**, *100*, 576. (b) Grethe, G.; Lee, H. L.; Mitt, T.; Uskoković, M. R. *J. Am. Chem. Soc.* **1978**, *100*, 581. (c) Taylor, E. C.; Martin, S. F. *J. Am. Chem. Soc.* **1974**, *96*, 8095. (d) Gates, M.; Sugavanam, B.; Schreiber, W. L. *J. Am. Chem. Soc.* **1971**, *93*, 205.

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