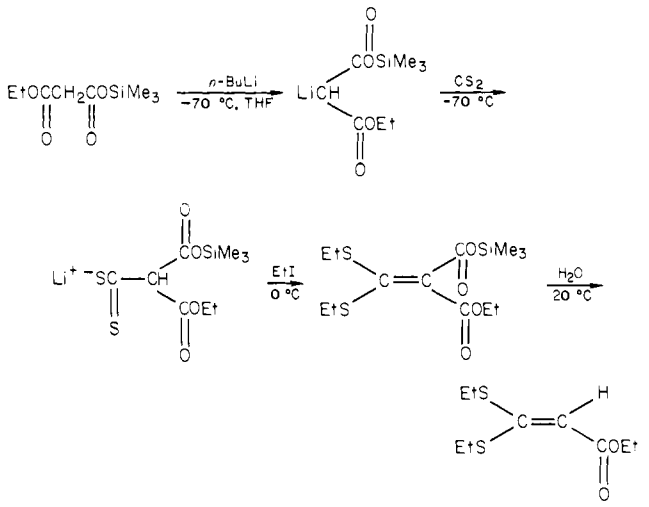
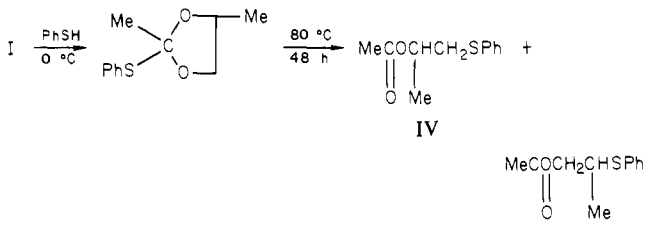
4 H), 2.08 (s, 3 H), and 1.20–1.50 ppm (m, 6 H). The absorption at 5.90 ppm is assignable to olefinic methine proton without any coupling, and the peaks at 5.21 and 3.02–3.40 ppm are due to methine and methylene protones adjacent to oxygen and sulfur atoms, respectively. Further, the peaks at 2.0, and 1.28–1.50 ppm are attributable to the methyl protones of acetate unit and propylene unit, respectively. From these data, P-I should be proposed as the structure of the copolymer.

In order to clarify this assumption, it was carried out to prepare the model compound [ethyl 2,-bis(ethylthio)acrylate (II)[7]] similar to the repeated unit by the following schemes.



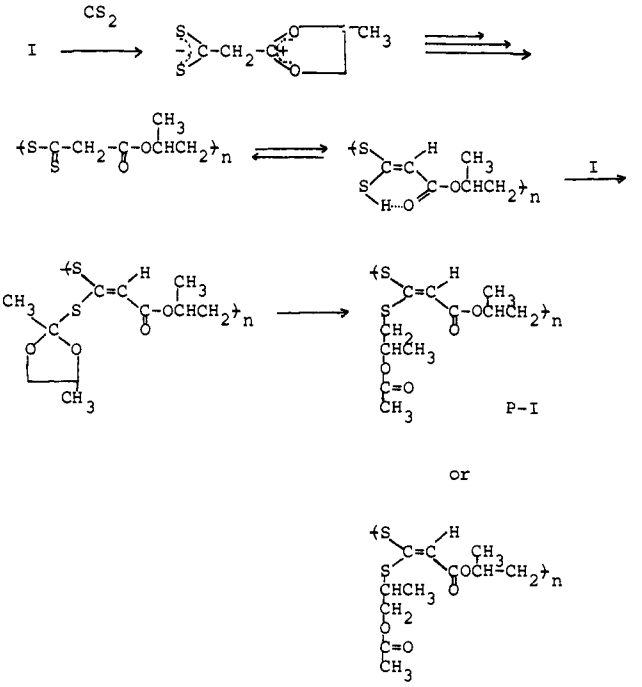
II

The reaction of I with thiophenol was also carried out to find that 2,4-dimethyl-2-(phenylthio)-1,3-dioxolane (III) was produced quantitatively by the equimolar reaction at 0 °C. Furthermore it was ascertained that III underwent the isomerization at 80 °C quantitatively to the mixture of 1-methyl-2-(phenylthio)ethyl acetate (IV) and 2-(phenylthio)propyl acetate (V).[8] The ratio



