Photochemical Studies on the Mechanism of the Oxadi-π-methane Rearrangement. An Example of a Stereospecific Rearrangement[1]

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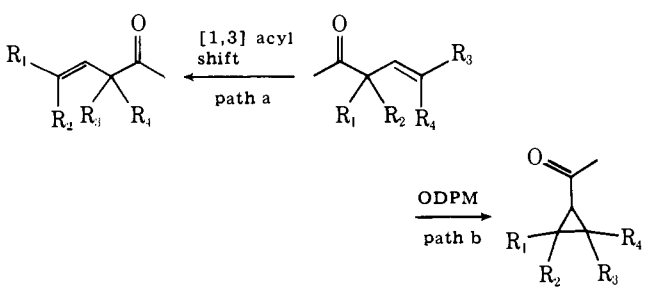
Abstract: The photochemistry of several 2-substituted-2-(1-cyclopentenyl)cyclopentanones **2** was studied. On direct irradiation, [1,3] acyl migrations were observed and, in the case of the optically active derivative **2c**, the migration was shown to be stereospecific in the forward direction, but some loss of optical purity was noted for the reverse reaction. Sensitized irradiations of **2** gave the oxadi-π-methane (ODPM) rearrangement products **6**. The ODPM rearrangement of optically active **2c** gave **6c** with inversion of stereochemistry at the "methane" carbon. A detailed discussion is presented with particular emphasis given to the relationship of this study with other studies of the stereochemistry of these reactions.

Since the first report of the photochemical rearrangement of a β,γ-unsaturated ketone in 1960,[3] a voluminous literature has evolved,[4] and a recent review[4c] cites more than 450 papers dealing with the photochemistry and spectroscopy of this intriguing chromophore. Although a variety of subtle structural features may affect the outcome of the photochemical transformations of individual compounds, it has generally been observed that the direct irradiation of β,γ-unsaturated ketones produces a [1,3] acyl shift (path a, Scheme I), whereas a [1,2] shift,[5a] the oxadi-π-methane rearrangement[5b] (ODPM), and [1,3] acyl shift occur with triplet sensitization[6] (path b).

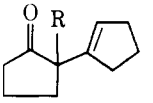
A number of mechanistic studies have been reported in which the nature of the excited state and the stereochemical outcome of these reactions have been investigated.[7-10] It has been generally assumed that the [1,3] acyl shifts observed on direct irradiation occur from the $^1n,\pi^*$ state, although very recent evidence suggests that some 1,3 shift occurs from the $^3n,\pi^*$ state.[23] The stereochemical outcome of the [1,3] acyl shift has been examined in several instances. In a number of cases the reaction has been shown to be stereospecific, and the stereochemical outcome has been consistent with a symmetry-allowed ${}_\sigma2_s + {}_\pi2_s$ rearrangement.[7] In other cases,[8] particularly with aryl β,γ-unsaturated ketones,[8b] the reaction was nonstereospecific and the experimental evidence was consistent with an initial type I cleavage.

The studies of the stereochemistry of the ODPM rearrangement have led to two suggested mechanisms for this reaction. (There is general agreement that initial type I cleavage is not involved in the ODPM rearrangement.) The first mechanism involves concerted, symmetry-allowed rearrangements following either a ${}_\sigma2_a + {}_\pi2_a$ or ${}_\sigma2_s + {}_\pi2_s$ pathway.[4e] Both pathways have been postulated,[5-7a,9] but in the case of many cyclic compounds the ${}_\sigma2_s + {}_\pi2_s$ pathway is not possible because of geometric constraints. However, a single example of the latter process has appeared.[9c] The second mechanism is a modification of the originally proposed ODPM mechanism.[5] Recent studies by Schaffner[10a] and Dauben[10b,c] have established that this pathway can operate in the ODPM rearrangement for the systems examined by these workers. This mechanism involves initial bonding between the carbonyl carbon and the β carbon followed by either a concerted rearrangement to the ODPM product or opening of the cyclopropyloxy radical to form a new 1,3 diradical which then closes to the product.[10] The conflicting results of these studies may indicate that no single mechanism operates in all ODPM rearrangements.

Scheme I. Structural Rearrangements of β,γ-Unsaturated Ketones



In a continuation of our studies of β,γ-unsaturated ketones



2a, R = CH_3
b, R = $CH_2CO_2C_2H_5$
c, R = CH_2CO_2H
d, R = $CH_2CO_2CH_3$

we have examined in detail the photochemistry of a series of 2-substituted-2-(1-cyclopentenyl)cyclopentanones (**2a,c**) and have delineated the stereochemistry of the direct and sensitized photorearrangements in this series by employing the chiral isomers of **2c**. This β,γ-unsaturated ketone provides a sensitive test for the stereochemistry of the ODPM and [1,3] acyl migration reactions, particularly in probing for the intermediacy of equilibrating diradicals proposed in mechanism b above (Chart I).

Results

Synthesis and Spectral Properties of 2-Substituted-2-(1-cyclopentenyl)cyclopentanones. Each of the β,γ-unsaturated ketones employed in this study was synthesized by the method outlined in Chart II. Keto acid **2c** was resolved as its cinchonidine salt by repeated recrystallization from 95% ethanol. Table I gives the ORD and CD data for the enantiomeric keto acids of **2c** obtained after hydrolysis of the cinchonidine salts. Optical purities of the enantiomeric esters **2d**, derived from the keto acids, were determined by integration of the separated $-CH_2CO_2CH_3$ NMR absorptions for each enantiomer in the presence of the chiral shift reagent, tris(3-heptafluoropropylhydroxymethylene-*d*-camphorato)europium (III).

The configuration of the levorotatory isomer ($[\alpha]^{28}_D$ −138°) was assigned as (*R*)-(−)-**2c** by correlation of the observed Cotton effect with the modified octant rule for β,γ-unsaturated ketones[11] as shown in Figure 1. This assignment was confirmed by a CD analysis of the saturated keto acid **3**, obtained by catalytic reduction of (−)-**2c**, which also displayed a negative Cotton effect.

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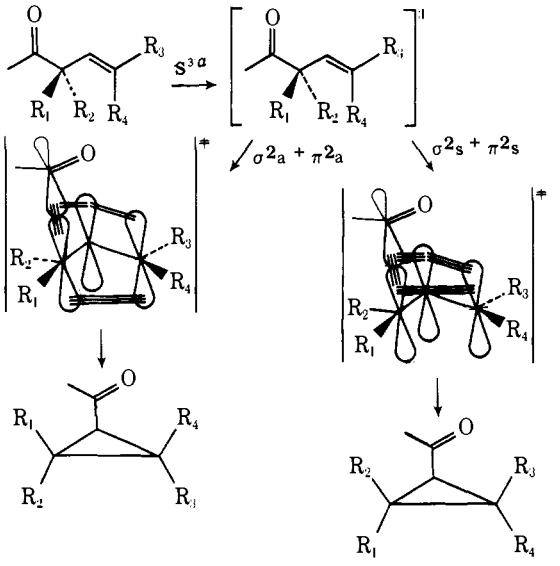
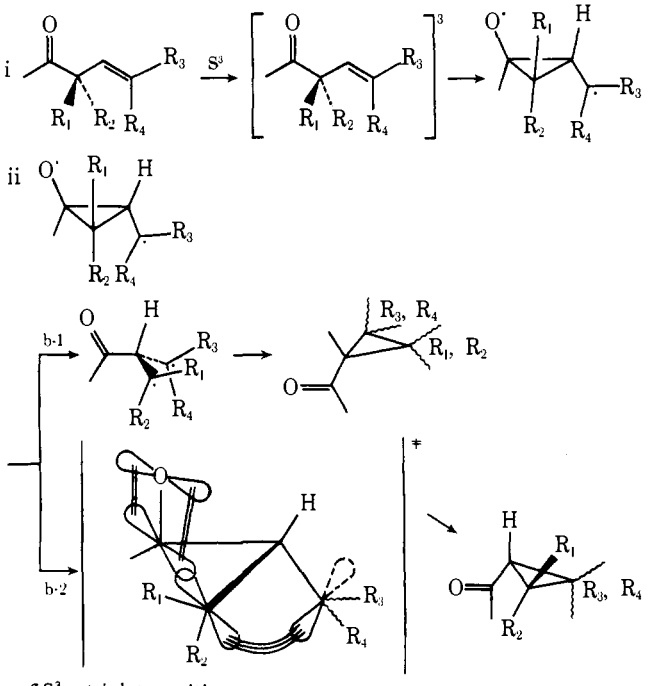
Chart I. Mechanisms Postulated for the Oxadi-π-methane Rearrangement of β,γ-Unsaturated Ketones: Stereochemical Consequences

(a) Concerted, Symmetry-Allowed $_\sigma 2_a + _\pi 2_a$ or $_\sigma 2_s + _\pi 2_s$



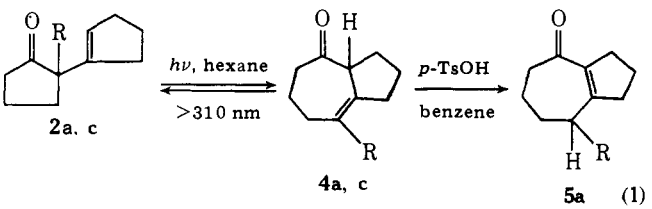
(b) Initial Carbonyl-Double Bond Bonding: the Stepwise Oxadi-π-methane Rearrangement



[a] S^3 = triplet sensitizer.

Ultraviolet spectra of each of the ketones revealed enhanced n,π* absorptivity and vibrational fine structure. The four maxima for the n,π* transitions at 325.3, 314.1, 303.8, and 294.4 nm correspond to a vibrational spacing of 1080 ± 30 cm^{-1}, which is the expected excited state carbonyl stretching frequency, while the 0,0 band at 325.3 nm corresponds to an energy of 87.9 kcal/mol expected for the S^1 state. Fluorescence was not observed preventing an independent confirmation of this value. Likewise, the triplet-state energy was not directly accessible, since phosphorescence emission was not detected.

