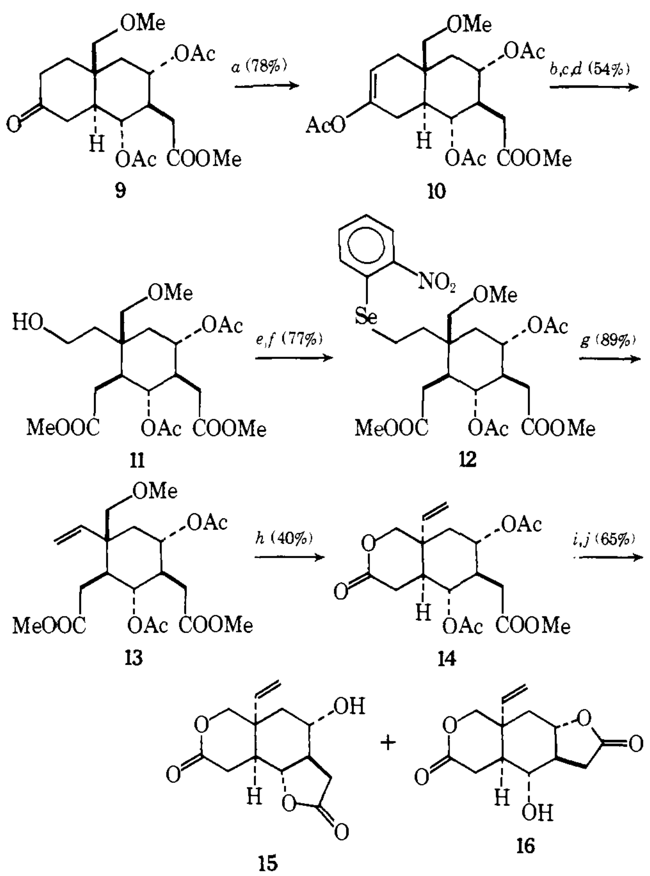
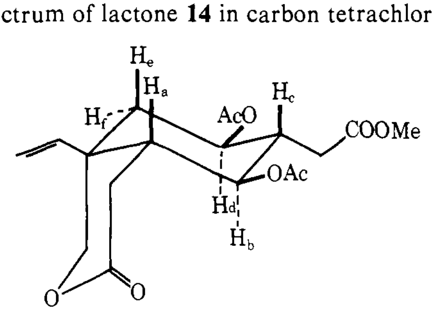
Chart II. Synthesis of Bisnorvernolepin and Bisnorvernomenin



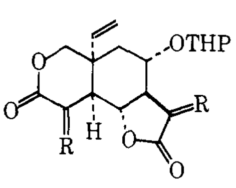
^{a} Isopropenyl acetate, TsOH, reflux, 9 h. ^{b} O_3, CH_2Cl_2–MeOH (1:1), −78°. ^{c} $NaBH_4$, −78°. ^{d} CH_2N_2, Et_2O. ^{e} MsCl, Py, 5°, 15 h. ^{f} o-$O_2NC_6H_4SeCN$, BH_4^-, DMF, room temp, 20 h. ^{g} 50% H_2O_2, THF, 24 h, room temp. ^{h} BBr_3, CH_2Cl_2, −78° (30 min) → −12° (4 h). ^{i} K_2CO_3, MeOH, 3 h, room temp. ^{j} TsOH, C_6H_6, reflux, 2 h.

accompanied by simultaneous lactonization to the bicyclic lactone **14**, mp 127–128°. Examination of the 250-MHz NMR spectrum of lactone **14** in carbon tetrachloride easily confirmed the assigned structure: δ 5.12 (triplet, 1 H, J_{ab} = J_{bc} = 11 Hz) and 4.94 (triplet of doublets, 1 H, J_{cd} = J_{de} = 11 Hz, J_{df} = 4.5 Hz). Acetate hydrolysis (77%) followed by lactonization (83%) provided a 2.5:1 mixture of bisnorvernolepin (**15**) and bisnorvernomenin (**16**) which, without separation, were converted to their respective tetrahydropyranyl ethers.

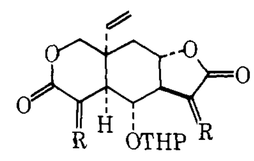


14

Bis-α-hydroxymethylation of the tetrahydropyranyl ethers of **15** and **16** was performed by generation of their respective dilactone enolates with lithium diisopropylamide in tetrahydrofuran containing 10% hexamethylphosphoramide followed by addition of formaldehyde as described previously.[9] Mesylation of the crude adducts **17** and **18** (R = H, CH_2OH) followed by β-elimination employing 1,5-diazabicyclo[5.4.0]undec-5-ene in benzene at room temperature gave **17** and **18** (R = $=CH_2$) in 16% overall yield.



