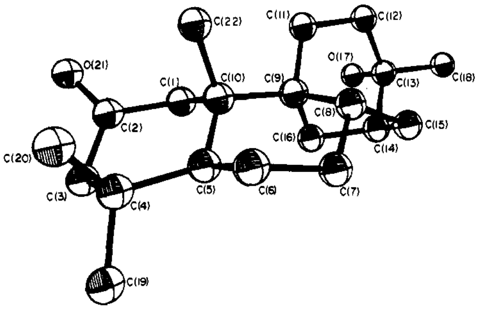

Figure 1. A computer generated perspective view of stemodinone (**5**).

system was effected through a single-crystal X-ray analysis of stemodinone (**5**). Crystals of stemodinone were grown from a solvent system of chloroform and ethyl acetate. The crystals belong to the orthorhombic crystal class with $a = 12.96$ (1), $b = 6.78$ (2) and $c = 20.16$ (1) Å. Systematic extinctions uniquely indicated space group $P2_12_12_1$, and a calculated density of 1.15 g/cm^3 for $Z = 4$ implied one molecule of stemodin per asymmetric unit. A total of 1675 unique reflections with $\theta \leq 55°$ were measured on a fully automated Hilger-Watts four-circle diffractometer with Ni-filtered Cu Kα (1.5418 Å) radiation. After correction for background, Lorentz, and polarization effects, a total of 1189 reflections were judged observed ($I \geq 3\sigma(I)$). Phases were assigned to 183 E's with magnitudes greater than 1.50 with a multiple solution, weighted tangent formula approach.[7] Three solutions with essentially identical phasing were strongly indicated. Inspection of the phased, three-dimensional E synthesis showed all 22 nonhydrogen atoms of the diterpene. Full-matrix least-squares refinement, with all atoms anisotropic and no hydrogens included, has lowered the crystallographic discrepancy index to 0.104.[8] Figure 1 is a computer generated drawing of the X-ray model indicating the structure and conformation of stemodinone.[9] All bond distances and angles agree well within estimated experimental error (0.02 Å and 2°) with generally accepted values.[10] There were no abnormally short intermolecular contacts. As can be seen from Figure 1 each of the six-membered rings is in the chair conformation and the five-membered ring in the envelope conformation with C(16) serving as the flap.

The structure of stemodinone (**5**), and thus stemodin (**1**), bears a close resemblance to that of the antibiotic aphidicolin, recently isolated from *Cephalosporium aphidicola*.[11] However, the stemodin stereochemistry differs from that reported for aphidicolin at C-9, 13, and 14 (stemodane numbering). The ORD of stemodinone exhibits a positive Cotton effect ($[\alpha]_{308} = 2460$), in agreement with an absolute configuration containing 5α-H and 10β-CH$_3$.[12] These results therefore add a further variant to the family of tetracyclic diterpene skeletons found in higher plants.

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Effect of Solvation on the Intrinsic Relative Acidity of Methanol and Ethanol

Sir:

It has been well known for many years that in solution *tert*-butoxide is a stronger base than ethoxide, and ethoxide in turn is a stronger base than methoxide. These observations lead to the conclusion that the relative order of acidity is $CH_3OH > C_2H_5OH > t\text{-}C_4H_9OH$.[1] Recently, however, Brauman and Blair reported that in the *gas phase* the relative order of acidities is reversed from that in solution.[2] This dramatic reversal in acid strengths indicates that the solvent assumes a major role in determining relative acidities.

Using the pulsed ion cyclotron resonance technique,[3] we have been able to determine quantitatively the relative gas-phase acidity of CH_3OH and C_2H_5OH. Methoxide ions, generated by electron impact on CH_3ONO,[4] react rapidly in the gas phase with C_2H_5OH to produce ethoxide ions. If a gaseous CH_3OH–C_2H_5OH mixture of known relative concentration is added to the spectrometer, a chemical equilibrium is established with respect to the reaction in eq 1.[5] This result confirms

$$CH_3O^- + C_2H_5OH = C_2H_5O^- + CH_3OH \quad K_1 = 23 \pm 2 \qquad (1)$$

that C_2H_5OH is a stronger acid than CH_3OH in the gas phase and is in agreement with the qualitative order reported by Brauman and Blair. By using the relation $\Delta G° = -RT \ln K$, the free energy change for reaction 1 at 298°K can be calculated as -1.9 ± 0.2 kcal/mol.