Photochemistry of 2-Substituted-2-(1'-cyclopentenyl)cyclopentanones. Direct Irradiations. Irradiations of hexane solutions of the β,γ-unsaturated ketones **2a** and **2c** gave a single major product identified as **4a** and **4c,** respectively (eq 1). Spectral properties for **4a** and **4c** as well as chemical transformations of **4a** provided the necessary structural information. In a typical irradiation, a 250-mL, 0.216 M hexane solution



of **2a** was irradiated with a Pyrex-filtered, 450-W Hanovia lamp for 33 h when an apparent photostationary state of **2** ⇆ **4** had been achieved.[12] GLC analysis indicated a 48% conversion to a single product. Silica gel chromatography and distillation provided an analytically pure sample of **4a.**

The structure of the isomeric product was assigned from its spectral data (IR 1710 cm^{-1}; NMR δ 1.61 (s, Me), 1.95-2.45

Table I. Specific Rotations, Optical Purities, and ORD or CD Maxima for Ketones **2c** and **3**

ketone	α-carbon config[a]	$[\alpha]^{28}_D$ (opt purity),[b] deg	CD or ORD[c]
(+)-**2c**	*S*	+131 (>95%)	$[\theta]_{300}$ +8381 $[\theta]_{214}$ −9713
(−)-**2c**	*R*	−130 (>95%)	$[\theta]_{300}$ −8686 $[\theta]_{214}$ +9996
(−)-**3**	*R*	−67 (not determined)	$[\Phi]_{314}$ −1988 $[\Phi]_{291}$ 0 $[\Phi_{270}$ +1626

[a] α to the cyclopentanone carbonyl. [b] 95% ethanol. [c] Ether.

Chart II. Synthetic and Resolution Scheme for β,γ-Unsaturated Ketones **2a–d**

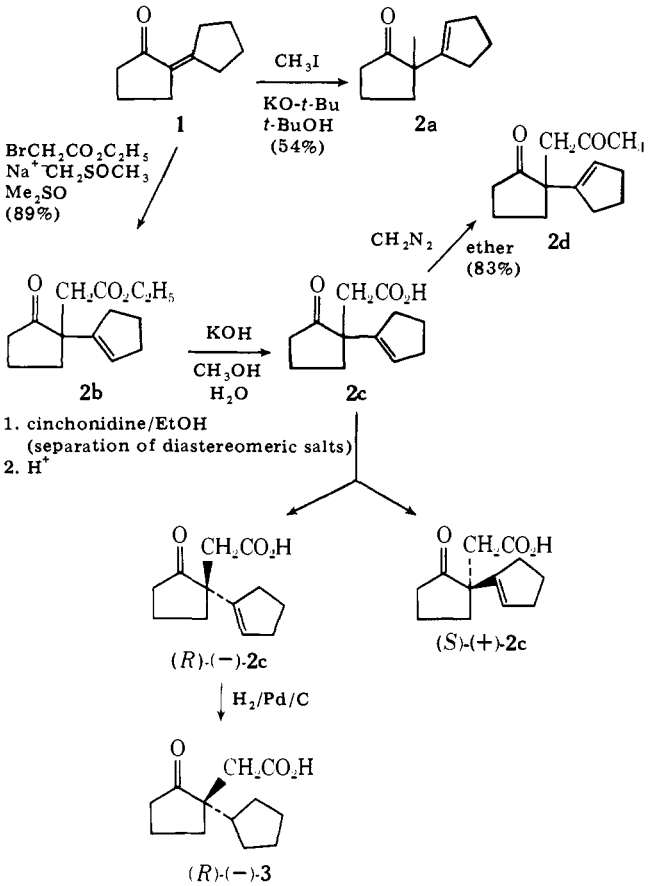
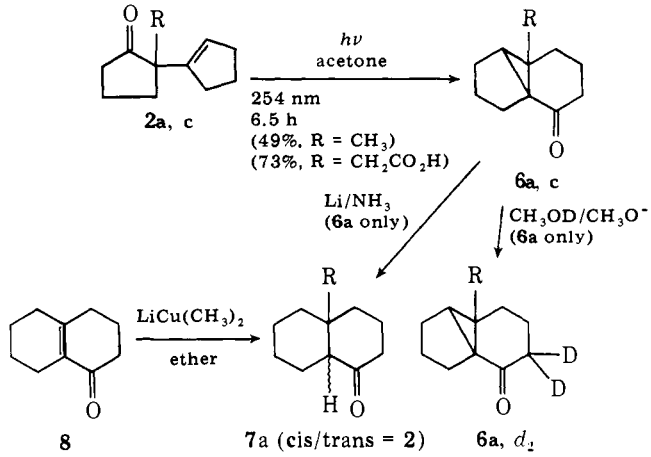


Chart III. Acetone Sensitization of **2a,c** and Structure Determination of Product **6a**



(m, 12 ring H), and 3.70–3.90 ppm (br m, H_1); UV λ_{max} 315 (ϵ 46), 304 (91), 295 (114), 286 (128), 276 (131), the n,π^* band with a vibrational spacing of 1121 ± 143 cm^{-1}, and 246 nm (1028), the π,π^* band; MS *m/e* 164 (M^+)). The absence of olefinic hydrogen absorptions in the NMR spectrum of **4a** was taken as evidence of a tetrasubstituted double bond, while the enhanced n,π^* absorptivity and the carbonyl stretching frequency indicated β,γ unsaturation. Of the two possible structures for the product (**4a** and **5a**), only the structure **4a** is both a nonconjugated ketone and contains a tetrasubstituted double bond.[13] Further evidence for the nonconjugated double bond was provided by acid-catalyzed isomerization of **4a** to **5a** in benzene. The structure of **5a** was firmly established as the conjugated ketone enone (IR 1660 cm^{-1}) with a ring-fused double bond by the position of the methyl group absorption in the NMR spectrum, now appearing as an upfield doublet at δ 1.17 ppm (J = 7 Hz). Additional evidence for the assignment of the product structure as **4a** was its conversion to **2a** on irradiation under identical conditions used for the forward reaction. A photostationary state of 1.2 for **2a** ⇆ **4a** was approached from each of the individual ketones using a merry-go-round apparatus with RPR 3000-Å lamps.

In a like manner, irradiation of the β,γ-unsaturated keto acid **2c** in ether gave the corresponding bicyclo[5.3.0]dec-1-en-6-one (**4c**). Spectral evidence (IR 1700 cm^{-1}; NMR δ 4.03 ppm (br m, 1 H); UV 285 nm (ϵ 145); and MS (*m/e*) 208 (M^+)) indicated the formation of the isomeric β,γ-unsaturated ketone **4c**.

Acetone-Sensitized Irradiations. In contrast to the direct irradiations, acetone-sensitized photolysis of **2a** and **2c** gave tricyclic ketones **6a** and **6c**. In the sensitized photolysis, a 6.5-h irradiation of 400 mL of an 18.8 mM acetone solution of **2a** at 254 nm gave an 80% conversion to a single product by GLC analysis. Product identification was again delineated by a combination of spectral evidence and partial degradation of the photoproduct **6a** and by spectral evidence for photoproduct **6c**. Chromatography followed by microdistillation of **6a** gave a 49% isolated yield of the photoproduct, which had the following spectral features: IR 1670 cm^{-1}; NMR δ 1.07 ppm (s, 3 H); UV 278 nm (ϵ 26); and MS (*m/e*) 164 (M^+).

The structural assignment of **6a** as 6-methyltricyclo-[5.3.0.$0^{1,6}$]decan-2-one, suggested by analogy with several known oxadi-π-methane conversions, was in accord with the spectral data and with the following chemical evidence (Chart III). A base-catalyzed deuterium exchange reaction revealed the presence of two exchangeable protons adjacent to the carbonyl group. The structure was established as **6a** by reductive opening of the cyclopropane ring with lithium in ammonia to give *cis*- and *trans*-10-methyl-1-decalone (**7a**). An

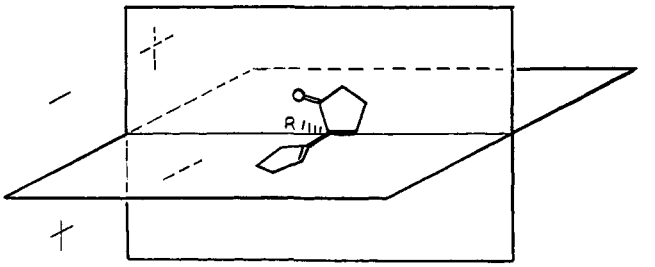
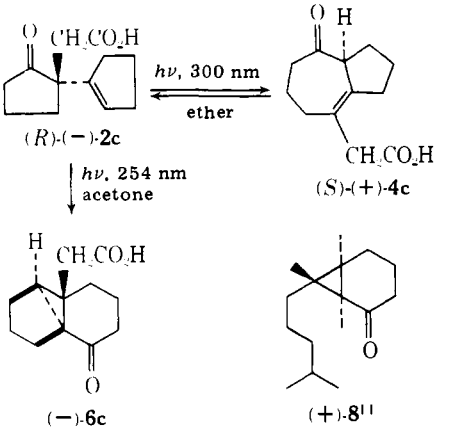


Figure 1. Application of the modified octant rule[11] to the (−)-keto acid **2c**.

Chart IV. Stereochemical Studies on the Direct and Acetone-Sensitized Irradiations of (*R*)-(−)-2-Carboxymethyl-2-(1-cyclopentenyl)cyclopentanone ((*R*)-(−)-**2c**)



identical cis–trans mixture of **7a** was independently generated by conjugate addition of lithium dimethylcuprate[28] to $\Delta^{9,10}$-1-octalone (**8**).

Similarly, keto acid **2c** was irradiated in acetone at 254 nm to give a 73% isolated yield of tricyclic keto acid **6c**; IR 1710, 1665 cm^{-1}; NMR δ 2.60 ppm (s, 2 H); UV λ_{max} 284 nm (ϵ 37). 2-Methylbicyclo[5.3.0]dec-1-en-6-one (**4a**) was also irradiated in acetone at 254 nm and a comparison was made of the relative photoconversion with **2a**. Both ketones gave the tricyclic ketone **6a**, although the efficiency for the conversion of **4a** to **6a** was substantially lower (approximately half) that for **2a**. In a parallel study with the keto acids, **4c** did not give the tricyclic, oxadi-π-methane product **6c**. Control experiments on **6a** and **6c** established that these photoproducts were stable to the acetone-sensitization conditions employed.

Stereochemical Studies. Each of the irradiations of keto acids **2c**, **4c**, and **6c** was repeated with the individual enantiomers. Optical purities of the derived methyl esters were determined by NMR studies employing the optically active europium shift reagent and are reported in Table II. Assignments of configurations were based on the CD and ORD results given in Table II and depicted schematically in Chart IV for the (*R*)-(−)-**2c** enantiomer. For example, low conversion, direct irradiations of (*R*)-(−)-**2c** gave (*S*)-(+)-**4c** of the same optical purity as **2c**. In higher conversion irradiations (e.g., run 4) the optical purity of both **2c** and **4c** decreased indicating that stereochemical equilibration does occur, albeit with a much lower efficiency. In an effort to explore the origin of this reaction, the direct irradiation of (+)-**4c** was also investigated. In this case, even the low conversion runs gave considerable loss of stereochemical integrity in forming 1,3-acyl migration product **2c**. However, the reactant (+)-**4c** was not extensively racemized, an indication that the photochemical ring contraction step occurs with racemization.

