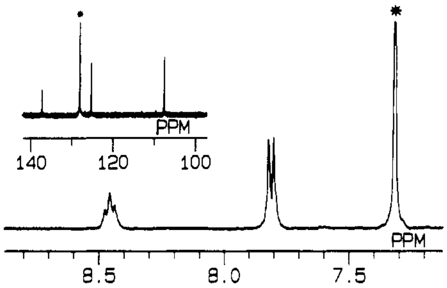

Figure 1. ^{1}H NMR spectrum of **1** (2:1 THF-d_8/CD_2Cl_2, −75 °C, 400 MHz): δ 8.45 (t, 2 H, J = 8.3 Hz, H5 and H10), 7.81 (d, 4 H, J = 8.3 Hz, H1, H4, H6, H9). Inset: ^{13}C NMR spectrum of **1** (CD_2Cl_2, −90 °C, ^{1}H-decoupled, 100 MHz): δ 137.1 (2 C, C5, and C10), 125.1 (4 C, C2, C3, C7, and C8), 107.5 (4 C, C1, C4, C6, and C9). Assignments verified by selective ^{1}H-decoupled ^{13}C NMR.

within **12** (trichloroacetic acid, acetonitrile–water, 23 °C, THPO → HO, 88%; triethylamine trihydrofluoride, methanol, 55 °C, TMSC≡C → HC≡C, 97%) then afforded **13**. Iodination of **13** to form **14** was readily achieved by the method of Hofmeister et al. employing *N*-iodosuccinimide (1.02 equiv) and silver nitrate (0.1 equiv) in acetone (0–23 °C, 81%).[10] Oxidation of **14** with the Dess–Martin periodinane (2.5 equiv, dichloromethane, 23 °C) provided the iodo aldehyde **8** in 85% yield.[11] Treatment of a dilute solution of **8** in rigorously deoxygenated THF at 0 °C with chromium(II) chloride (2.5 equiv) doped with nickel(II) chloride (0.01%) for 3 h afforded the cyclization product **6** in 40% yield after purification by flash column chromatography.[6] Due to the extreme sensitivity of **6** toward adventitious decomposition when neat, this product was typically handled in solution in the presence of a free radical inhibitor.

Initial studies designed to transform **6** to **1** via the corresponding mesylate[9] established that **1** has no appreciable lifetime above −40 °C. For example, treatment of **6** with methanesulfonic anhydride and triethylamine in deoxygenated THF-d_8 at −40 °C led to slow disappearance of the starting material with concomitant formation of 1,5-dideuterionaphthalene (^{1}H NMR analysis, $t_{1/2} \approx 1.5$ h); signals attributable to the presumed intermediate mesylate or to **1** were not observed, leading to the conclusion that mesylate formation is rate-determining and that cyclization of **1** to the biradical **5** is rapid at −40 °C. By contrast, variable-temperature NMR analysis of the reaction of **6** with trifluoromethanesulfonic anhydride and triethylamine at −90 °C showed clean and rapid conversion of **6** to a product assigned as **1**. ^{1}H and ^{13}C NMR data (Figure 1) are consistent with static or time-averaged D_{2h} symmetry for **1** at −90 °C. The proton-decoupled ^{13}C NMR spectrum consists of three singlets whose chemical shifts are approximated by averaging the anticipated chemical shifts for corresponding carbons in the two canonical resonance structures. The ^{1}H NMR chemical shifts show clear evidence of a diamagnetic ring current, supporting the notion that **1** is an "aromatic" compound (Figure 1). Samples of **1** were stable for extended periods at −90 °C but at higher temperatures cyclized readily to form naphthalene (50–85% yield, varying with the medium). In deuterated solvents, incorporation of deuterium was evident at the 1 and 5 positions of naphthalene. The kinetics for the cyclization reaction was determined in CD_2Cl_2 in the presence of 1,4-cyclohexadiene (0.6 M) and found to be first-order (k = (4.6 ± 0.9) × 10^{-4} s^{-1}, $\Delta G^* = 16.3 \pm 0.1$ kcal/mol, −51 ± 1 °C, 85% yield of naphthalene). Thus, the half-life for cyclization of **1** at −51 °C is ~25 min, making this the most rapid biradical-forming cycloaromatization yet reported. The next most rapid cyclization of which we are aware is that of the neocarzinostatin cumulene intermediate (**15** → **16**, $t_{1/2} \approx 2$ h at −38 °C, $\Delta G^* = 18.0 \pm 0.1$ kcal/mol).[4d–f] With the assumption that both processes have negligible entropies of activation, the free energies of activation may be compared directly, leading to a 1.7 kcal/mol lower barrier for cyclization of **1** versus **15**. This is an interesting and unexpected outcome because it would appear that **15** is the more strained molecule. It should be pointed out that the exceedingly facile cyclization of **1** to **5** does not argue against the aromatic stabilization of the former. The stability usually associated with an aromatic compound relates to a reaction pathway in which aromaticity is invariably lost in transition; in the case of **1**, aromaticity is not disrupted in the transformation to **5**.