IV

of IV and V was estimated to be 90:10 by the ^{1}H NMR spectrum. The IR spectra of the mixture of II and IV–V were in good agreement with that of the resulting copolymer (P-I). From these data the plausible mechanism of the reaction of I with CS_2 might be as follows.



We can expect to prepare new compounds or new types of polymers by developing the reactions of cyclic ketene acetals with heterocumulenes such as carbon dioxide, isocyanates, isothiocyanates, carbodiimides, etc. on the basis of this reaction.

Registry No. I, 85079-89-6; II, 18224-54-9; III, 90369-21-4; IV, 32300-28-0; V, 32300-63-3; (I)·(CS_2) (copolymer), 90369-22-5; CS_2, 75-15-0; EtI, 75-03-6; PhSH, 108-98-5; $EtO_2CCHLiCO_2SiMe_3$, 49775-36-2.

(7) To a solution of 20 mL of tetrahydrofuran containing 4.1 g (0.02 mol) of ethyl trimethylsilyl malonate, prepared by the reaction of monoethyl malonate and trimethylsilyl chloride, 15 mL of *n*-butyllithium in hexane (1.6 mmol/mL) was added dropwise at −70 °C, and the mixture was left at −70 °C for 10 min. After 2.3 g (0.03 mol) of CS_2 was added dropwise to the solution at −70 °C, 6.2 g (0.04 mol) of ethyliodide was added to the mixture. After reaction mixture was allowed to warm to 0 °C overnight, 50 mL of water was added, and the solvent was removed by a rotary evaporator. The residue was poured into 100 mL of water and the organic layer was extracted with ether 3 times. After the etheral solution was dried over magnesium sulfate, the solvent was removed and the residue was distilled under reduced pressure to give 2.52 g (57%) of II; bp 124–125 °C (4 mmHg); ^{1}H NMR (100 MHz, $CDCl_3$) δ 1.20–1.48 (3 t, 9 H, CH_3), 2.85–3.20 (2 q, 4 H, SCH_2), 4.25 (q, 2 H, OCH_2), 5.78 (s, 1 H, C=CH). Anal. Calcd for $C_9H_{16}O_2S_2$: C, 49.05; H, 7.33; S, 29.10. Found: C, 48.90; H, 7.62; S, 29.20.

(8) To a mixture of 1.1 g (0.01 mol) of thiophenol and 5 mL of carbon tetrachloride 1.0 g (0.01 mol) of I was added dropwise at 0 °C. A portion of the reaction mixture was poured into a NMR tube, and then NMR measurement was carried out to find that 2,4-dimethyl-2-(phenylthio)-1,3-dioxolane (III) was obtained quantitatively. After the solvent was removed by using a rotary evaporator, the oily residue was heated at 80 °C for 48 h and then distilled under reduced pressure to give 1.92 g (87%) of 1-methyl-2-(phenylthio)ethyl acetate (IV) containing 10% of 2-(phenylthio)propyl acetate (V): bp 109–111 °C (3 mmHg); ^{1}H NMR (100 MHz, $CDCl_3$) δ 1.50 (d, 3 H, CH_3), 1.96 (s, 3 H, CH_3CO), 2.90–3.20 (m, 2 H, SCH_2), 5.10 (m, 1 H, OCH), 7.40–7.70 (m, 5 H, Ar H's). Anal. Calcd for $C_{11}H_{14}O_2S$: C, 62.81; H, 6.72; S, 15.25. Found: C, 62.80; H, 6.78, S, 15.21.