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(3) (a) R. T. McIver, Jr., and J. R. Eyler, *ibid.*, **93**, 6334 (1971); (b) R. T. McIver, Jr., and R. C. Dunbar, *Int. J. Mass Spectrom. Ion Phys.*, **7**, 471 (1971); (c) R. T. McIver, Jr., *Rev. Sci. Instrum.*, **41**, 555 (1970).

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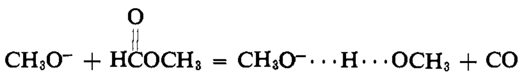
(5) Reaction 1 has previously been studied by D. K. Bohme, E. Lee-Ruff, and L. B. Young, *J. Amer. Chem. Soc.*, **93**, 4608 (1971). A value of $K_1 = 3$ was obtained using the flowing afterglow technique to measure the rate constants for both the forward and reverse direction of proton transfer.

The principal advantage of the gas-phase experiments to date has been the ability to measure the acidity of molecules in the absence of solvent effects. Blair, Isolani, and Riveros have recently reported, however, that ions such as $CH_3O^- \cdots H \cdots OCH_3$ can be generated in the gas phase by the reaction of alkoxide ions with alkyl formates.[6] These ions can be viewed as



$$CH_3O^- + \overset{\overset{\displaystyle O}{\|}}{H}COCH_3 = CH_3O^- \cdots H \cdots OCH_3 + CO \qquad (2)$$

alkoxide ions "solvated" by a single alcohol molecule.[7] $CH_3O^- \cdots H \cdots OCH_3$ reacts rapidly with C_2H_5OH to generate $C_2H_5O^- \cdots H \cdots OCH_3$, an ethoxide ion solvated by a CH_3OH molecule.[6]

These alkoxide cluster ions provide the intriguing possibility of bridging the gap between studies in the gas phase and in solution. Using reaction 2 as a source of alkoxide cluster ions, we have been able to measure equilibrium constants for reactions 3 and 4. Figure 1 shows the pulsed icr results for a reaction mixture produced by adding CH_3ONO to a partial pressure of 1×10^{-7} Torr, HCO_2CH_3 to a partial pressure of 2×10^{-6} Torr, and a 5:1 mixture of CH_3OH–C_2H_5OH to a partial pressure of 1×10^{-5} Torr. Each trace of Figure 1 shows the relative abundance of a particular mass ion *vs.* reaction time. Methyl nitrite captures low-energy electrons efficiently to generate methoxide ions in the gas phase.[4] The upper trace in Figure 1 shows that a 10-msec pulse of the electron beam produces a large initial abundance of CH_3O^-, *m/e* 31, which then decreases due to reaction with HCO_2CH_3 (reaction 2) to form $CH_3O^- \cdots H \cdots OCH_3$, *m/e* 63. Subsequent reaction of *m/e* 63 with ethanol (reactions 3 and 4) leads to the alkoxide cluster ions $C_2H_5O^- \cdots H \cdots OCH_3$, *m/e* 77, and $C_2H_5O^- \cdots H \cdots OC_2H_5$, *m/e* 91, which increase in abundance and then level out. Chemical equilibrium is attained once the abundance of the ions has reached a steady-state value.[8] Double resonance experiments confirm the occurrence of reactions 3 and 4 in this system. Furthermore, consistent values of both K_3 and K_4 can be obtained from the same reaction mixture by working with CH_3OH–C_2H_5OH ratios from 2:1 to 15:1.