In conclusion, it seems both reasonable and useful to classify the biradical-forming cycloaromatization reactions into two categories: those involving cycloaromatization to form a biradical syn about the newly-formed σ bond, of which the Bergman reaction[4a–c] may be considered prototypical, and those involving cycloaromatization to form a biradical anti about the newly-formed σ bond,[2e,f,4d–i] perhaps now best illustrated by the transformation of **1** to **5**. Though rigorous comparisons are not possible, it would appear that the latter class of cyclization is generally a more facile reaction. On the basis of ab initio calculations it has been suggested that this effect has its origin in the differences in in-plane π–π repulsion in the two systems, this being exacerbated in the former class and diminished in the latter.[12] Finally, with regard to the enediyne antibiotics, it will clearly be of interest to design a molecule which will undergo a transformation analogous to **1** → **5** after an appropriate "chemical activation" step; perhaps such a molecule already exists in nature.

Acknowledgment. Generous financial assistance from the David and Lucile Packard Foundation, Pfizer Inc., and American Cyanamid Company is gratefully acknowledged.

Supplementary Material Available: Listings of IR and ^{1}H and ^{13}C NMR spectral data for **6** and synthetic precursors to **6** (4 pages). Ordering information is given on any current masthead page.

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High-Intensity, Argon Ion Laser-Jet Photochemistry. Reactions between Transient Species: The Addition of Diphenylcarbene to the Photoenol of 2-Methylbenzophenone

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In principle, reactions between short-lived photochemical transients, transient–transient reactions, offer many possibilities for novel chemistry. Transient–transient reactions between identical species, such as radical coupling, are well-known, and while their efficiencies are enhanced at higher light intensities, they can frequently be observed at lower light levels in the absence of competing processes.[1] In contrast, very few examples of

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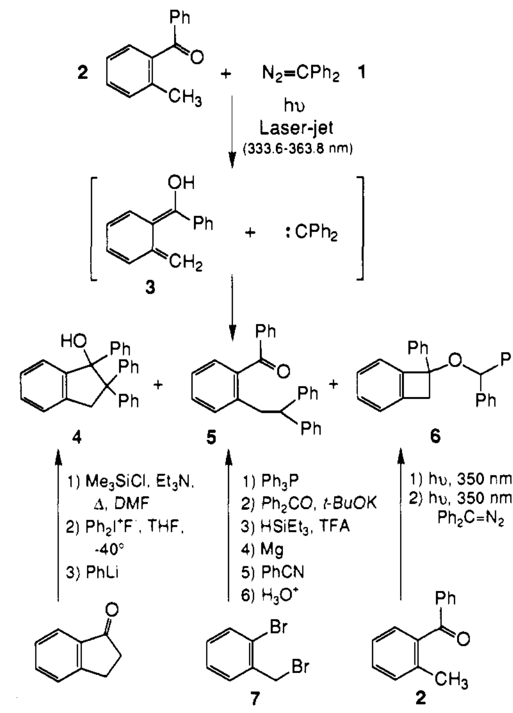
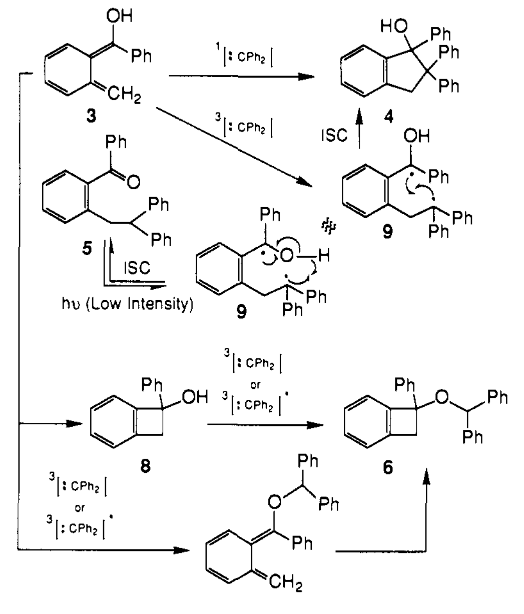
Scheme I