17



18

Hydrolysis (60% aqueous acetic acid, 3 h, 45°) of the tetrahydropyranyl ethers afforded (71%) crude vernolepin (**1**) and vernomenin (**2**) as a mixture (ca. 3:1). Vernolepin and vernomenin were cleanly separated by preparative layer chromatography on 0.25-mm silica gel plates (one elution with chloroform–acetone (3:1)). (±)-Vernolepin, mp 210–211°, was identical with a sample of natural vernolepin,[10] mp 181–182°, by thin layer chromatographic and spectral comparisons. (±)-Vernomenin, mp 186–188°, was identical according to spectral comparisons with spectra kindly provided by Professor S. M. Kupchan.

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References and Notes

(1) S. M. Kupchan, R. J. Hemingway, D. Werner, A. Karim, A. T. McPhail, and G. A. Sim, *J. Am. Chem. Soc.*, **90**, 3596 (1968); S. M. Kupchan, R. J. Hemingway, D. Werner, and A. Karim, *J. Org. Chem.*, **34**, 3903 (1969).

(2) P. A. Grieco, J. A. Noguez, and Y. Masaki, *Tetrhedron Lett.*, **4213** (1975), and references cited therein.

(3) Cf. D. H. R. Barton, R. H. Hesse, M. M. Pechet, and E. Rizzardo, *J. Am. Chem. Soc.*, **95**, 2748 (1973).

(4) Compound **3** was prepared from its corresponding cis isomer by equilibration with sodium methoxide in methanol. The preparation of the cis isomer is described in ref 2.

(5) All intermediates were characterized by ir and NMR (60 and 250 MHz) spectroscopy and the spectral data are fully consistent with the structures assigned. All intermediates gave satisfactory combustion analyses or exact mass data. Yields reported are for chromatographically pure substances unless indicated otherwise.

(6) For a recent review of selenium chemistry see K. B. Sharpless, K. M. Gordon, R. F. Lauer, D. W. Patrick, S. P. Singer, and M. W. Young, *Chem. Scr.*, in press.

(7) This reaction was developed in our laboratory by Dr. T. Oguri. Complete details concerning a variety of α-substituted epoxy ketones will be reported in due course.

(8) K. B. Sharpless and M. W. Young, *J. Org. Chem.*, **40**, 947 (1975); P. A. Grieco, Y. Masaki, and D. Boxler, *J. Am. Chem. Soc.*, **97**, 1597 (1975).

(9) P. A. Grieco and K. Hiroi, *J. Chem. Soc., Chem. Commun.*, 1317 (1972).

(10) We are indebted to Professor S. M. Kupchan (University of Virginia) for providing us with a sample of natural vernolepin.

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Reaction Rate Difference in the Laser Excitation of Different Vibrational Modes of CF_2ClCF_2Cl

Sir:

When a molecular vibrational mode of a gaseous system is excited by a laser tuned to the frequency of that mode, intermolecular collisions and intramolecular mode coupling act to transfer the excitation to other vibrational and translational modes. If the tranfer rates are sufficiently rapid,

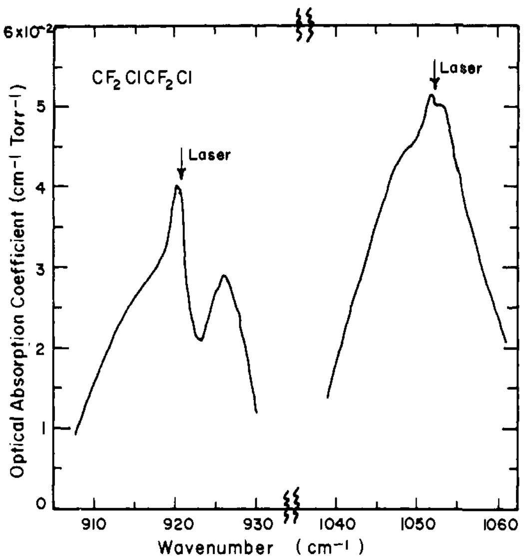

Figure 1. Normalized optical absorption coefficient (cm^{-1} Torr^{-1}) vs. wavenumber over two bands of CF_2ClCF_2Cl. Absorption measured at 200 Torr with instrumental slit resolution of 1 cm^{-1}.

the selectivity of the excitation is destroyed and the result is pure thermal heating by the laser.

This note reports the first observation, to our knowledge, of a significant difference in reaction rates induced by steady-state laser excitation of two different vibrational modes of the same molecule (CF_2ClCF_2Cl). Moreover, this occurs under conditions in which the excitation rate of either mode ($\sim 10^4$ photons absorbed per second per molecule) is very much less than the collision frequency ($\sim 10^9$ per second per molecule). The results suggest that collisions play an important role in the activation process leading to reaction, and at a rate which successfully competes with thermalization.