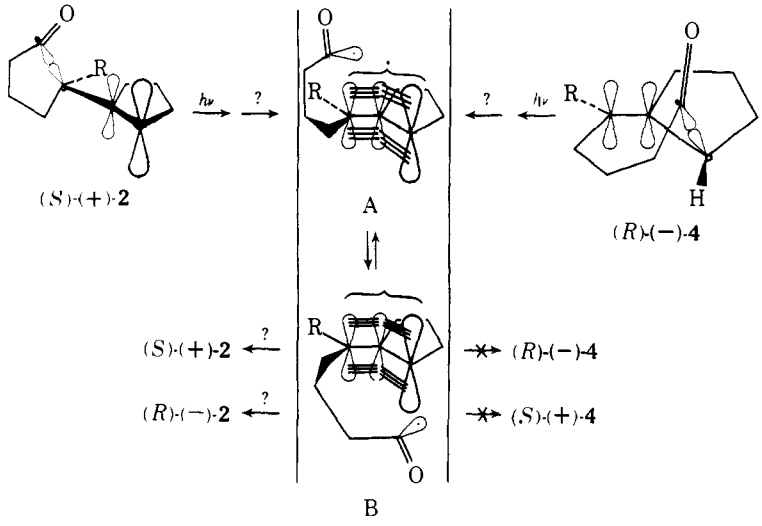
From the acetone-sensitized irradiations, the tricyclic keto acid **6c** was obtained with essentially the same optical purity

Table II. Specific Rotations and Optical Purities for Photoproducts of **2c**

	keto acids reactant/ product	run	conv, %	config of α-C reactant/ product	opt[a] purity recovd reactant/ product	$[\alpha]^{28}_D$ product, deg	yield,[b] %
direct	**2c**/**4c**	1	37	*R*/*S*	90%/95%	+147	57
		2	45	*S*/*R*	80%/95%	−150	66
		3	47	*R*/*S*	90%/85%	+133	45
		4[c]	65	*R*/*S*	23%/26%	+41	55
	4c/**2c**	5	30	*S*/*R*	85%/55%	−80	41
		6[d]	44	*S*/-	87%/-		
		7	61	*S*/*R*	78%/45%	−71	21
acetone sensitized	**2c**/**6c**	8	58	*S*/*S*	81%/95%	+52	97
		9	81	*R*/*R*	80%/95%	−52	73
		10[e]		*R*/*R*	-/95%	−52	60
		11[e]		*R*/*R*	-/86%	−47	55
		12[e]		*S*/*S*	-/86%	+47	52

[a] The error is less than ±5%. [b] Based on recovered reactant. [c] An extended irradiation, t = 4187 min. [d] Product was not isolated. [e] Reactant was not isolated.

Scheme II



as the reactant at low to moderate conversion (runs 8 and 9). At high conversion (runs 10–12), the optical purity dropped slightly. This racemization probably is attributable to a less efficient, competing photoracemization of the keto acid **2c**. It should be noted that **4c** was not detected in these runs, suggesting that the [1,3] acyl migration pathway was not the competing stereochemical equilibrating pathway. This was firmly established by examination of the acetone-sensitized irradiation of (−)-**4c**, which did not give **2c** and gave only a trace of the ODPM product **6c** (2%). Evidently, degradation and photoracemization are the principal reaction pathways for the triplet of **4c**. The very low efficiency of the **4a** to **6a** conversion under acetone-sensitized reaction conditions was in accord with these results.

Finally, the assignment of the absolute configuration of the ODPM product (−)-**6c** was of importance (vide infra). As shown in Chart IV, the configuration of acetone-sensitized product was deduced to be (−)-**6c** from the ORD–CD spectra by application of the modified octant rule for cyclopropyl ketones.[11] Furthermore, a comparison with the spectra of (+)-**8** of known absolute stereochemistry[14] also confirmed this stereochemical assignment for **6c**.

Quantum Yield Studies. The efficiency for the direct irradiation conversion of **2a** to **4a** in ether at 300 nm was 0.054 mol/einstein for the appearance of **4a** and 0.09 mol/einstein for the disappearance of **2a**. A greater quantum efficiency was found for the ODPM rearrangement where irradiation of an acetone solution of **2a** at 254 nm produced **6a** with an efficiency of 0.25 mol/einstein and a disappearance efficiency of 0.35 mol/einstein.

Discussion

A. Direct Irradiation. The principal reactions from direct irradiations of **2a, 2c, 4a,** and **4c** can be summarized as [1,3] carbonyl migrations. The interesting observation in this series is the apparent change in mechanism for the forward (**2** → **4**) and reverse (**4** → **2**) photoisomerizations.[15] The ring expansion step proceeds stereospecifically as shown by the high degree of optical purity of the product **4c** in low conversion runs. This is not the case for the reverse reaction, where approximately half of the product obtained is formed with racemization, even in low conversion irradiations of **4c**. This loss of stereochemical integrity must occur during the ring contraction step since recovered reactant is obtained with little loss of optical purity. The results rule out a common intermediate (biradical, Scheme II) as well as a common mechanism for the two processes.

It is indeed interesting to speculate on why these different pathways are taken and to explore the nature of the forward (stereospecific) and reverse (stereoequilibrating) [1,3] rearrangements found here and in related studies on the [1,3] rearrangements of other β,γ-unsaturated ketones.[4b,c,7,8] Examination of molecular models of **2** and **4** provides some insight. For the bicyclo[5.3.0]decenones **4a,c,** the carbonyl and double bond cannot easily attain an orientation which will

Scheme III. The π-Complexed Acyl Radical Mechanism According to Nakanishi[7b-d]

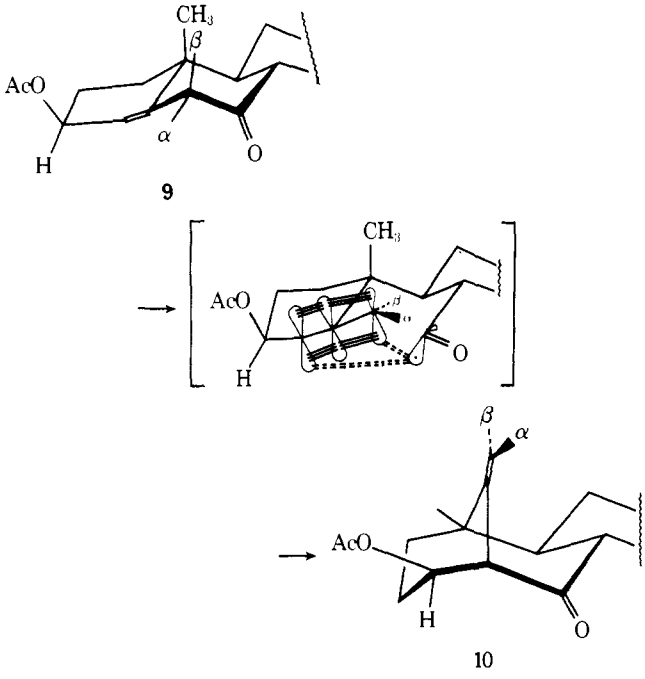
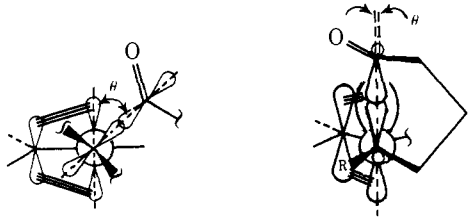


Chart V. Dihedral Angles of the π Orbitals and the Carbon–Carbonyl σ Bond



I, θ = 40 ± 3° (see text)

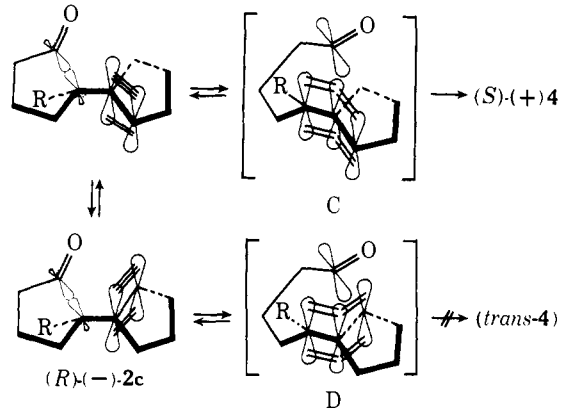
II, θ = 0° (2)

allow initial maximum overlap of the σ orbital (i.e., the developing radical center) with the π orbital of the double bond (Chart V, I). In the conformationally restricted ring, type I ketone cleavage and other singlet excited-state reactions typical of the carbonyl function (e.g., intersystem crossing, oxetane formation, etc.) are competitive with and may dominate the photochemistry of the β,γ-unsaturated ketone.[4b,15,16] Recombination with stereoequilibration would be expected; however, the five-membered ring formation would be kinetically much faster than seven-membered ring formation,[18] thus giving stereoequilibration in the ring contraction process only (Scheme II, (+)-**2** ← A ⇄ B → (−)-**2**). A very similar argument has been presented by Yang and Chen[15c] for the stereoequilibration of 1-hydroindanone and 1-decalone derivatives.

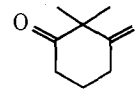
In contrast, the α-cleavage reaction for the excited singlet of **2** is most favorable from a conformation in which the developing radical center can delocalize the odd electron into the π bond (Chart V, II). Here, initial formation of a radical pair such as A or B (Scheme II) is less likely than either a suprafacial migration or, alternatively, the π-complexed acyl radical (Scheme III) suggested by Nakanishi.[7b-d] This latter mechanism cannot be dismissed since it also predicts preservation of stereochemistry throughout the acyl migration.

Interestingly, this mechanism has the added feature that it can provide an alternative explanation for the low quantum efficiency measured for the **2a** → **4a** reaction. In previous studies, the acyl radical was either conformationally restricted

Scheme IV. Acyl–Allyl Biradical Mechanism for (*R*)-(−)-**2c**



to one face of the allyl radical (e.g., **9** and **10**)[7b-d] or both faces were equivalent (e.g., **11**).[17b] However, for **2** both faces are



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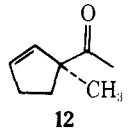
conformationally accessible[19] and the two acyl–allyl biradicals are nonequivalent.