Scheme II



transient–transient reactions between different species have been observed due to the low concentrations of the transients afforded by conventional low-intensity irradiation conditions.[2] If a method were available for the generation of reactive intermediates in significantly high concentrations, many fascinating reactions between transient species might be observed. In an effort to determine whether the recently developed technique of argon ion laser-jet irradiation[3] can be effectively applied to this problem of "transient–transient" reactions, we have examined the reaction of diphenylcarbene with a photoenol.

Diphenylcarbene (DPC), generated photochemically from diphenyldiazomethane (**1**), has a lifetime in the microsecond range.[4] The photoenol (**3**) of 2-methylbenzophenone (**2**) has a much longer lifetime of a few seconds.[5] In spite of the relatively long lifetime of **3**, no products derived from the reaction of DPC with **3** are observed when **1** is irradiated in the presence of **2** under conventional low-intensity conditions (Rayonet photochemical reactor, 360 nm). However, under high-intensity, laser-jet conditions (all UV lines, 333.6–363.8 nm, 4.0 W), three new products incorporating the elements of DPC and **3** can be isolated (Scheme I). These high-intensity photoproducts consist of the indanol **4**, the benzophenone **5**, and the benzocyclobutyl diphenylmethyl ether **6** (**4**:**5**:**6** = 8:4:1).[6]

The structures of these materials have been confirmed by the syntheses shown in Scheme I. The indanol **4** was prepared by a sequence involving the diphenylation of the silyl enol ether of 1-indanone with diphenyliodonium fluoride.[7] The benzophenone **5** was prepared via a Wittig reaction using the benzylic phosphonium salt of the dibromide **7**, followed by triethylsilane reduction of the resulting double bond,[8] and a Grignard ketone synthesis with benzonitrile. Of particular significance was the observation that the cyclobutyl ether **6** could be prepared by either the low- or high-intensity irradiation of **1** in the presence of the cyclobutanol **8**, which in turn is readily prepared photochemically from **2**.[9]

Of these products, **4** and **5** are clearly derived from transient–transient reactions. In support of this mechanistic pathway, irradiation of **1** and **2** under high-intensity, laser-jet conditions using the visible output of the argon ion laser (all visible lines, 454.5–514.5 nm, 6.1 W) completely destroys **1** to yield tetraphenylethylene, but affords neither **4** nor **5**. Thus, the formation of DPC in the absence of the photoenol **3** does not lead to the generation of **4** or **5**.

