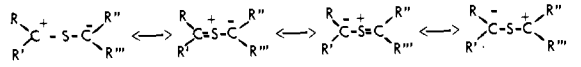
## Simple Generation of Thiocarbonyl Ylides

*Sir:*

Thiocarbonyl ylides are species represented by **1**.[1] They can be generated by the thermal extrusion of nitrogen from thiadiazolines (**2**) yielding thiiranes (**3**) as final products (eq 1).[2,3] Unfortunately, preparation of the thiadiazoline pre-



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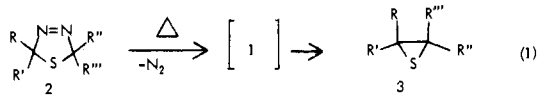
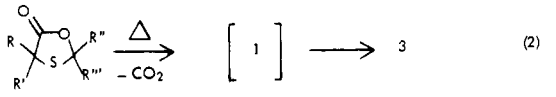
cursors is not trivial.[2,3] We report a new method for the generation of thiocarbonyl ylides which is simple and promises to be very general.



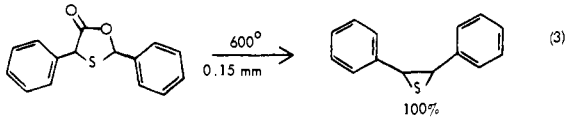
(1)

Our approach to these reactive intermediates is outlined in eq 2. Analogous loss of nitrogen is well established (eq 1)[2,3] and



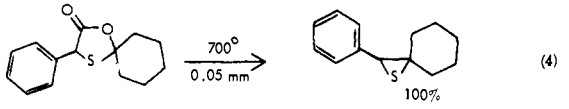
(2)

loss of carbon dioxide by a 1,3 cycloreversion is precedented in $\Delta^2$- and $\Delta^3$-oxazolinones,[4] but never before has carbon dioxide elimination been used successfully for the formation of an allylic ylide like **1**. In particular, 2,4-diphenyl-1,3-oxathiolan-5-one[5,6] undergoes loss of carbon dioxide at 600 °C to give a quantitative yield of thiirane (eq 3).[7] The reaction also



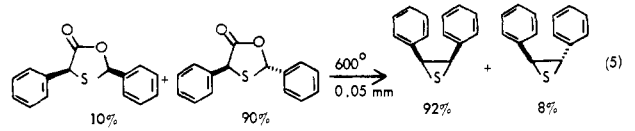
(3)

procedes well with only one phenyl substituent in the molecule, but a slightly higher temperature is required (eq 4).[8,9]



(4)

If the loss of carbon dioxide illustrated in eq 3 and 4 is concerted, the conversion of a 1,3-oxathiolan-5-one into a thiirane should be stereospecific. Furthermore, the overall process should procede with inversion of configuration based on orbital symmetry considerations.[10,11] Indeed, the initial reaction of eq 3 gave encouraging results since the original mixture of starting 1,3-oxathiolan-5-ones was 62% cis and the resulting thiirane mixture was 65% trans. In addition, another mixture of these 2,4-diphenyl-1,3-oxathiolan-5-ones containing 40% cis isomer yielded 37% trans product upon pyrolysis. This seems to rule out thermal isomerization of the thiiranes; however, in order to remove any possible ambiguity, fractional sublimation was used to obtain the nearly pure cis and trans isomers of 1,2-diphenyl-1,3-oxathiolan-5-one and these were pyrolyzed separately (eq 5 and 6). These results show that the conversion is almost 100% stereospecific and this supports the hypothesis of a *concerted loss of carbon dioxide.*



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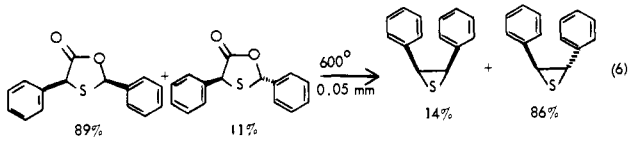