As shown in Scheme IV, the chemistry of biradical C is summarized as a partitioning between return to (+)-**2** or formation of (−)-**4**, while biradical D is restricted to return to (+)-**2** (with retention of configuration), the formation of **4** with a trans double bond being too endothermic. This latter "energy-wasting" process is consistent with the observed low ($\phi_{2\rightarrow 4}$ = 0.054) quantum yield, if it is assumed that the energy barrier leading to D is approximately the same as that leading to C (Figure 2). Although direct application of arguments based on the ground-state conformational populations to the rationalization of excited state behavior is hazardous, examination of molecular models (Drieding or CPK) does not reveal significant differences between the two rotamers (θ = 0° and θ = 180°, Chart V). Indeed, attempts to determine the conformational population of **2a** and **12**[20] (also under investigation



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in our laboratories)[20a,b] by microwave spectroscopy were unsuccessful due to the absence of strong spectra which in and of itself can be construed as evidence for the presence of several significantly populated rotomers in the gas phase.[21] If α cleavage occurs from either geometry (θ = 0, 180°) with equal facility to a π-complexed radical, then a real distinction does exist between this mechanism and the one-step, $_{\pi}2_s + {}_{\sigma}2_s$ mechanism, a distinction not recognized previously,[4b] in that the second step of the Nakanishi mechanism becomes the difficult step for D (cf. Scheme IV and Figure 2).

Regardless of these mechanistic uncertainties, it is clear that the forward reaction **2** → **4** is a useful synthetic entry into the hydroazulene ring system.[22] Because the rearrangement is stereospecific, the requisite substituent stereochemistry may be introduced either before or after the photochemical ring expansion step, thereby enhancing the versatility of this method.

B. Sensitized Irradiations. For the triplet-sensitized reaction, the mechanistic details are especially intriguing. The conversion of **2** to the 6-substituted-tricyclo[5.3.0.$0^{1,6}$]decan-6-ones (**6**) proceeds in high yields[22] and with good efficiency (ϕ_{6a} =

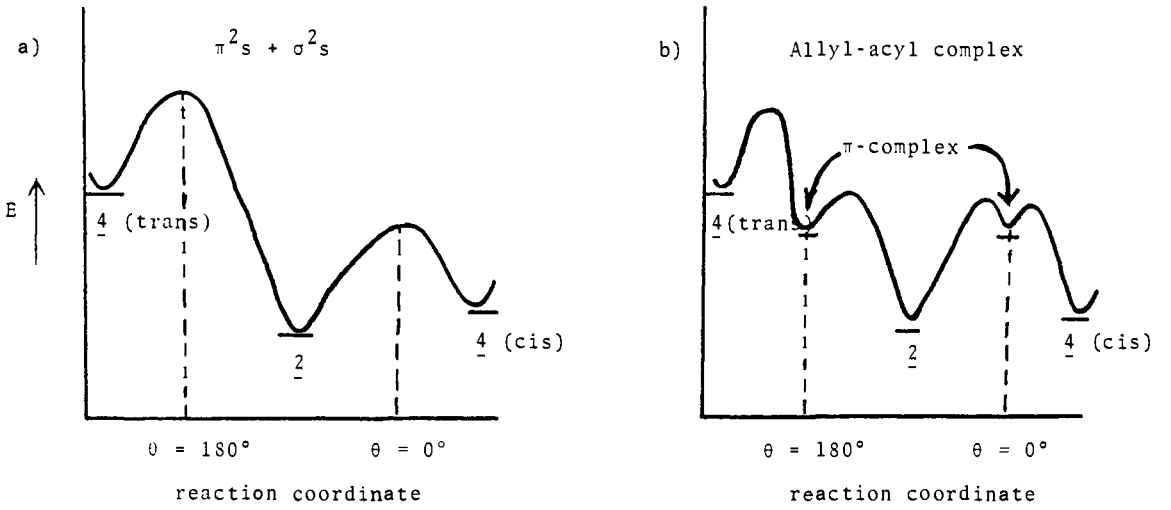


Figure 2. Energy diagrams for $_{\pi}2_s + _{\sigma}2_s$ and π-allyl-acyl complex pathways.

0.25). No evidence of a sequential rearrangement (**2** → **4** → **6**) or other major competing processes was uncovered.[23] In fact, no other products were observed in several instances where isolated yields exceeded 95% for the rearranged product **6** (see Experimental Section, Acetone-Sensitized Irradiation of (*S*)-(+)-**2c**, for an example). For the methyl derivative **2a**, however, the yields were somewhat lower and a significant amount of unidentified polymeric material was obtained. GLC yields were generally higher than the isolated yield of **6a**, especially in low conversion runs as evidenced by the quantum efficiency studies ($(\phi_{6a}/\phi_{2a}) \times 100 = 71\%$).

In view of the high yield and efficiency and the ready availability of the two antipodes of **2c**, a study of the stereochemistry of the triplet-sensitized transformation was initiated in order to distinguish among several of the mechanistic possibilities outlined in Chart I insofar as the "methane" carbon stereochemistry was involved.[9,10,24] Furthermore, a comparison of the oxadi-π-methane reaction with the di-π-methane rearrangment was in order. Recent studies by Zimmerman[25] have shown that at least two structurally different reactants undergo stereospecific singlet di-π-methane reactions that require inversion of configuration at the methane carbon.[25] Within the series of stereochemical studies on the oxadi-π-methane rearrangement, the entire gamut of possible stereochemical results has been reported, from retention of configuration at the "methane" carbon (Ziffer[9c]), to partial or total racemization (Dauben,[10b,c] Schaffner,[9a,10a] and Nakanishi[9d]), to inversion of configuration (Matsura,[9b] Plank,[9b] and our work[7]). From this extreme range of stereochemical results, it is apparent that seemingly minor structural changes can have a profound influence on the course of this rearrangement. Unlike the singlet di-π-methane rearrangement, a single mechanistic pathway for the triplet-sensitized β,γ-unsaturated ketone to cyclopropyl ketone rearrangement (the ODPM rearrangement) is unlikely. The bichromophoric functional group is extremely sensitive to structural modifications that alter the nature and mechanistic details of the photorearrangement. It remains, however, to define some of the parameters which affect the reactivity.

Clearly, the relative orientation of the two chromophoric groups and extended conjugation must play significant roles in the triplet- (and singlet-) state chemistry. An examination of each of the structures studied to date shows that extended conjugation either with a second keto group or an aryl group greatly alters the photochemistry and photophysics of the β,γ-unsaturated ketone. Specific examples include the 2,3-unsaturated 1,5-diketones **13**[9a] and **14**[9b] and the 3- and 4-phenyl 3,4-unsaturated ketones **15–18**.[4d,5b,8c,10b,c,26] For example, phosphorescence has been observed from several of these ketones (e.g., **13**[9a] and **14**[9b]), an indication that the triplet state is accessible on direct irradiation, and the sensitizers employed have been of very low triplet energy (e.g., chrysene for **15b**),[10b,c] significantly lower in energy than the simple β,γ-unsaturated ketone chromophore (estimated to be 76 kcal/mol[22]). The observation of phosphorescence without noting any oxadi-π-methane rearrangement on direct irradiation for ketones **13**[9a] and **18**[8c,26] is particularly puzzling. The authors[8c,26] suggest that the partitioning of the excited states for **13** and **18** between photochemical and photophysical pathways may govern this temperature dependence. Unfortunately, no results are available from temperature studies in the critical range from −100 to 20 °C, the range between no reaction (only phosphorescence) and a 1,3 acyl migration and type I reactions.[26]

The effect of the extended conjugation, in addition to lowering the initial triplet-state energy, also would be to stabilize any accessible diradical-like intermediate that might be in competition with the stereospecific $_{\pi}2 + _{\sigma}2$ rearrangements, a possibility previously suggested by Dauben.[10b] Such intermediates, pictured in Chart I (mechanism b) would allow

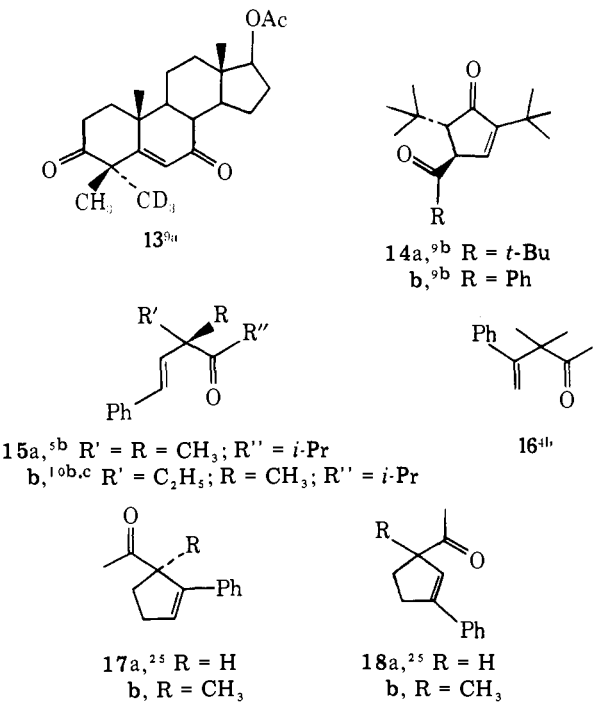
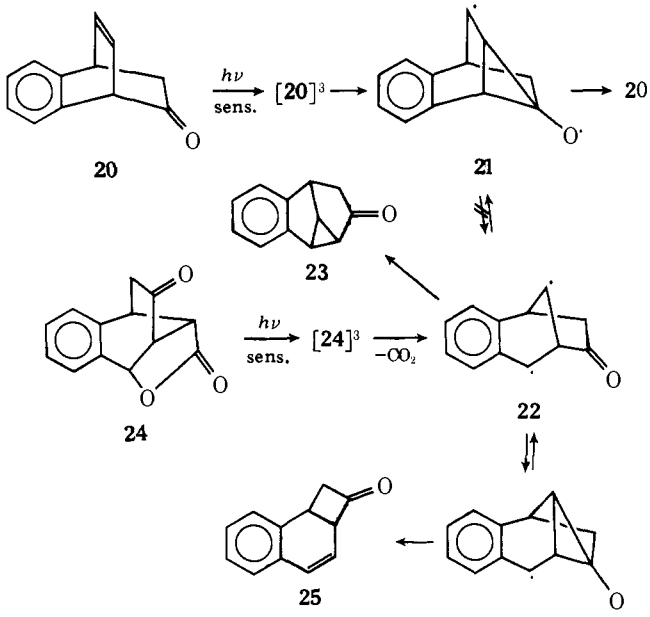
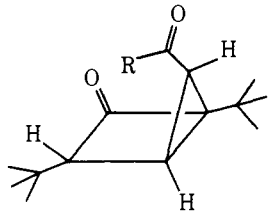