$$CH_3O^- \cdots H \cdots OCH_3 + C_2H_5OH = C_2H_5O^- \cdots H \cdots OCH_3 + CH_3OH \quad K_3 = 7.5 \pm 2 \qquad (3)$$

$$C_2H_5O^- \cdots H \cdots OCH_3 + C_2H_5OH = C_2H_5O^- \cdots H \cdots OC_2H_5 + CH_3OH \quad K_4 = 2 \pm 0.5 \qquad (4)$$

$$CH_3ONO + e^- = CH_3O^- + NO \qquad (5)$$

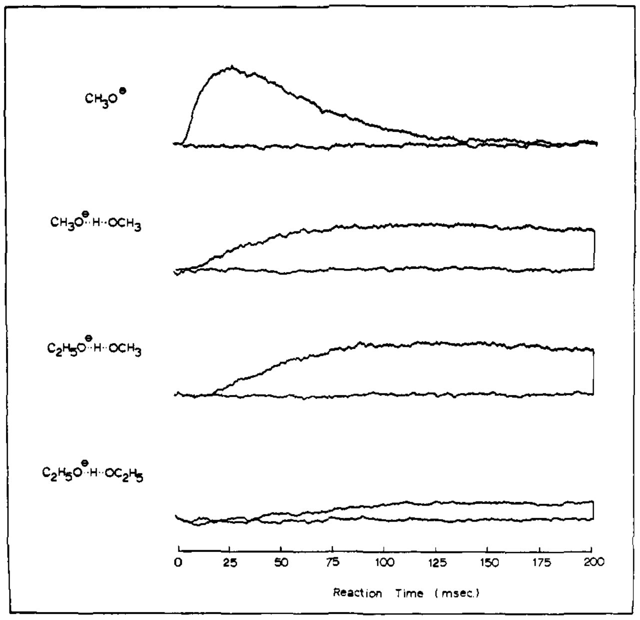


Figure 1. Pulsed icr spectra showing the relative abundance of negative ions *vs.* reaction time in a 5:1 mixture of CH_3OH–C_2H_5OH. CH_3O^- is generated by electron impact on CH_3ONO, and $CH_3O^- \cdots H \cdots OCH_3$ is initially formed by reaction of CH_3O^- with HCO_2CH_3.

Comparison of reactions 1 and 3 illustrates the effect of a single solvent molecule on the intrinsic relative acidity of CH_3OH and C_2H_5OH. Reaction 3 is identical with reaction 1 except that a single CH_3OH is allowed to solvate both the methoxide and ethoxide ions. The free energy change for reaction 3 is -1.2 ± 0.2 kcal/mol, compared to -1.9 ± 0.2 kcal/mol for reaction 1. The first methanol solvent molecule, therefore, produces a *decrease* of about 0.7 kcal/mol in the apparent relative acidity of CH_3OH and C_2H_5OH. This is consistent with the expected trend in going from the gas phase to solution, but obviously more than one solvent molecule is required to reverse the relative acidity order. Reaction 3 can be broken down into a thermodynamic cycle consisting of three reactions. Reactions

$$CH_3O^- + C_2H_5OH = C_2H_5O^- + CH_3OH \quad \Delta G^\circ = -1.9 \pm 0.2 \qquad (6)$$

$$CH_3O^- \cdots H \cdots OCH_3 = CH_3O^- + CH_3OH \quad \Delta G^\circ_{1.0}(CH_3O^-) \qquad (7)$$

$$C_2H_5O^- + CH_3OH = C_2H_5O^- \cdots H \cdots OCH_3 \quad -\Delta G^\circ_{1.0}(C_2H_5O^-) \qquad (8)$$

$$CH_3O^- \cdots H \cdots OCH_3 + C_2H_5OH = C_2H_5O^- \cdots H \cdots OCH_3 + CH_3OH \quad \Delta G^\circ = -1.2 \pm 0.2$$

7 and 8 are a measure of the free energy of dissociation for the alkoxide–methanol cluster ions. Summing the free energies for reactions 6–8 and rearranging terms gives $\Delta G^\circ_{1.0}(CH_3O^-) - \Delta G^\circ_{1.0}(C_2H_5O^-) = 0.7$ kcal/mol. These results show that the free energy of dissociation of the methoxide–methanol cluster ion is approximately 0.7 kcal/mol greater than the free energy of dissociation of the ethoxide–methanol cluster ion. Methoxide, a stronger base than ethoxide in the gas phase, forms stronger hydrogen bonds to a single methanol solvent molecule. This is in agreement with trends reported by Payzant, Yamdagni, and Kebarle for the dissociation of negative ion hydrates.[9]

Reaction 4 can be interpreted as a measure of the relative solvating ability of CH_3OH and C_2H_5OH toward ethoxide ion. The measured free energy value of 0.4 ± 0.2 kcal/mol shows that C_2H_5OH, the stronger acid, forms slightly stronger hydrogen bonds to the

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(6) L. K. Blair, P. C. Isolani, and J. M. Riveros, *J. Amer. Chem. Soc.*, **95**, 1057 (1973).