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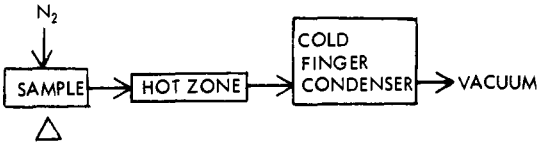


**Figure 1.** Flash vacuum pyrolysis unit.

We have used flash vacuum pyrolysis to carry out all of the thermal reactions. This technique is characterized by high temperatures, low pressures, and short contact times.[12] In particular, the compounds were slowly swept with a stream of nitrogen into a hot quartz tube with a cold finger condenser at the exit (see Figure 1). This should allow the isolation of even thermally labile products on preparative scales.[12]

We are currently studying the scope of the reaction and trapping of the thiocarbonyl ylides as well as extension to oxygen and nitrogen analogues. Complete details of the present work and the results of other efforts in this area are forthcoming.

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(6) All new compounds have satisfactory combustion analyses and IR and NMR spectra.
(7) The crude product was pure by NMR and TLC but was recrystallized for an analytical sample, mp 34–37 °C, 83% yield.
(8) Pyrolysis at 600 °C as in the diphenyl system (eq 3) gives only a 65% conversion. It is tempting to correlate necessary pyrolysis temperature with apparent stability of the ylide, but is rather speculative with only two systems.
(9) The pure, crude thiirane was distilled to obtain a boiling point: bp 74–75 °C (0.001 mm), 91% yield.
(10) Woodward, R. B.; Hoffmann, R. "The Conservation of Orbital Symmetry"; Verlag Chemie: Weinheim/Bergstr., Germany, 1970.
(11) This is a consequence of disrotatory ring opening with loss of carbon dioxide followed by conrotatory ring closure of the ylide.
(12) For example, see the excellent review: Seybold, G., *Angew. Chem., Int. Ed. Engl.* **1977,** *16,* 365.

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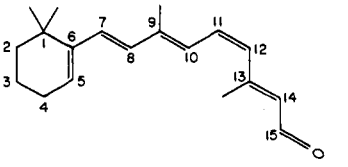
## Polyene Chain Conformations of 13-Demethylretinals

*Sir:*

Considerable recent attention has been focussed upon the conformation of the polyene chain portion of 11-*cis*-retinal (I), the visual pigment chromophore. A number of experimental



and theoretical studies[1,2] have contributed to the mounting body of evidence that the conformation about the 12–13 single bond, while distorted *s*-cis in the crystal state, is labile in solution, so that a mixture of conformers of 11-*cis*-retinal exists in solution. It has been proposed that the conformation when bound to the protein is 12-*s*-trans and that the wavelength of

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**Table I.** $^1$H NMR Chemical Shifts of 13-Demethylretinal Isomers and Chemical-Shift Differences between 13-Demethylretinals and Normal Retinals

| proton | 13-demethylretinal chemical shifts[a] | | chemical-shift differences[b] | |
|---|---|---|---|---|
| | all-trans | 11-cis | all-trans | 11-cis |
| 1,1′-$CH_3$ | 0.974 | 0.979 | −0.003 | 0.014 |
| 5-$CH_3$ | 1.640 | 1.652 | −0.006 | 0.025 |
| 9-$CH_3$ | 1.910 | 1.906 | −0.009 | 0.025 |
| 7-H | 6.248 | 6.271 | 0.030 | 0.066 |
| 8-H | 6.061 | 6.121 | −0.007 | 0.081 |
| 10-H | 6.146 | 6.498 | 0.094 | 0.058 |
| 11-H | 6.867 | 6.616 | −0.118 | 0.106 |
| 12-H | 6.286 | 6.065 | 0.068 | 0.294 |
| 13-H | 6.913 | 7.410 | | |
| 14-H | 5.948 | 5.961 | 0.167 | 0.068 |
| 15-H | 9.456 | 9.505 | −0.525 | −0.466 |

[a] Chemical shifts measured relative to internal hexamethyldisiloxane (HMDS), in perdeuteriocyclohexane at 32 ± 1 °C (HMDS resonates 0.02 ppm downfield of $Me_4Si$). Olefinic shifts were fitted using LAOCN3. [b] Shift differences (13-demethylretinal–normal retinal) in parts per million for all samples in $C_6D_{12}$; negative value means downfield shift of normal retinal relative to 13-demethylretinal.