Multisite Kinetics by Quantitative Two-Dimensional NMR

Charles L. Perrin* and Robert K. Gipe

Department of Chemistry, D-006
University of California, San Diego
La Jolla, California 92093

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Two-dimensional NMR[1] is a promising technique for kinetics,[2] especially in multisite systems. Previous applications[3,4] have been qualitative, designed to display exchange pathways. Quantitative application has been limited, owing to the use of absolute-value transforms to produce suitable peak shapes. We now report that rate constants can be evaluated from two-dimensional NMR spectra obtained with a program of phase cycling[5] that produces

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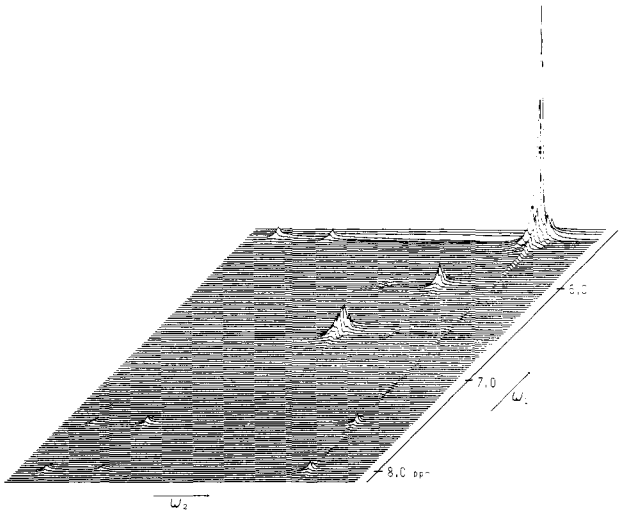
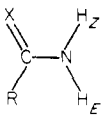


Figure 1. Two-dimensional pure-absorption-phase spectrum of acrylamide in ethylene glycol at measured pH 1.75. The peaks along the diagonal, from bottom left to top right, are H_E, H_Z, CH (vinylics), CH (vinylic), and H_S (OH of solvent); CH_2 of solvent is off scale at lower ω_1 and ω_2. Also, every other ω_1 value has been omitted. Peak intensities (arbitrary units): I_{SS} = 720, I_{SZ} = 33, I_{SE} = 36, I_{ZS} = 28, I_{ZZ} = 31, I_{ZE} = 14.3, I_{ES} = 39, I_{EZ} = 15.3, I_{EE} = 25.4.

pure absorption-mode spectra in both dimensions.

Figure 1 shows a portion of a 2D NMR spectrum of acrylamide (**1**, X = O; R = CH_2CH) in acidified ethylene glycol. This was



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obtained with the pulse sequence 90°–t_1–90°–HS–t_m–14°–t_2–(acquisition). Since proton concentrations are high, an observation pulse of 14°, rather than the conventional 90°, was used to reduce sensitivity. This then necessitated a homospoil pulse,[2] HS, to eliminate residual *xy* magnetization. The mixing time t_m was 150 ms, chosen to match both the spin–lattice T_1, which had been measured previously, and the reaction rate, which was adjusted by adding HCl. A single cycle of 16 phase settings[5] was used to obtain pure absorption-mode spectra, selected by phasing the t_1 = 0 spectrum. A total of 512 t_1 values was used, each with a spectral width of 2200 Hz at 360 MHz, and 1024-point FIDs were acquired in the t_2 dimension. A line broadening of 4 Hz was imposed in each dimension prior to Fourier transformation.

The sizable off-diagonal peaks in Figure 1 show qualitatively that there is exchange among all sites, H_E, H_Z, and H_S (solvent OH). Each peak intensity, I_{ij} (i,j = *E*,*Z*,*S*) was evaluated as a volume by integrating peak areas with respect to ω_2 and summing those areas over ω_1. Intensities are given in Figure 1. The requirement that $I_{ij} = I_{ji}$ is satisfied with an average deviation of 10%, so we may have confidence in these values.