(7) Blair, Isolani, and Riveros performed an extensive series of experiments which all supported the proposed structure of the alkoxide cluster ion (see ref 6). These ions have also been postulated to form in solution; see D. J. Cram, B. Rickborn, C. A. Kingsbury, and P. Haberfield, *ibid.*, **83**, 3678 (1961).

(8) The equilibrium constant for reaction 3 is calculated from the expression, $K_3 = (I_{77^-}/I_{63^-})(77/63)([CH_3OH]/[C_2H_5OH])$, where I_{63^-} is the equilibrium abundance of the $CH_3O^- \cdots H \cdots OCH_3$ ion; 63 the mass of the ion, a mass correction factor; and $[CH_3OH]$ the pressure of CH_3OH in the spectrometer.

(9) J. D. Payzant, R. Yamdagni, and P. Kebarle, *Can. J. Chem.*, **49**, 3308 (1971).

ethoxide ion. This is in qualitative agreement with recently reported measurements of hydrogen bond energies to Cl^- ions.[10]

A wide variety of negative cluster ions can be generated in the pulsed icr spectrometer. In favorable cases it may be possible to measure the free energy of dissociation for cluster ions containing more than one solvent molecule. By measuring the thermodynamics for sequential solvation of ions in the gas phase, the process of ion solvation can be studied at its most fundamental level.

Acknowledgment. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and to the Conselho Nacional de Pesquisas of Brazil for support of this research.

(10) R. Yamdagni and P. Kebarle, *J. Amer. Chem. Soc.*, **93**, 7139 (1971).

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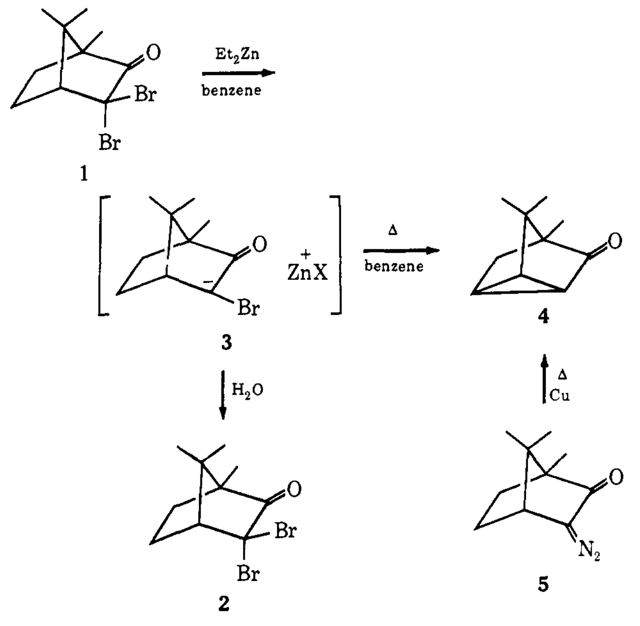
Ketocarbenoids by α Elimination. Intramolecular Trapping by Carbon-Hydrogen Insertion

Sir:

Although α-elimination reactions provide the best route to most classes of carbenes and carbenoids, the decomposition of diazo ketones has stood for over half a century as the sole source of *keto*carbenes.[1] The lack of synthetically useful alternatives to this frequently unsatisfactory diazo route, together with the mechanistic mysteries surrounding the metal-catalyzed decomposition of diazo ketones, has sparked substantial recent activity in this area of carbene chemistry.[2,3] We should now like to report the first example of a ketocarbenoid generated by α elimination in high yield and the efficient trapping of this intermediate by intramolecular C-H insertion.