Chart VI.[6] Sensitized Rearrangements of Benzobicyclo[2.2.2]-octadienone (**20**) and Lactone **24**



equilibration of the stereochemistry of the methane carbon provided that rotation of the radical centered carbon ($\dot{C}R_1R_2$) was faster than cyclopropyl ring formation (ii, a, in the ODPM rearrangement). Indeed, of the studies on the stereochemistry of the methane carbon for those ketones which do undergo the sensitized oxadi-π-methane rearrangement (**13, 14, 15,** and **18**), all except **14** occur with extensive stereoequilibration of the "methane" carbon. For **14,** it is uncertain whether or not the product formed (**19**) is simply the more stable one produced



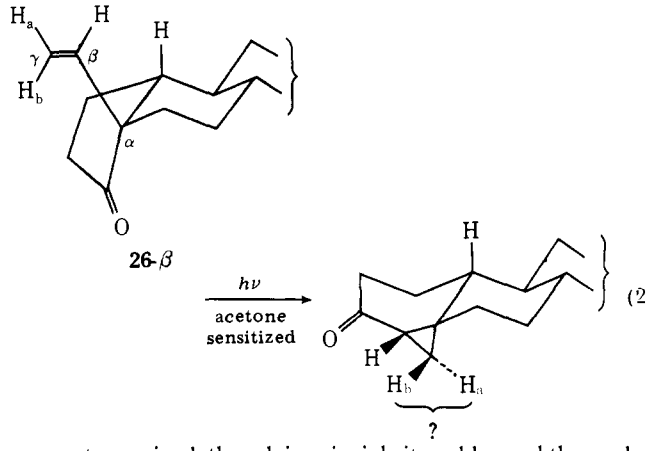
19a, R = *t*-Bu
b, R = Ph

from the 1,3-diradical closure.[8c,26] The tentative conclusion at this time is that the oxadi-π-methane mechanism (b) will dominate when extended conjugation is present in the reactant chromophores. Equilibration of the stereochemistry of the "methane" carbon is to be expected.

Earlier, we probed this reaction pathway for benzobicyclo[2.2.2]octadienone **20** and found that the diradical intermediate **21** (generated independently from lactone **24**) was not involved in the acetone- or acetophenone-sensitized rearrangement of **20**.[5a,b] This result is consistent with the pattern developed in Chart VI: the initially bridged intermediate **21** required for oxadi-π-methane rearrangements receives little or no stabilization from the aryl ring. Significant aryl stabilization occurs only during the second step, i.e., the formation of **22**. The alternative, a $_\pi2_a + {}_\sigma2_a$ rearrangement, dominates in this delicately balanced trifunctional molecule.

Several studies have restricted the chromophore to just the β,γ-unsaturated ketone. However, the studies conducted to date on unsubstituted acyclic β,γ-unsaturated ketones have shown that the oxadi-π-methane rearrangement is not observed, presumably due to more efficient, competing reactions.[4] Therefore, interpretable results aimed at delineating the stereochemical fate of the methane carbon are limited to alicyclic β,γ-unsaturated ketones. Within the alicyclic β,γ-unsaturated ketones, two systems have been examined: β,γ-unsaturated cyclanones in which the double bond is (1) an attached vinyl group or (2) an endocyclic double bond.

The study by Seeman and Ziffer,[9c] which represents the former functional arrangement, remains the only example to date of the $_\pi2_s + {}_\sigma2_s$ stereospecific oxadi-π-methane process. The stereochemistry of the vinyl carbon (C-2, H_a, H_b, eq 2)

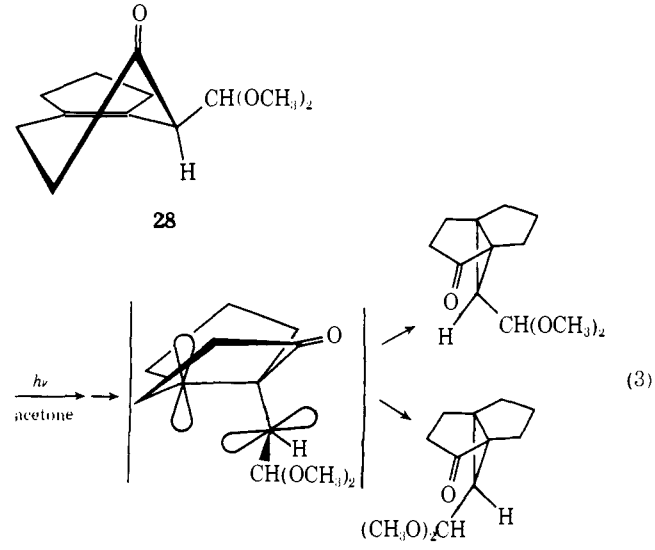


(2)

was not examined, though in principle it could reveal the modes of bonding in this transformation.[4c] Thus, although a suprafacial migration of the carbonyl to the β carbon is demanded from the product studies of **26**-β and its diastereomer, **26**-α, the fate of the γ-carbon stereochemistry precludes a complete analysis of this system. Therefore, the $_\pi2_s + {}_\sigma2_s$ mechanism has yet to be fully established.

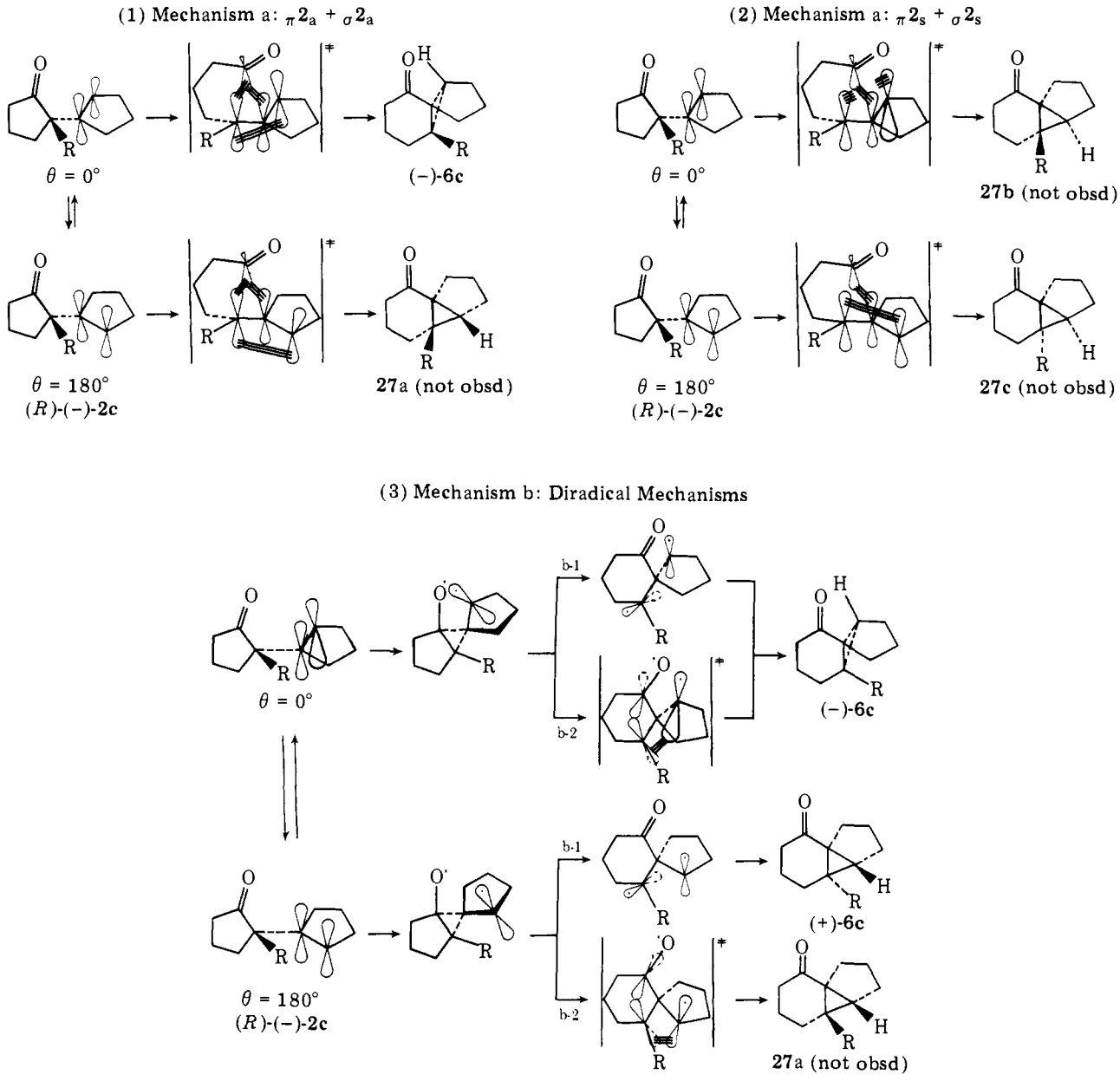
The three remaining studies have both of the two interacting chromophores within rings: these are **27**,[9d] **28**,[10a] and our system **2c**. The first two are β,γ-unsaturated indanones or decalones, while the latter is a cyclopentenylcyclopentanone. For both of the former ketones, the stereochemical fate of the α carbon is summarized as a high degree of stereoisomerization, during the oxadi-π-methane reaction, yielding a mixture of stereoisomers. This result is not surprising, for these ketones are locked in a geometry which effectively precludes the combination of effective overlap of the C_α–CO bond and the $\pi_{C=C}$ bond (θ = 53 ± 3°) with simultaneous α,γ overlap. Referring again to Chart V, the difficulty of effective antarafacial (or suprafacial) 1,3 bonding is increased for the oxadi-π-methane reaction when compared with the [1,3] migration because of the additional requirement that the physically separated 1,3 carbons must bond while the acyl group migrates.

For **28** (eq 3), the conformational preference of a pseudoequatorial substituent undoubtedly dictates the initial bonding

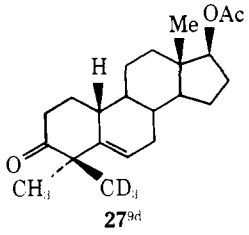


(3)

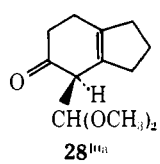
Chart VII. Applications of Mechanisms a and b to (*R*)-(−)-**2c** for the $\theta = 0°$ and $\theta = 180°$ Conformations



of the carbonyl double bond in forming an oxy-carbon diradical intermediate, but the added strain of backside (or frontside) C_{α}–C_{γ} bonding prevents this from occurring simultaneously, thereby leading to the diradical structure proposed by Schaffner.[10a] Thus, the product is obtained with loss of stereochemistry at the methane carbon but as only one of the two possible diastereomeric pairs. For **27**, all four isomers are



27[9d]



28[10a]

produced, since there is little preference for either conformationally isomeric transition state.