**Table II.** Vicinal Coupling Constants of 13-Demethylretinal Isomers and Coupling Constant Differences with Normal Retinal Isomers

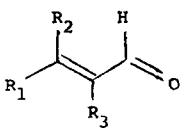
| coupling | 13-demethylretinal | | differences | |
|---|---|---|---|---|
| | all-trans | 11-cis | all-trans | 11-cis |
| 7H,8H | 16.0 | 16.2 | −0.1 | +0.1 |
| 10H,11H | 11.6 | 13.1 | +0.2 | +0.1 |
| 11H,12H | 14.5 | 10.3 | −0.6 | −0.6 |
| 12H,13H | 11.3 | 11.6 | | |
| 13H,14H | 15.3 | 15.1 | | |
| 14H,15H | 7.6 | 7.5 | +0.4 | +0.3 |

maximum absorption in visual pigments is in part governed by the precise 12–13 torsional angle. It is the C-13 methyl group of 11-*cis*-retinal which is a major contributor to the distortion from planarity about the 12–13 bond of the chromophore in solution; so, in order to understand fully the interactions governing this conformation, it is important to know with certainty the structure of the compound having *no* methyl group at C-13, namely 11-*cis*-13-demethylretinal. Nelson et al.[3] demonstrated that of two isomers of 13-demethylretinal which would combine with opsin to form synthetic visual pigments, the one designated "*cis*-II", and presumed to be 11-*cis*-13-demethylretinal, reacted with opsin much more slowly than did 11-*cis*-retinal, and the pigment formed was markedly less stable than was native rhodopsin. In the present communication we first establish using high resolution $^1$H NMR that the "*cis*-II" isomer of Nelson et al.[3] is indeed a single isomer, namely 11-*cis*-13-demethylretinal, and, secondly, show that the conformation of this analogue visual chromophore free in solution is planar *s*-trans, including in particular the 12–13 and 14–15 single bonds. Finally, we present preliminary results of continuous photoirradiation of *all-trans*-13-demethylretinal.

The $^1$H NMR chemical shifts and vicinal coupling constants are summarized in Tables I and II. These data, especially in comparison with data for the corresponding normal retinal isomers, provide evidence for the planar structure of both isomers. Considering first the coupling constants, we see that, for the all-trans isomer, the couplings between adjacent protons along the chain are consistent with trans vicinal couplings across alternating single and double bonds; the values are almost identical with those obtained for *all-trans*-retinal under the same conditions.[4] The differences between the normal retinal parameters and the corresponding 13-demethyl parameters are shown in column 3 of Table II. For 11-*cis*-13-demethylretinal, $J_{11H,12H}$ = 10.3 Hz, which is proof of the cis configuration about the 11–12 double bond (see ref 4 for detailed discussion of possible range of values for cis and trans vicinal coupling contrasts in these systems). Again, this and the other corresponding coupling constants are quite similar for both the 11-*cis*-13-demethyl compound and the normal 11-*cis*-retinal. Although long-range coupling constants were quite helpful in determining the structures in acetone solution of the normal retinal isomers,[4] the signal to noise ratio and resolution of the 13-demethylretinal spectra do not allow a similar analysis here.