In principle, ^{1}DPC might add to the photoenol **3** in a concerted fashion to form the indanol **4** directly (Scheme II).[10] However, the extremely short lifetime of ^{1}DPC makes this pathway seem improbable. Far more likely is the addition of ^{3}DPC to **3**, which would lead to the triplet biradical **9**. Upon intersystem crossing, **9** might either cyclize to the indanol **4** or disproportionate to the benzophenone **5**. Confirmation of the cyclization of the biradical **9** to the indanol **4** was obtained through the independent generation of biradical **9** by the low-intensity irradiation of **5**[11] to form **4** in 27% yield.[12]

The mechanism(s) of formation of the cyclobutyl ether **6** is less certain (Scheme II). Low-intensity control experiments show that ^{3}DPC reacts with the cyclobutanol **8** to form **6**. However, the excited state of ^{3}DPC (^{3}DPC*) is known to be much more reactive toward alcohols than ^{3}DPC itself.[13] Thus, under high-intensity

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(6) All new compounds reported here have spectroscopic properties in accord with their proposed structures: **4**, mp 131.6–132.7 °C, ^{1}H NMR (250 MHz, $CDCl_3$) δ 4.14 (d, J = 15.8 Hz, 1 H), 3.81 (d, J = 15.8 Hz, 1 H); **5**, mp 82.1–83.2 °C, ^{1}H NMR (250 MHz, $CDCl_3$) δ 4.26 (t, J = 7.5 Hz, 1 H), 3.45 (d, J = 7.5 Hz, 2 H); **6**, colorless oil, ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.55 (d, J = 7.5 Hz, 1 H), 5.52 (s, 1 H), 3.71 (d, J = 14 Hz, 1 H), 3.42 (d, J = 14 Hz, 1 H).

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(12) The indanol **4** is accompanied by a mixture of cyclobutanol isomers that are formed via γ-hydrogen abstraction, photoenol formation, and cyclization.

conditions, ^{3}DPC and ^{3}DPC* might both contribute to the formation of **6** through reactions with either cyclobutanol **8** or photoenol **3** followed by cyclization.

These simple experiments clearly demonstrate the viability of targeting one transient species with another under high-intensity, laser-jet conditions. In many cases, this transient–transient reaction strategy promises to provide access to fascinating novel reactions, as well as new insights into the chemistry of transient intermediates.

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High-Resolution Two-Dimensional In-Phase Multiplets in Nuclear Magnetic Resonance Correlation Spectroscopy

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In multidimensional nuclear magnetic resonance,[1] selective methods such as “soft COSY”[2-5] allow one to boost the resolution in comparison with conventional, nonselective correlation spectroscopy (“hard COSY”). Improved resolution, obtained by “zooming in” on multiplets of interest, allows one to measure the magnitudes and signs of scalar coupling constants with very high accuracy. In various forms of COSY, however, the proximity of peaks with opposite signs (antiphase multiplets) may lead to distortions and partial peak cancellation. In nonselective experiments, this problem may be overcome by switching to “total correlation spectroscopy” (TOCSY),[6] which yields in-phase multiplets. However, these multiplets usually suffer from limited resolution, their fine structure is difficult to interpret, and unlike the situation prevailing in COSY, the mere presence of a TOCSY cross-peak at frequency coordinates (Ω_A, Ω_X) does not imply that $J_{AX} \neq 0$. So far, no techniques are available which can deliver high-resolution in-phase multiplets that are easy to interpret. This communication describes a new selective method which fills this gap.