The choice of structure **2c** remains the best, though not ideal, test of the stereochemistry for the oxadi-π-methane reaction. The conformational preference is lacking[27] (vide supra) and the structural constraints imposed on the alicyclic ketones examined earlier are for the most part absent. The pathways outlined in Chart I are specifically applied to the two rotamers of (*R*)-(−)-**2c** in Chart VII. If each mechanism is considered for *both* the 180 and 0° rotamers, the number of pathways that yield a stable product is quickly reduced to just three.

For example, in mechanism a, the $_{\pi}2_a + {}_{\sigma}2_a$ pathway yields the observed (−)-**6c** for only the 0° rotamer. The 180° rotamer gives a thermodynamically unfavorable trans-fused bicyclo[4.1.0]heptane skeleton **27a**. Within the same mechanism, the $_{\pi}2_s + {}_{\sigma}2_s$ rearrangement gives an unstable trans-fused bicyclo[3.1.0]hexane skeleton (**27b** and **27c**) for both the 0 and 180° rotamer. Thus, only one of the symmetry-allowed pathways is available, the 0°, $_{\pi}2_a + {}_{\sigma}2_a$ rearrangement.

A similar analysis of mechanism b, the diradical pathways shown in Chart VII for the two rotamers of (*R*)-(−)-**2c**, reveals two possible routes to **6c**. From the 0° rotamer, routes b-1 and b-2 both will lead to (−)-**6c**. The only difference between the two paths is the requirement in b-2 that the second step of the reaction be an internal backside displacement, a restriction that Schaffner[10a] and Dauben[10b,c] have invoked in order to account for the apparent stereoselectivity observed in their studies.

Dauben has termed this pathway a least motion route,[10c] with which we concur.

Consideration of these same two pathways for the 180° rotamer is revealing. For the stepwise pathway labeled b-1, the stable product is (+)-**6c**, the enantiomer of the observed product. In comparing the b-1 stepwise process for the two rotamers, there appears to be no obvious preference for 0° rotamer to the total exclusion of the 180° rotamer. Interestingly, this also involves a least motion pathway from the initially formed diradical. Our results do not accord with this pathway.

Mechanism b-2 for the 180° rotamer leads to the strained **27a** just as in the ${}_{\pi}2_a + {}_{\sigma}2_a$ route. For **2c**, the structural constraints of the cyclopentene ring do not allow us to distinguish between this mechanism and the ${}_{\pi}2_a + {}_{\sigma}2_a$ pathway. However, these mechanisms both yield net inversion of configuration at the methane carbon, a result which has been observed in most of the previous examples where the stereochemistry has been determined.

Thus, our observation is a highly stereospecific sensitized photorearrangement of (+)-**2c** to (+)-**6c**, inconsistent with the diradical oxadi-π-methane process illustrated in b-1. The results are consistent with both the concerted ${}_{\pi}2_a + {}_{\sigma}2_a$ process as well as the radical displacement mechanism b-2; we do not try to distinguish between these two mechanisms with this study.

This study was initiated to explore the stereochemistry of the photosensitized rearrangement of **2**. The result that inversion of configuration at the "methane" carbon takes place in this transformation accords with the studies by Zimmerman on the di-π-methane reaction. In addition, the observation of a *stereospecific, triplet* rearrangement for **2** joins a growing number of similar photosensitized reactions in which migrations occur with inversion of configuration at a tetrahedral carbon.[28] Most of these rearrangements also show a remarkable similarity in their stereospecificity for the less stable diastereoisomer. Work is in progress in which we plan to explore these phenomena in detail.

Conclusions

The conclusions from the analysis of previous studies and the current investigation on β,γ-unsaturated ketones are fourfold: For ketone **2**:

(1) The ring expansion, singlet rearrangement (**2** → **4**) is best described as suprafacial [1,3] migration.

(2) The reverse rearrangement (**4** → **2**), a ring contraction process, is best summarized as a diradical process with extensive stereoequilibration.

(3) The "oxadi-π-methane" (ODPM), triplet-sensitized rearrangement (**2** → **6**) is best described as a [1,2] suprafacial carbonyl migration with inversion of configuration at the methane carbon.

General features of the photorearrangements of other β,γ-unsaturated ketones:

(4) Both the [1,3] and [1,2] rearrangements, but especially the [1,2] migration, are extremely sensitive to conformation and substituent effects. The geometry which yields stereospecific rearrangements in both cases appears to be that in which the CO–C_α σ bond and the C_β=C_γ π bond are aligned for maximum overlap (θ = 0 and 180°). The conformational angles favoring diradicals from a type I cleavage are when these bonds are orthogonal (θ = 90 and 270°). Aryl substitution sufficiently stabilizes the diradical intermediates so that stereochemical equilibration can compete effectively with stereospecific pathways.

Experimental Section

Infrared (IR) spectra were recorded on either a Beckman Model IR-8, Model IR-33, or Acculab 3 infrared spectrometer as solutions in carbon tetrachloride or chloroform. The nuclear magnetic resonance (NMR) spectra were recorded with either a Varian EM-360, A-60A, or HA-100 spectrometer with tetramethylsilane as an internal standard and carbon tetrachloride or chloroform-*d* as solvent. The mass spectra were obtained with a Varian CH-5 single focusing mass spectrometer. Optical rotations were measured with a Perkin-Elmer Model 141 polarimeter in 95% ethanol. The circular dichroism and optical rotary dispersion curves were recorded with a Cary Model 60 spectrometer in diethyl ether. Elemental analyses were performed in the Department of Medicinal Chemistry, University of Kansas.

Spectral grade acetone was used without further purification. *tert*-Butyl alcohol was distilled from calcium hydride and stored over Linde Type 4A molecular sieves. Hexane was washed with concentrated sulfuric acid until the acid wash remained clear. The hexane was then distilled. Hexane for chromatographic use was simply distilled. Diethyl ether was distilled from and stored over sodium. Dimethyl sulfoxide was distilled from calcium hydride and stored over Linde Type 4A molecular sieves. Magnesium sulfate (anhydrous) was used as the drying agent unless otherwise stated.

2-Methyl-2-(1-cyclopentenyl)cyclopentanone (2a). To a solution of potassium *tert*-butoxide prepared from 25.0 g (0.61 g-atom) of potassium in 800 mL of *tert*-butyl alcohol was added 85.0 g (0.57 mol) of 2-cyclopentylidenecyclopentanone[29] over a period of 15 min under nitrogen. After an additional 15 min, 142.0 g (1.06 mol) of methyl iodide was added dropwise over a period of 1 h while maintaining the temperature below 20 °C. The solution was stirred an additional 30 min and the *tert*-butyl alcohol was removed under reduced pressure. To the milky-white residue was added 250 mL of water and 250 mL of ether, the layers were separated, and the aqueous layer was thoroughly extracted with ether. The combined ether extracts were washed with saturated sodium bicarbonate and brine, dried, and filtered. The ether was removed to afford 79.0 g of crude product as an orange liquid. Distillation gave 50.5 g (54%) of **2a** as a clear liquid, bp 60–64 °C (0.10 Torr). The distilled product contained a minor impurity (GLC, 6-ft UCW-98 column at 150 °C). A 697-mg sample of the distillate was chromatographed on silica gel and gave 122 mg of a mixture of ketone **2a** and impurities and 275 mg of pure **2a**, which was distilled in a short path still to give pure **2a** as a clear colorless liquid: bp 64 °C (0.10 Torr); IR 3090, 1740, 1650, 1460, 1410, 1370, 1335, 1205, 1155, 1055, 958, 933 cm^{-1}; NMR δ 5.36 (m, 1 H), 2.00–2.40 (m, 6 H), 1.80–2.00 (m, 6 H), and 1.04 ppm (s, 3 H); UV (isooctane) λ_{max} 323 (63), 313 (120), 311 (120), 308 (113), 302 (129), 287 (105), 258 (342); mass spectrum *m/e* 164 (M^+), 146, 121, 109 (base peak), 93, 91, 79, 77.

Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.46; H, 9.71.

Direct Irradiation of 2-Methyl-2-(1-cyclopentenyl)cyclopentanone (2a). A solution of 8.830 g (54 mmol) of **2a** in 250 mL of hexane was degassed with prepurified nitrogen for 30 min and irradiated for 33 h with a Hanovia 450-W medium pressure lamp fitted with a Pyrex filter sleeve. The solvent was removed to give 8.914 g of clear liquid. Analysis by GLC (6-ft UCW-98 at 150 °C) indicated approximately 48% conversion to a single major product. Column chromatography of 3.70 g of the clear liquid on silica gel gave 1.960 g of a mixture of starting ketone **2a** and ring-expanded ketone **4a** and 0.820 g of pure **4a**, which was distilled to give 0.407 g of 2-methylbicyclo[5.3.0]dec-1-en-6-one (**4a**) as a clear liquid: IR 2950, 1710, 1460, 1440, 1420, 1380, 1340, 1305, 1295, 1185 cm^{-1}; NMR δ 3.70–3.90 (br m, 1 H), 1.95–2.45 (m, 12 H), 1.61 ppm (s, 3 H); UV (isooctane) λ_{max} 315 (46), 304 (91), 294 (114), 286 (128), 276 (131), 246 (1028); mass spectrum *m/e* 164 (M^+), 121, 108 (base peak), 93, 79, 77.

Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.48; H, 9.65.

Isomerization of 2-Methylbicyclo[5.3.0]dec-1-en-6-one (4a) with *p*-Toluenesulfonic Acid in Benzene. A solution of 587 mg of a 1:1 mixture of ketones **2a** and **4a** in 50 mL of benzene was refluxed overnight with a catalytic amount of *p*-toluenesulfonic acid. The benzene was removed under reduced pressure and the residue treated with 15 mL of saturated sodium bicarbonate solution and 15 mL of ether. The layers were separated and the aqueous layer extracted with two portions (15 mL) of ether. The combined organic extracts were washed with saturated sodium bicarbonate solution and brine, dried, filtered, and concentrated under reduced pressure to afford 336 mg of a dark liquid. Dry column chromatography of this material on silica gel using 10% ether–hexane as eluent gave 157 mg (54%) of **5a**. Distillation of 55 mg of this material in a microstill gave 2-methylbicy-

clo[5.3.0]dec-1-en-6-one (**5a**) as a clear liquid: IR 2950, 2880, 1660, 1620, 1450, 1370, 1335, 1305, 1270, 1210, 900 cm^{-1}; NMR δ 2.35–2.80 (m, 7 H), 1.55–2.95 (m, 6 H), 1.17 ppm (d, 3 H, J = 7.0 Hz); UV (isooctane) λ_{max} 300 (76), 245 (10 500); mass spectrum *m/e* 164 (M^+), 121 (base peak), 108, 93, 92 (base peak), 91, 79, 77.

Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.14; H, 9.52.

Acetone-Sensitized Irradiation of 2-Methyl-2-(1-cyclopentenyl)-cyclopentanone (2a). A solution of 1.235 g (7.53 mmol) of ketone **2a** in 400 mL of acetone in a quartz vessel was degassed with prepurified nitrogen for 30 min and irradiated with RPR 2537-Å lamps for 3.5 h. Evaporation of the solvent afforded 1.882 g of crude product as a yellow liquid. Analysis by GLC (6-ft UCW-98 at 150 °C) indicated approximately 80% conversion to a single, new product. Chromatography of 1.185 g of this material on silica gel gave 42.0 mg of **2a** and 396.0 mg (55%) of **6a.** Distillation in a microstill gave pure 6-methyltricyclo[5.3.0.$0^{1,6}$]decan-2-one (**6a**) as a clear liquid: IR 2970, 1670, 1475, 1455, 1395, 1342, 1315, 1275, 1180, 1130, 1055, 920 cm^{-1}; NMR δ 2.50–2.90 (m, 2 H), 1.20–2.30 (br m, 11 H), 1.07 ppm (s, 3 H); UV (isooctane) λ_{max} 278 (26); mass spectrum *m/e* 164 (M^+), 149, 146, 136, 135, 131, 121, 108, 107, 93 (base peak), 91, 79, 77, 67.

Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.65; H, 9.55.

Deuterium Exchange of 6-Methyltricyclo[5.3.0.$0^{1,6}$]decan-2-one (6a) with Methoxide–Methanol-*O-d*. To a solution of 41.6 mg (0.254 mmol) of ketone **6a** in 8 mL of methanol-*O-d* was added 60.3 mg of sodium methoxide. The solution was stirred for 11 h and then quenched with 5 mL of deuterium oxide and 2 drops of hydrochloric acid. Isolation by extraction with ether afforded 18.1 mg (43%) of dideuterated **6a.** The percent deuterium incorporation was determined by mass spectral analysis: (M), 5.82%; (M + 1), 8.41%; (M + 2), 85.76%.

Reduction of 6-Methyltricyclo[5.3.0.$0^{1,6}$]decan-2-one (6a) with Lithium in Liquid Ammonia. To a solution of 432 mg (61 mmol) of lithium in 100 mL of liquid ammonia was added, with stirring, 507 mg (3.08 mmol) of ketone **6a** over a period of 10 min. After an additional 30 min, 7 g of ammonium chloride was added and the ammonia allowed to evaporate. Water (100 mL) was added, the layers were separated, and the aqueous layer was extracted with ether. The combined ether extracts were washed with brine, dried, and concentrated under reduced pressure to afford 403 mg (79%) of **7.** Distillation of a small amount of this material in a microstill gave a 2:1 mixture of *cis*- and *trans*-10-methyl-1-decalone (**7**): IR 2960, 2890, 1710, 1445, 1425, 1380, 1310, 1300, 1230, 1200, 1150, 1080, 1040 cm^{-1}; NMR δ 1.20–2.30 (m, 15 H), 0.78 and 1.00 ppm (2 singlets, totaling 3 H). These spectra are identical with those obtained for the product of the addition of lithium dimethylcopper to $\Delta^{9,10}$-1-octalone (**8**) (vide infra).

Addition of Lithium Dimethylcopper to $\Delta^{9,10}$-1-Octalone (8). To a stirred slurry of 1.49 g (7.77 mmol) of cuprous iodide in 32 mL of ether at 0 °C under nitrogen was added 19.5 mL (14.7 mmol) of 0.754 M methyllithium in ether. After an additional 30 min, a solution of 300 mg (2.00 mmol) of ketone **8**[30] in 5 mL of ether was added dropwise. The reaction mixture was stirred for 24 h at 0 °C, poured into 30 mL of saturated ammonium chloride solution, and extracted with ether. The combined ether extracts were washed with saturated sodium bicarbonate solution and brine, dried, and concentrated under reduced pressure to afford 252 mg of a yellow oil. Column chromatography of 230 mg of this material on silica gel gave 112 mg of a mixture of **2a** and **7b.** Distillation gave the same 2:1 mixture of *cis*- and *trans*-methyl-1-decalone (**7**) as above.

Direct Irradiation of 2-Methylbicyclo[5.3.0]dec-1-en-6-one (4a). A solution of 64.0 mg of ketone **4a** in 15 mL of hexane in a Pyrex tube was degassed with prepurified nitrogen for 30 min and irradiated with RPR 2537-Å lamps. Analysis by GLC (6-ft UCW-98 at 150 °C) during the photolysis indicated the appearance of **2** as the only product. After 326 min no further conversion of **4a** to **2a** was detected. The photostationary state composition consisted of approximately a 1.2:1 ratio of **4a** to **2a.** The same photostationary state was obtained in a simultaneous photolysis of **2a** in 15 mL of hexane.

Acetone-Sensitized Irradiation of 2-Methylbicyclo[5.3.0]dec-1-en-6-one (4a). A solution of 80 mg of ketone **4a** in 15 mL of spectral grade acetone in a quartz tube was degassed with purified nitrogen for 30 min and irradiated in a merry-go-round apparatus with RPR 2537-Å lamps. Analysis by GLC (UCW-98 at 150 °C) during the photolysis indicated the appearance of a new product with retention time corresponding to tricyclic ketone **6a.** After 395 min the ratio of **4a** to **6a** in the reaction mixture was approximately 45% ketone **4a** and 54% ketone **6a.** Photolysis of an 84-mg sample of **2a** in 15 mL of acetone for the same period of time resulted in the total disappearance of **2a.**

General Procedure for Determination of Quantum Yields. A solution of the ketone in 5 mL of solvent in either a Pyrex or quartz tube was degassed with purified nitrogen and placed in the merry-go-round apparatus. Irradiations were carried out with either RPR 3000-Å or RPR 2537-Å lamps. Light output was monitored by potassium ferrioxalate actinometry according to the method of Hatchard and Parker.[31]

Samples were removed and the contents analyzed directly by GLC using cyclodecane as an internal standard. A 1/8 in. × 6 ft 10% SE-30 column at 140 °C in a Varian 1200 fid instrument was used for analysis. Limiting quantum yields were determined by extrapolation of the apparent quantum yield at various conversions to zero conversion.

In the direct irradiation of **2a** the following data were obtained: initial ketone concentration, 4.10×10^{-2} M (ether); RPR 3000-Å lamps, light output, 0.2559 mEinstein/h; $\Phi_{dis(2a)} = 0.09$; $\Phi_{app(4a)} = 0.054$.

In the acetone-sensitized irradiation of **2a** the following data were obtained: initial ketone concentration, 4.43×10^{-2} M (acetone); RPR 2537-Å lamps, light output, 0.4590 mEinstein/h; $\Phi_{dis(2a)} = 0.35$; $\Phi_{app(6a)} = 0.25$.

Emission Studies with 2-Methyl-2-(1-cyclopentenyl)cyclopentanone (2a). Fluorescence and phosphorescence studies employing solutions of **2a** in ether or hexane at ambient temperatures or methanol, methylcyclohexane, isopentane, or methylcyclohexane–isopentane mixtures at 77 K were carried out by standard methods. *No emission was observed.*

2-Carboxymethyl-2-(1-cyclopentenyl)cyclopentanone (2c). To a solution of 0.38 mol of sodium methylsulfinylmethide in 500 mL of dimethyl sulfoxide was added dropwise a solution of 50.0 g (0.33 mol) of 2-cyclopentylidenecyclopentanone (**1**) in 400 mL of dimethyl sulfoxide. The solution was stirred for an additional hour and 64.2 g (0.385 mol) of ethyl bromoacetate in 300 mL of dimethyl sulfoxide was added dropwise with cooling. After 30 min the reaction mixture was quenched with 1 L of a saturated solution of ammonium chloride. Isolation by extraction with pentane gave 69.8 g (89%) of a red liquid. A solution of 62.9 g (266 mmol) of crude keto ester **2b** and 44.7 g (798 mmol) of potassium hydroxide in 1.5 L of methanol was heated at reflux overnight. The methanol was removed under reduced pressure, 350 mL of ether and 400 mL of water were added, and the layers were separated. The aqueous layer was acidified with hydrochloric acid and thoroughly extracted with ether. The combined ether extracts were dried and filtered, and the ether was removed under reduced pressure to afford 50.0 g (90%) of a dark solid. Sublimation of 2.35 g of this material gave 1.24 g of white solid, mp 92–94 °C. Recrystallization of 1.16 g of this material from ether–hexane gave 0.75 g of 2-carboxymethyl-2-(1-cyclopentenyl)cyclopentanone (**2c**) as colorless crystals: mp 93–95 °C; IR 3060, 2970, 2860, 1745, 1715, 1410, 1220, 1160 cm^{-1}; NMR δ 14.41 (s, 1 H), 5.53 (m, 1 H), 2.71 (d of d, 2 H, J = 17 Hz), 1.5–2.5 ppm (m, 12 H); UV (ether) λ_{max} 300 (198), 211 (1340) end abs.; mass spectrum *m/e* 208 (M^+), 190, 162, 149, 131, 120, 119, 107, 93, 92, 91 (base peak), 79, 77.

Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.51; H, 7.94.

On a larger scale, purification of the keto acid was accomplished by filtration of the crude acid through silica gel (Mallinckrodt SilicAR CC-4) with 30% ether–hexane is eluent, followed by recrystallization from ether–hexane.

Resolution of 2-Carboxymethyl-1-(1-cyclopentenyl)cyclopentanone (2c). Keto acid **2c** (10.30 g, 49.5 mmol) and 14.90 g (50.5 mmol) of cinchonidine were dissolved in 200 mL of boiling 95% ethanol and, on cooling, 26.45 g (105%) of solid was precipitated. Systematic recrystallization of this material from 95% ethanol, followed by acid hydrolysis of the salt, gave the following quantities of resolved and partially resolved acid **2c** (total recovery, 8.62 g, 84%) (Table III).