Considering next the chemical shifts of the 13-demethyl compounds in relation to those of the corresponding normal retinal isomers, the most striking difference among the chemical shifts of the two trans isomers is the relative shielding experienced by 15-H in *all-trans*-13-demethylretinal (Table I, column 3). A similar upfield shift of the 15-H resonance was noted[8] in the spectra of 13-demethyl-14-methylretinal, in comparison with the value for normal *all-trans*-retinal. These authors concluded, because of the shift of 15-H, that the conformation about the 14–15 single bond was *s*-cis for this structural isomer of retinal. However, comparison of the aldehyde proton chemical shifts for a number of α,β-unsaturated aldehyde compounds, shown in Table III, leads us to the *opposite* conclusion, namely that the upfield shift of the 15-H resonance in *all-trans*- (and 11-*cis*- as well) 13-demethylretinal, and probably in the 13-demethyl-14-methylretinal compounds as well, implies a 14-*s*-trans conformation. The upfield shift of 15-H arises *from the removal of the 13-methyl group*. In lines 1 and 2 of Table III, the resonance positions for

**Table III.** Aldehyde Proton Chemical Shifts for α,β-Unsaturated Aldehydes




| | $R_1$ | $R_2$ | $R_3$ | compd | chemical shift[a] | solvent | ref for shift | ref for conformation |
|---|---|---|---|---|---|---|---|---|
| 1 | H | $CH_3$ | H | *cis*-crotonaldehyde | 10.04 | neat | 5 | 9 |
| 2 | H | H | H | acrolein | 9.49 | | 6 | |
| 3 | $CH_3$ | H | H | *trans*-crotonaldehyde | 9.40 | neat | 5 | 9 |
| 4 | $CH_3$ | H | $CH_3$ | tiglaldehyde | 9.33 | | 6 | |
| 5 | $C_{16}H_{23}$ | $CH_3$ | H | *all-trans*-retinal | 10.12 | $CDCl_3$ | 7 | 4 |
| 6 | $C_{16}H_{23}$ | H | $CH_3$ | *all-trans*-14-methyl-13-demethylretinal | 9.44 | $CDCl_3$ | 8 | |
| 7 | $C_{16}H_{23}$ | H | H | *all-trans*-13-demethylretinal | 9.48 | $C_6D_{12}$ | this work | |

[a] Chemical shifts relative to $Me_4Si$.

the aldehyde proton in acrolein (no "13-methyl" group) and *cis*-crotonaldehyde can be seen, and the acrolein shift is substantially upfield. Comparison of the aldehyde proton chemical shifts for *trans*-crotonaldehyde and tiglaldehyde, lines 3 and 4 of Table III, shows that the effect of methyl substitution $\alpha$ to the aldehyde carbon is very small. In lines 5 and 7 can be seen the aldehyde chemical shifts of *all-trans*-retinal and *all-trans*-13-demethylretinal, showing that the effect of $\beta$-methyl substitution is the same in the conjugated polyene aldehydes as it is in the model compounds. The $\alpha$–$\beta$ single bond conformation for the compounds in lines 1, 3, and 5 has been shown to be planar *s*-trans, in the reference given in the last column of the table. Concerning the *cause* of the upfield shift accompanying the removal of an adjacent ($\beta$-) methyl group, it is at least partly explained as the removal of a source of steric polarization (a deshielding effect) of the aldehyde proton.[10,11]

Considering now the even more important C-10–C-13 region of 11-*cis*-13-demethylretinal, we note in Table I that the resonances of both 10-H and 13-H are considerably deshielded, relative to their positions in the trans isomer of this model chromophore. The shielding is the result of the kind of steric interaction[12] previously noted for the aldehyde proton. Interaction between 10-H and 13-H can occur in the 12-*s*-trans conformer of 11-*cis*-13-demethylretinal.

To confirm the structure and conformation of 11-*cis*-13-demethylretinal, several nuclear Overhauser experiments were performed.[13] When the 10-H resonance was saturated, a 17% enhancement was observed for 13-H, confirming the proximity of 10-H and 13-H in the molecular structure. When 13-H was irradiated, a 23% enhancement of 15-H was found; this enhancement is in close accord to the corresponding experiment on *trans*-crotonaldehyde in acetone-$d_6$ solution, where a 26% enhancement of the aldehyde proton resonance was found when the $\beta$ proton was saturated.[9] The 15-H[13-H] result is indicative of a 14–15 planar *s*-trans conformation.