The relationship between 2D peak intensities and rate constants is given by eq 1, adapted from eq 9 of Macura and Ernst.[6] Here

$$I_{ij}(t_m) = (e^{-\mathbf{R}t_m})_{ij}M_j^\circ \quad (1)$$

M_j° is the equilibrium magnetization of the nuclei in site j and **R** has off-diagonal elements $\mathbf{R}_{ij} = -k_{ji}$, where k_{ji} is the first-order rate constant for chemical exchange from site j to site i. It is then possible to solve for the rate-constant/relaxation matrix **R** through eq 2, where $\mathbf{A}_{ij} = I_{ij}(t_m)/M_j^\circ$, **X** is the square matrix of eigenvectors

$$\mathbf{R} = -t_m^{-1} \ln \mathbf{A} = -t_m^{-1}\mathbf{X}(\ln \Lambda)\mathbf{X}^{-1} \quad (2)$$

of **A**, such that $\mathbf{X}^{-1}\mathbf{A}\mathbf{X} = \Lambda = \mathrm{diag}(\lambda_i)$, and $\ln \Lambda = \mathrm{diag}(\ln \lambda_i)$.[7]

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Table I. Site-to-Site Rate Constants (s^{-1}) for Acid-Catalyzed Proton Exchange of Acrylamide (in Ethylene Glycol) and Thioacetamide (in Glycerol–Me_2SO-d_6) at 22 °C

	acrylamide 2D NMR	acrylamide saturation transfer[9]	thioacetamide 2D NMR
$[H_S]/[H_{EZ}]$	7.15	10.90	19.4
k_{EZ}	2.5	2.5 ± 0.5	<0.14
k_{ZE}	2.2	2.5 ± 0.5	<0.15
k_{ZS}	2.5	3.1 ± 0.5	0.55
k_{ES}	4.9	4.6 ± 0.5	0.54
k_{SE}	0.51	0.43 ± 0.05	0.038
k_{SZ}	0.39	0.34 ± 0.05	0.038

It is also necessary to evaluate M_j°. An easy method is to use only ratios of M_j° values, determined from the relative populations of nuclei in the various sites. This would suffice to calculate rate constants but not the spin–lattice times that contribute to the diagonal elements of **R**. An alternative method is to repeat the experiment with $t_m = 0$. According to eq 1, M_j° can then be evaluated as the intensity of the diagonal peaks in the 2D spectrum. However, for effective homospoil operation it was necessary to use t_m = 10 ms. The resulting intensities were I_{SS} = 1520, I_{ZZ} = 185, I_{EE} = 179.

Table I gives site-to-site rate constants for the proton exchange, calculated according to eq 2 from the peak intensities. A rate constant of 1.4 s^{-1} for uncatalyzed rotation about the C–N bond[8] has been subtracted from the calculated k_{EZ} and k_{ZE}, so the values in Table I are rate constants purely for acid-catalyzed exchange. The data satisfy, within ±25%, the requirement that forward and reverse rates be equal. For comparison, Table I includes rate constants previously determined under nearly the same conditions by saturation-transfer techniques.[9] The agreement is remarkably good, especially in view of the fact that the new values are obtained with a single t_m of 150 ms. (Two-dimensional accordion spectroscopy[10] would overcome this limitation). This t_m was chosen to optimize accuracy, but t_m = 75 or 300 ms gave the same values, within experimental error. Moreover, these rate constants show clearly that within experimental error $k_{EZ} = k_{ZE} = k_{ZE} < k_{ES}$. This is the quantitative result to support the N-protonation mechanism for exchange, via $RCONH_3^+$ in which deprotonation is competitive with rotation about the C–N single bond.[9] Thus rate constants determined by 2D NMR are sufficiently reliable that we may draw mechanistic conclusions from them.