CF_2ClCF_2Cl has two strong absorption bands of comparable strength within the frequency range of a CO_2 laser. Figure 1 shows the absorption coefficient of the compound over these bands and the laser frequencies chosen for irradiation. The absorption is recorded at low light intensity and is expected to decrease at laser intensities (transparency effect). Laser powers from 2.5 to 4.6 W (CW) were used with a beam diameter of 1 mm, and in all experiments the beam was totally absorbed along the 50-mm path length of the sample cell. Reaction rates were obtained by monitoring the growth of the 1344-cm^{-1} absorption band of one of the reaction products (C_2F_4) during irradiation.

Both laser frequencies appear to give the same reaction but at different rates. With a starting gas pressure of 300 Torr of CF_2ClCF_2Cl, the reaction rate for 921-cm^{-1} radiation is 160 ± 35 times larger than for 1052-cm^{-1} radiation at identical power levels. Within experimental error, this ratio of rates seems independent of laser power over the range 2.5–4.6 W. The rates increase approximately as the eighth power of laser intensity. It should be noted that the optical absorption coefficients at 921 and 1052 cm^{-1} are 0.040 and 0.051 cm^{-1} Torr^{-1}, respectively, so that the slower reaction in fact occurs for the more strongly absorbing band, i.e., where the power absorbed per unit volume is the larger. In a purely thermal reaction, therefore, 1052-cm^{-1} radiation would actually produce the faster reaction.

We observe also that the rate ratio falls with increasing pressure. At 400 Torr starting pressure, for example, the ratio is one-half that for 300 Torr.

At 300 Torr, the classical kinetic model of hard spheres[1] gives a collision frequency $\sim 10^9$ s^{-1}. The rate of photon absorption per molecule is given by the expression $\alpha I/N$, where α is the optical absorption coefficient, I is the photon flux density (photons per second per unit area), and N is the number of molecules per unit volume. At 300 Torr, $\alpha I/N$ is $\sim 10^4$ s^{-1} for our experiments. This is an upper limit, since α will be reduced at the intensity of the laser.

There have been some studies of the thermal[2] and flow-tube pyrolytic[3] decomposition of CF_2ClCF_2Cl. Decomposition occurs readily at temperatures over 600 °C. Thermodynamic and kinetic data do not appear to be available. Borchardt[3] writes the initial reaction as

$$CF_2ClCF_2Cl \rightarrow CF_2Cl_2 + CF_2{:} \qquad (1)$$

followed by polymerization and insertion products of the diradical. Infrared analysis of the laser induced reaction clearly shows the immediate appearance of characteristic bands of C_2F_4 and also the presence of CF_2Cl_2. Under continued irradiation a series of further reactions occurs in which initial and subsequent products participate. At various stages the bands of $CClF_3$, CF_2CCl_2, and C_2F_3Cl, among others, are observed. An alternate route to the production of C_2F_4 may be:

$$CF_2ClCF_2Cl \rightarrow CF_2ClCF_2\cdot + Cl\cdot \qquad (2)$$

$$CF_2ClCF_2\cdot \rightarrow C_2F_4 + Cl\cdot \qquad (3)$$

$$CF_2ClCF_2Cl + Cl\cdot \rightarrow CF_2ClCF_2\cdot + Cl_2 \qquad (4)$$

$$Cl\cdot + Cl\cdot \rightarrow Cl_2 \qquad (5)$$

The initial reaction induced by laser irradiation of either of the bands mentioned appears to be similar to that of pyrolysis. Presumably the decomposition of CF_2ClCF_2Cl proceeds via the breaking of the weakest bond, either the C–C bond as suggested by Borchardt[3] or the C–Cl bond. If the route to reaction involves energy transfer from either of the laser-excited modes to a third (predominantly C–C or C–Cl stretch) mode by way of intramolecular coupling or resonant collision, then the difference in reaction rates could be attributed to differences in the probabilities, or rates, of transfer. Alternatively, in each of the laser-excited vibrational modes there might be a significant fraction of the total energy in C–C or C–Cl stretching motion, but in different amounts for the two modes. A normal mode analysis of the molecule would be of great value for evaluating various explanations of the reaction rate differences but a literature search has revealed only the assignment of a C–F stretch of the gauche isomer for each of the two bands excited here.[4,5]

Acknowledgment. We wish to thank the Organic Chemicals Department of DuPont for supplying CF_2ClCF_2Cl containing less than 2% CF_3CFCl_2.

References and Notes

(1) See, for example, E. A. Desloge, "Statistical Physics", Holt, Rinehart and Winston, New York, N.Y., 1966, pp 69–73.
(2) J. A. Callighan, *ASHRAE J.*, **11**, 65 (1969).
(3) H. J. Borchardt, *Du Pont Innovation*, **6, No. 2,** 1 (1974).
(4) D. Simpson and E. K. Plyler, *J. Res. Natl. Bur. Stand.*, **50**, 223 (1953).
(5) R. E. Kagarise, *J. Chem. Phys.*, **26**, 380 (1957).

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