Treatment of α,α-dibromocamphor (**1**)[4] with 1 molar equiv of diethylzinc in anhydrous benzene causes a rapid disappearance of starting material. Quenching the reaction mixture with water at this stage gives *endo*-α-bromocamphor (**2**) quantitatively,[5] suggesting the initial formation of bromoenolate **3** (see Scheme I). If the reaction mixture is refluxed for 22 hr before quenching, however, tricyclic ketone **4** is produced in 80% yield,[6,8] while the yield of **2** drops to 10%. Longer reaction times give slightly more **4** at the expense of **2**. When considered with respect to Bredt's preparation of the same tricyclic ketone[9] by C-H insertion of the ketocarbene derived in the classical way from diazo ketone **5**, our results argue convincingly for the intermediacy of a ketocarbenoid[10] in this α elimination.

Scheme I



The use of only 0.5 molar equiv of diethylzinc in the above reaction changes the product distribution very little (60% **4**:11% **2**:5% **1**). Evidently the α elimination does not require an ethyl group as ligand X in intermediate **3**. The formation of tricyclic ketone **4** from dibromocamphor (**1**) in *ca.* 35% yield by the action of either zinc dust or zinc-copper couple[11] in hot dimethylformamide supports this conclusion, although both reactions fail in benzene or ether solvents.

In accord with the α elimination of Br_2 adjacent to a ketone, the corresponding α elimination of HBr likewise yields a ketocarbenoid (Scheme II). Thus, the relatively slow reaction between diethylzinc and *endo*-α-bromocamphor (**2**) in refluxing benzene furnishes **2**, **4**, and **7** in comparable amounts after 48 hr. Production of the tricyclic ketone **4** again implicates most likely the bromoenolate **3**, formed in this instance by deprotonation of the starting material. Competitive removal of the bromine from **2** by diethylzinc undoubtedly accounts for the camphor **7** found in this reaction, whereas the bromocamphor **2** may either

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(1) W. Kirmse, "Carbene Chemistry," 2nd ed, Academic Press, New York, N. Y., 1971.

(2) H. O. House, W. F. Fischer, Jr., M. Gall, T. E. McLaughlin, and N. P. Peet, *J. Org. Chem.*, **36**, 3429 (1971).

(3) B. W. Peace and D. S. Wulfman, *Tetrahedron Lett.*, 3799 (1971); B. W. Peace and D. S. Wulfman, *Chem. Commun.*, 1179 (1971); D. S. Wulfman, B. W. Peace, and E. K. Steffen, *ibid.*, 1360 (1971); B. W. Peace, F. Carman, and D. S. Wulfman, *Synthesis*, 658 (1971); D. S. Wulfman and B. W. Peace, *Tetrahedron Lett.*, 3903 (1972).

(4) Dibromocamphor was prepared from *d*-camphor by a modification of the procedure of B. Shive, W. W. Crouch, and H. L. Lochte, *J. Amer. Chem. Soc.*, **63**, 2979 (1941).

(5) Identified by comparison with an authentic sample.

(6) The combustion analysis, ir, nmr, and mass spectral properties of this compound are all consistent with the structure assigned; mp 165-166° (lit.[7] 168-170°); oxime mp 127-129° (lit.[7] 132°).

(7) J. R. A. Pollock and R. Stevens, Ed., "Dictionary of Organic Compounds," 4th ed, Oxford University Press, New York, N. Y., 1965, p 3190.

(8) Yields based on dibromocamphor were determined by vpc, using α-methylnaphthalene as internal standard, and have been corrected by the detector response factor for each compound.

(9) The correct structure for tricyclic ketone 4 was first assigned by J. Bredt and W. Holz, *J. Prakt. Chem.*, **95** (2), 133 (1917), although the compound had been prepared previously by R. Schiff, *Chem. Ber.*, **14**, 1375 (1881). See also P. Yates and S. Danishefsky, *J. Amer. Chem. Soc.*, **84**, 879 (1962), for a more recent examination of diazocamphor (**5**) and related diazo ketones.

(10) We support the commonly accepted definition of "carbenoid" found on p 6 in ref 1. The ketocarbenoids (metal-complexed carbenes) formed by copper-catalyzed decomposition of diazo ketones and by our α eliminations are clearly distinct from the "free" ketocarbenes generated by diazo ketone photolysis, for only the latter suffer Wolff rearrangement.[1]

(11) The zinc-copper couple was prepared by the method of E. LeGoff, *J. Org. Chem.*, **29**, 2048 (1964).