A 2D NMR spectrum, with t_m = 350 ms, of thioacetamide (**1**, X = S, R = CH_3) in 1:1 (v/v) glycerol–Me_2SO-d_6 containing 0.15 M HCl gave peak intensities I_{SS} = 1890, I_{SZ} = 21, I_{SE} = 18.5, I_{ZS} = 15.4, I_{ZZ} = 63, I_{ZE} < 3, I_{ES} = 13.2, I_{EZ} < 3, and I_{EE} = 47. (The downfield NH peak has been assigned as H_Z.[11]) Qualitatively, the absence of off-diagonal *EZ* and *ZE* peaks would suggest that there is no intramolecular proton exchange. However, according to eq 1, the stoichiometry renders these peaks inherently weak, relative to the other off-diagonal peaks. Therefore it is essential to be quantitative. Table I gives site-to-site rate constants for exchange, calculated from the intensities. It is clear that the intramolecular rate constants, k_{EZ} and k_{ZE}, are significantly less than the intermolecular rate constant k_{ZS} (or k_{ES}). This result is inconsistent with the N-protonation mechanism, and it is strong evidence for the imidic acid mechanism, involving $CH_3C(SH)$=NH as intermediate. Such a mechanism had been suggested[12] on the basis of a comparison of the rate of acid-catalyzed proton exchange in a secondary thioamide with the rate of acid-catalyzed rotation about the C–N bond in a tertiary thioamide. However, that comparison is not as conclusive as the one obtained here.

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The total acquisition time for Figure 1 was 8 h. However, adequate kinetic data could be obtained in 2 h and trial spectra in 30 min. Thus this technique can be competitive with the previous saturation-transfer technique. Moreover, the time required for the 2D experiments is nearly independent of the number of sites (if chemical shifts are well separated), whereas the time required for the multiple saturations increases with the number of sites. Therefore, the 2D technique is likely to be preferable with many sites, but not with only two sites.

The 2D technique is essential for thioacetamide. Hydroxylic solvents are required for proton exchange, and viscous solvents are required to sharpen NH resonances. In such solvents the peak separation between H_E and H_Z is quite small—0.06 ppm in the solvent mixture used here. Such a close spacing would not permit selective irradiation for a saturation-transfer study. However, the 2D technique does provide quantitative kinetic data.

Acknowledgment. We are greatly indebted to Dr. John Wright for programming the Nicolet 293-B programmer and 1180-E computer to cycle through the pulse phases and to manipulate the data efficiently. Dr. Eric R. Johnston performed some preliminary experiments. This research was supported by National Science Foundation Grant CHE 81-16800.

Registry No. $CH_3C(SH)=NH$, 65680-21-9; acrylamide, 79-06-1; thioacetamide, 62-55-5.

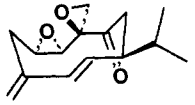
Cyclobutene Bridgehead Olefin Route to the American Cockroach Sex Pheromone, Periplanone-B

Stuart L. Schreiber*[1] and Conrad Santini

Department of Chemistry, Yale University
New Haven, Connecticut 06511

Received April 5, 1984

Periplanone-B, the potent sex attractant and sex excitant pheromone of the American cockroach, *Periplaneta americana*, escaped complete stereochemical assignment of structure for the first 25 years of combined studies from several research groups. Persoons and his co-workers were able to isolate and purify a small quantity (200 μg) of periplanone-B, and in 1976, on the basis of their extensive spectroscopic studies, established the constitution as shown in **1**.[2] Through conformational analysis of germacranoid



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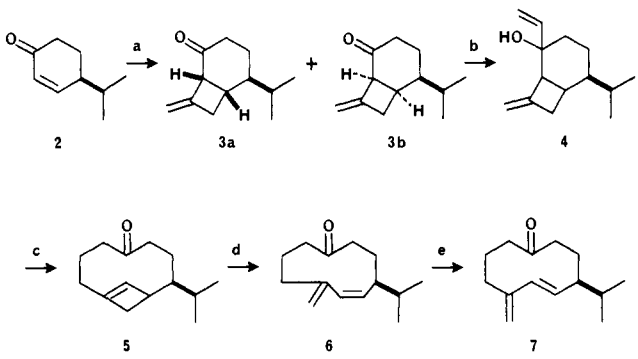
synthetic intermediates, Still was able to deduce the relative stereochemistry of periplanone-B on route to the first total synthesis of this substance.[3] A combination of X-ray, synthetic, and chiroptical techniques finally established the absolute configuration of periplanone-B as shown in **1**.[4]

The challenging structural features of periplanone-B in combination with the practical implications of the potent attractant property[5] of the cockroach pheromone render **1** as an attractive target for further synthetic studies. Herein, we report on our investigations which have resulted in a new total synthesis of (±)-periplanone-B.