Direct Irradiation of 2-Carboxymethyl-2-(1-cyclopentenyl)cyclopentanone (2c). A solution of 790 mg of **2c** in 200 mL of anhydrous ether in a Pyrex vessel was degassed with purified nitrogen for 30 min and irradiated with the RPR 3000-Å lamps for 826 min (37% disappearance of **2c**). Removal of the ether under reduced pressure afforded

929 mg of a white solid which was chromatographed on silica gel to give 495 mg of keto acid **2c** and 148 mg (50%) of keto acid **4c** as a fluffy white solid: mp 92–93 °C. Recrystallization of **4c** from ether gave colorless needles: mp 130–131 °C, IR 3050, 2960, 2900, 1700, 1410, 1395, 1308 cm^{-1}; NMR δ 9.13 (br s, 1 H), 4.03 (br m, 1 H), 3.12 (s, 2 H), 2.80–1.60 ppm (m, 12 H); UV (ether) λ_{max} 285 (145), 212 (5650); mass spectrum *m/e* 208 (M^+), 190, 107, 93 (base peak), 91, 79, 77, 67.

Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 68.92; H, 7.84.

Acetone-Sensitized Irradiation of 2-Carboxymethyl-2-(1-cyclopentenyl)cyclopentanone (2c). A solution of 193 mg of **2c**, in 15 mL of spectral grade acetone in a quartz vessel, was degassed with purified nitrogen for 15 min and irradiated with RPR 2537-Å lamps for 50 min (81% disappearance of **2c**). Removal of the solvent under reduced pressure gave 240 mg of a light yellow oil which was chromatographed on silica gel to give 36 mg of keto acid **2c** and 114 mg (73%) of keto acid **6c**. Keto acid **6c** was recrystallized from ether to give pure 6-carboxymethyltricyclo[5.3.0.$0^{1,6}$]decan-2-one (**6c**) as a colorless solid: mp 112–113 °C; IR 3060, 2975, 1710, 1665, 1405, 1340, 1275 cm^{-1}; NMR δ 10.06 (br s, 1 H), 2.60 (s, 2 H), 1.30–3.00 ppm (m, 13 H); UV (ether) λ_{max} 284 (37); mass spectrum *m/e* 208 (M^+), 190, 163, 162, 149, 135, 134, 133, 131, 121, 119, 110 (base peak), 107, 106, 105, 93, 92, 91, 79, 77.

Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.54; H, 7.67.

Direct Irradiation of (*R*)-(−)-2-Carboxymethyl-2-(1-cyclopentenyl)cyclopentanone ((*R*)-(−)-2c). A solution of 953 mg of (*R*)-(−)-**2c**, $[\alpha]^{28}_D$ −131°, in 250 mL of anhydrous ether in a Pyrex vessel was degassed with purified nitrogen for 15 min and irradiated with the RPR 3000-Å lamps for 18 h (50% disappearance of (*R*)-(−)-**2c**). Removal of the ether at reduced pressure afforded 938 mg of a white solid, which was chromatographed on silica gel to give 482 mg of keto acid **2c**, $[\alpha]^{28}_D$ −129°, and 224 mg (48%) of keto acid **4c**, $[\alpha]^{28}_D$ +150°. Data for additional examples of the conversion of optically active **2c** to **4c** are listed in Table II.

Acetone-Sensitized Irradiation of (*S*)-(+)-2-Carboxymethyl-2-(1-cyclopentenyl)cyclopentanone ((*S*)-(+)-2c). A solution of 221 mg of (*S*)-(+)-**2c**, $[\alpha]^{28}_D$ +131°, in 15 mL of spectral grade acetone in a quartz tube was degassed with purified nitrogen for 15 min and irradiated with RPR 2537-Å lamps for 60 min (58% disappearance of (*S*)-(+)-**2c**). Removal of the solvent under reduced pressure gave 265 mg of a yellow liquid that was chromatographed on silica gel to give 81 mg of keto acid **2c**, $[\alpha]^{28}_D$ +118°, and 136 mg (97%) of keto acid **6c**, $[\alpha]^{28}_D$ +52°. Data for additional examples of the conversion of optically active **2c** to **6c** are listed in Table II.

Direct Irradiation of (*S*)-(+)-2-Carboxymethylbicyclo[5.3.0]dec-1-en-6-one ((*S*)-(+)4c). A solution of 73 mg of (*S*)-(+)-**4c**, $[\alpha]^{28}_D$ +143°, in 25 mL of ether in a Pyrex tube was degassed with purified nitrogen for 15 min and irradiated with RPR 3000-Å lamps for 23 min (38% disappearance of (*S*)-(+)-**4c**). The ether was removed under reduced pressure to give 69 mg of an oil that was chromatographed on silica gel to give 9.1 mg (32%) of keto acid **2c**, $[\alpha]^{28}_D$ −80°, and 45 mg of keto acid **4c**, $[\alpha]^{28}_D$ +132°. Data for additional examples of the conversion of optically active **4c** to **2c** are recorded in Table II.

Attempted Acetone-Sensitized Irradiation of (*R*)-(−)-2-Carboxymethylbicyclo[5.3.0]dec-1-en-6-one ((*R*)-(−)4c). A solution of 125 mg of (*R*)-(−)-**4c**, $[\alpha]^{28}_D$ −150°, in 15 mL of spectral grade acetone in a quartz tube was degassed with purified nitrogen for 15 min and irradiated in a merry-go-round apparatus with RPR 2537-Å lamps for 1.5 h. Removal of the solvent under reduced pressure gave 127 mg of a viscous yellow oil which was filtered through silica gel to afford 75 mg of material that was chromatographed on silica gel (Mallinckrodt SilicAR CC-4) to give 47 mg of recovered keto acid **4c**, $[\alpha]^{28}_D$ −105°.

In a separate experiment, irradiation of 36 mg of keto acid **4c** under the same conditions for 0.5 h, a time in which the keto acid had been shown to partially racemize, resulted in only small (2%) conversion to the tricyclic keto acid **6c** as detected by GLC (5% OV-17, 135 °C) of the reaction mixture after esterification with diazomethane.

Catalytic Reduction of (*R*)-(−)-2-Carboxymethyl-2-(1-cyclopentenyl)cyclopentanone ((*R*)-(−)-2c). Hydrogenation of 206 mg of (*R*)-(−)-**2c**, $[\alpha]^{28}_D$ −128°, over 30 mg of 10% Pd/C in ethanol at 1 atm of hydrogen for 2 h, followed by filtration and removal of the solvent at reduced pressure, gave 165 mg (80%) of a white solid which was recrystallized from ether to give (*R*)-(−)-2-carboxymethyl-2-cyclopentylcyclopentanone ((*R*)-(−)-**3**): $[\alpha]^{28}_D$ −67°; white solid; mp 86–87 °C; IR 3010, 2960, 2870, 1725, 1705, 1400, 1155, 1120 cm^{-1}; NMR δ 10.36 (br s, 1 H), 2.63 (d of d, 2 H, J = 17 Hz), 2.20–2.50 (m, 2 H), 1.80–2.10 (m, 4 H), 1.30–1.75 ppm (br s, 8 H); UV (ether) λ_{max} 294 (38); mass spectrum *m/e* 210 (M^+), 151, 142, 124 (base peak), 97, 96, 95, 94, 93, 91, 81, 79.

Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63. Found: C, 68.28; H, 8.81.

Table III

recovd keto acid, g	$[\alpha]^{28}_D$ (ethanol), deg
0.60	−139
0.94	−138
0.96	−131
0.83	−128
0.71	−30
2.97	+136
1.61	+105

General Procedure for Optical Purity Determinations. Greater than 95% optical purities of the individual enantiomers of keto acids **2c**, **4c**, and **6c** were demonstrated by measuring the 100-MHz NMR spectrum of the derived methyl esters (diazomethane) in the presence of varying amounts of the chiral shift reagent, tris(3-heptafluoropropylhydroxymethylene-*d*-camphorato)europium(**III**).

General Procedure for Esterification of Keto Acids. The acid **2c**, 3.94 g (18.9 mmol), was treated with an ethereal solution of diazomethane[32] (prepared from 10 g of methylnitrosourea) at 0 °C. After 1 h, 8 mL of acetic acid was added. The mixture was extracted with saturated sodium bicarbonate and brine, dried, and filtered and the ether was removed under reduced pressure to afford 3.48 g (83%) of a yellow liquid. Distillation of this material gave 1.37 g of 2-carbomethoxymethyl-2-(1-cyclopentenyl)cyclopentanone (**2d**) as a clear liquid: bp 99–100 °C (0.45 Torr); IR 2974, 2870, 1750, 1445, 1410, 1355, 1200, 1165 cm^{-1}; NMR δ 5.40–5.50 (m, 1 H), 3.55 (s, 3 H), 2.55 (d of d, 2 H, J = 15 Hz), 1.70–2.40 ppm (m, 12 H).

Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.04; H, 8.24.

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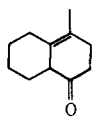

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Reactions of Photoradicals with Nitroxide Spin Labels[1]

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Abstract: The kinetics of reactions of radicals R· with nitroxide spin labels have been studied, the radicals R· being produced by laser photodecomposition of alkylcobalt complexes having the general formula $Co(CN)_5^{3-}R$. The rate of reaction of the radicals R· and nitroxide radicals is shown to be a sensitive function of the molecular environment of the nitroxide group, i.e., whether it is bound to a membrane or is free in solution. The ease with which a variety of alkylcobalt compounds $Co(CN)_5^{3-}R$ can be prepared with the corresponding radicals R· having different physical and chemical properties, and the ease with which the rate of generation of radicals R· can be varied with laser power, indicates that a number of applications of this photochemistry to biophysical and biochemical problems may be possible.

Introduction

In a recent communication Sheats and McConnell[3] reported the photochemical reaction of an alkylcobalt complex, carboxymethylpentacyanocobaltate, with the nitroxide 4-hydroxytetramethylpiperidine-1-oxyl (Tempol, or R_2NO) according to the equation

$$Co(CN)_5^{3-}CH_2CO_2^- + R_2NO \xrightarrow{h\nu} Co(CN)_5^{3-} + (R_2)NOCH_2CO_2^- \quad (1)$$

Since then a number of applications to the study of phospholipid membranes have appeared[4,5] which illustrate the considerable scope and versatility of this class of reactions in biophysical chemistry. Although our interest in these reactions has been primarily in applications based on the stoichiometry of radical–radical reactions, we have recently found that a quantitative analysis of the kinetics of these reactions may also yield significant biophysical information. Here we report our results on two different alkylcobalt complexes, and describe preliminary applications to the structure and dynamics of model membranes (lipid bilayers).

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