In the pulse sequence shown in the upper right part of Figure 1, the initial 270° Gaussian pulse[7] excites in-phase coherence I_x^A of a selected spin A. Evolution during t_1 leads to four terms, I_x^A, I_y^A, $2I_x^AI_z^X$, and $2I_y^AI_z^X$, modulated as usual by scalar coupling constants and chemical shifts.[8,9] In the mixing period of duration τ_{DSI}, a doubly selective irradiation is applied by placing the carrier frequency half-way between two chosen chemical shifts at $\omega_0 = {}^1/_2(\Omega_A + \Omega_X)$ and by modulating the amplitude with cos ($\omega_a t$), where $\omega_a = {}^1/_2(\Omega_A - \Omega_X)$. This generates two sidebands at $\omega_0 \pm \omega_a$, which coincide with the chemical shifts of the two selected spins.[10,11] During the doubly selective irradiation, I_x^A is converted into in-phase magnetization I_x^X, which gives rise to a pure absorptive in-phase multiplet. An ideal transfer is obtained for $\tau_{DSI} = 1/J_{AX}$.[11] The terms I_y^A and $2I_x^AI_z^X$ do not lead to any observable coherence on spin X. The terms I_x^A and $2I_y^AI_z^X$ can only be converted into $2I_z^AI_y^X$ and I_x^X, respectively, if $\tau_{DSI} \neq 1/J_{AX}$. The term $2I_y^AI_z^X$, however, can be converted into an undesirable term $2I_z^AI_y^X$, which leads to a contamination of the multiplet by dispersive antiphase signals. This transfer is negligible if the amplitude of the radio frequency (rf) field of each sideband accidentally or deliberately fulfills the condition $\omega_1 = \pi J[n(n+1)]^{1/2}$, with n integer.[12] In practice, the $2I_z^AI_y^X$ term can be purged by applying another 270° Gaussian pulse to spin A while one continues to spin-lock the desirable I_x^X coherence by a phase-modulated rf field (see Figure 1).

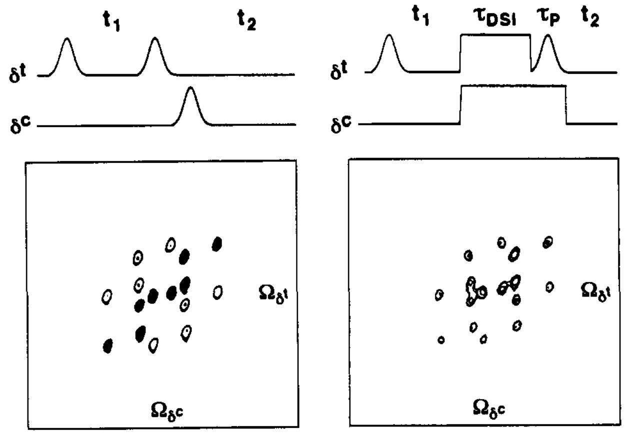

Figure 1. Top: Pulse sequences for soft COSY (left) and PICSY (right). Bottom: Corresponding multiplets of cyclo-(L-Pro-L-Pro-D-Pro),[15] correlating the proton resonances of δ^{trans} (3.23 ppm) with δ^{cis} (3.81 ppm) of the D-proline residue. The doubly selective irradiation period τ_{DSI} was set to 80.7 ms, i.e., to an integer (14-fold) multiple of the inverse of the frequency separation $(\Omega_A - \Omega_X)/2\pi = 173.5$ Hz while being close to $1/J$, and the purging pulse τ_P was set to 30 ms. The rf amplitude for each sideband was $\nu_1 = 55$ Hz. Two scans were recorded for each t_1 increment with alternation of the phase of the first pulse and of the receiver. For PICSY, the spectral widths were 75 Hz in ω_1 and 3000 Hz in ω_2; the matrix consisted of 128 × 8K data points before and 256 × 8K after zero-filling. For soft COSY, the spectral widths were 75 Hz in both dimensions and the matrix consisted of 128 × 1K data points before and 256 × 1K after zero-filling. In both cases, a Lorentz–Gauss transformation was applied (LB = −0.3, GB = 0.05) before Fourier transformation. The experiments were carried out on a Bruker MSL 300 spectrometer equipped with an Oxford Research Systems selective excitation unit.

It can be shown that the transfer of in-phase coherence occurs in much the same way in systems with more than two spins. The in-phase multiplets obtained therefore feature the same square patterns as soft COSY spectra, which are reminiscent of those in E.COSY[13] or *z*-COSY.[14] The soft COSY multiplet of cyclo-(L-Pro-L-Pro-D-Pro),[15] shown for comparison on the left of Figure 1, is composed of four antiphase square patterns, each with an active splitting $J(\delta^{cis}, \delta^{trans})$, which are displaced with respect to each other by passive splittings to the protons γ^{trans} and γ^{cis} of D-proline. In the multiplet shown on the right, one recognizes

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