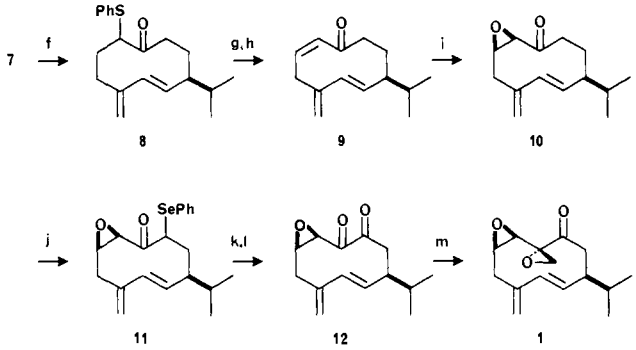
Our synthesis commenced with photocycloaddition of allene and 4-isopropyl-2-cyclohexen-1-one[6] (10.6 g), which provided a 2:1 mixture of the anti (**3a**)[7] and syn (**3b**)[8] head-to-head[9] photoadducts (9.9 g, 72% yield)[10] (Scheme I). Although **3a** and **3b** can be isolated by HPLC (10-μm Porasil, 9% EtOAc/hexane)

Scheme I[a]



[a] (a) $CH_2=C=CH_2$, Et_2O, $h\nu$ (450-W Hanovia lamp equipped with a Pyrex filter), 72% (**3a**:**3b** = 2:1), 30 °C. (b) $CH_2=CHMgBr$, Et_2O, -78 °C, 63%. (c) KH, 5 equiv of 18-Cr-6, THF, 60 °C, 25 min. (d) Toluene, 175 °C, 20 h, 77%. (e) Benzene, $h\nu$ (450-W Hanovia lamp equipped with a Vycor filter), 82%.

Scheme II[a]



[a] (f) THF, $LiN(SiMe_3)_2$, -78 °C, $PhSSO_2Ph$, regioselectivity = 16:1. (g) aqueous MeOH, $NaIO_4$, 71% from 7. (h) Toluene, 110 °C, 45%. (i) THF, *t*-BuOOH, KH, 0 °C, 83% (4:1) mixture of β:α epoxides). (j) THF, $LiN(SiMe_3)_2$, -78 °C, PhSeBr, 83%. (k) 30% H_2O_2, THF, 97%. (l) THF, Ac_2O, NaOAc; then MeOH, H_2O, K_2CO_3, 60%. (m) Me_2SO, THF, $(Me)_3S^+I^-$, dimsyl (NaH), 62%.

(1) Searle Scholar, 1982-1985.

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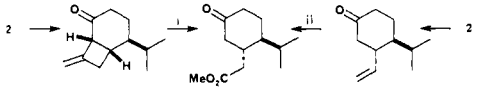
(7) The stereochemistry was assigned on the basis of chemical correlation (eq 1) with the product of the copper-catalyzed conjugate addition of vinylmagnesium bromide to cryptone 2, a reaction process known to occur with trans stereoselectivity.[11]



i: O_3, MeOH, K_2CO_3. ii: (1) disiamylborane; $H_2O_2^-$, OH; (2) Jones oxidation; (3) CH_2N_2.

(8) For another example of predominant "anti" addition and a discussion, see: Cargill, R. L.; Morton, G. H.; Bordner, J. *J. Org. Chem.* **1980**, *45*, 3929.

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