Nelson et al.[3] reported the presence of only two isomers when *all-trans*-13-demethylretinal was irradiated with visible light. These were separated chromatographically and tentatively identified as 9-cis and 11-cis isomers by their reaction with opsin. In view of the well-known difficulty of separating 11-cis from 13-cis isomers of retinal-like compounds (before the advent of high pressure liquid chromatography), the possibility existed that the isomer called *cis*-II, and identified as 11-cis, might actually be contaminated with 13-*cis*-demethylretinal. A photoisomerization experiment was done with a degassed dilute solution of the *all-trans*-13-demethylretinal compound irradiated continuously with light while held in a flat quartz cell. The resulting isomerate solution was transferred directly to an NMR sample tube and pulsed overnight. The spectra revealed considerable isomerization: 21% 9-cis, 4% 11-cis, and 75% all-trans was the isomeric composition of the product. There were no peaks in the isomerate spectrum which could be attributed to 13-*cis*-13-demethylretinal.[14] This is strikingly different photoisomerization behavior from that of normal *all-trans*-retinal, which under identical conditions yields 12% 9-cis, no detectable 11-cis, 20% 13-cis, and 60% all-trans.

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(15) Deceased. Address correspondence to Brian D. Sykes, Department of Biochemistry, University of Alberta, Edmonton, Alberta T6G 2H7.

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## 1,2-Dioxetane Formation in an Indole System[1]

*Sir:*

The cleavage of the 2,3 double bond of indoles by molecular oxygen has long been known in many chemical[2] and biological[3] oxygenations. In most cases 1,2-dioxetane has been assumed to be the precursor of the $C_2$–$C_3$ ring cleavage product,[2,4] while such a highly strained arene 1,2-dioxetane has not yet been proved experimentally. We now report the preparation and characterization of the 1,2-dioxetane in the low-temperature photooxygenation of *tert*-butylated indoles, the first example of the direct observation of the long-sought 1,2-dioxetane derived from indoles. We previously observed that singlet oxygenation of *N*-methylindoles results in the formation of the ring-cleavage products in high yield.[2a,6] In order to detect 1,2-dioxetane intermediates we have carried out the photooxygenations of a number of 2- and 2,3-substituted *N*-methylindoles at low temperature, and found that 2-*tert*-butyl-1,3-dimethylindole (**1**) gives a 1,2-dioxetane which has a long enough lifetime to allow chemical and spectroscopic characterization.

Photosensitized oxygenation of **1** (1.4 mmol) in $CFCl_3$ at −78 °C with tetraphenylporphyrin as sensitizer using a tungsten–bromine lamp gave rise to the formation of a peroxidic product which rapidly liberated iodine from aqueous alcohol solution of potassium iodide. Warming of the low-temperature solution to room temperature resulted in the formation of the ring-cleavage product **2** in a quantitative yield (Scheme I). The $^1$H NMR spectrum ($CFCl_3$) of the low-temperature solution at −70 °C showed resonances at $\delta$ 1.22 (s, 9 H, *tert*-butyl), 2.01 (s, 3 H, *C*-methyl), 3.04 (s, 3 H, *N*-methyl), and 6.60–7.35 (m, 4 H, aromatic H).[7] The $^1$H NMR signals completely disappeared within a few minute at 0 °C with the appearance of the peaks ascribable to **2**. The chemical shifts of the resonances of the unstable peroxide are inconsistent with the formulation as the zwitterion **3** which would be expected to have the *N*-methyl and *tert*-butyl resonances considerably downfield of the position of the spectrum, whereas the chemical shifts of the deshielded *C*-methyl protons[8] ($\delta$ 2.01) as well as *N*-methyl and *tert*-butyl protons are in the

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