

Influence of Substitution on the Photochemistry of Rigid Cyclopentenones¹

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The rigid cyclopentenones **1c**, **1d**, and **1e** were synthesized and photolyzed for comparison with the behavior of **1a**, which undergoes normal [2 + 2] photocyclization to **2a**, and **1b**, which undergoes intramolecular energy transfer from the cyclopentenone chromophore to the isolated double bond and a subsequent series of intramolecular hydrogen transfers. In solution, **1c** underwent competitive [2 + 2] photocyclization to **2c** and type 1 cleavage followed by steps eventuating in an oxycarbene rearrangement to **11**. **1d** underwent photodimerization, whereas **1e** underwent [2 + 2] photocyclization to **2d**. The absence of products resulting from intramolecular hydrogen transfer is ascribed to the circumstance that **1c** and **1e**, like **1a** and unlike **1b**, have low-lying $n-\pi^*$ enone triplets (77 K, phosphorescence). The difference in the results between **1c** and **1e** is explained in terms of the different values of the triplet energies (75 and 72 kcal/mol).

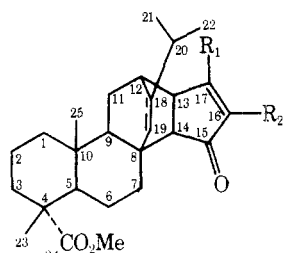
The photochemistry of the rigid cyclopentenones **1a** and **1b** exhibits surprising differences.²⁻⁵ Whereas irradiation of **1a** yielded the expected [2 + 2] photocyclization to **2a**, irradiation of **1b** produced not only **2b** by a reversible photochemical reaction, but also irreversibly **3** by a then² unprecedented intramolecular energy transfer from cyclopentenone chromophore to the isolated double bond followed by hydrogen abstraction by C-19 from the C-10 methyl group.²⁻⁴ In turn, **3** undergoes further photochemically induced hydrogen transfer to form **4a**²⁻⁴ and **5**.⁵ The photochemical mechanism of these unusual reactions has been investigated in some detail.⁵ The difference between the photochemical behavior of **1a** and **1b** was attributed to the nature of the lowest lying triplet ($^3n,\pi^*$, in the case of **1a**, $^3\pi,\pi$ in the case of **1b**) and the possibility that more than one enone triplet may be involved in the formation of **2b** and **3** from **1b** and the formation of **4** and **5** from **3**.⁵

It seemed of interest to synthesize other derivatives of **1a** and to study their photochemical behavior. Details of such a study are reported herewith.

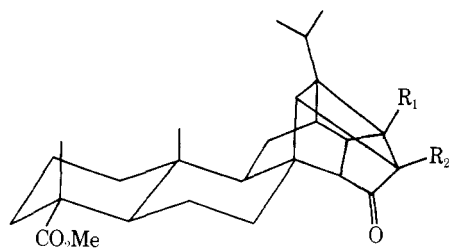
Syntheses of Starting Materials. In analogy with the initial step in the conversion of **1b** to **1a**,³ reaction of **6** with

lithium reagents was expected to furnish a series of 3-substituted cyclopentenones. Thus, addition of methyllithium to **6** at -70°C in ether for 15 min and acid workup yielded **1c** quantitatively. The UV spectrum exhibited the characteristic absorption of a β -substituted α,β -unsaturated cyclopentenone and the NMR spectrum displayed the typical α -proton frequency at 5.7 ppm allylically coupled to the β -methyl signal at 1.85 ppm. Other signals corresponded to those previously observed.³ In a similar fashion reaction of **6** with phenyllithium afforded a quantitative yield of **1d**. Again, UV and IR spectra exhibited the characteristic absorption of a β -substituted α,β -unsaturated cyclopentenone; in this instance, the H-16 singlet was sharp owing to absence of long-range coupling with the five protons of the phenyl group which appeared as a complex band in the 7.5-ppm region.⁶

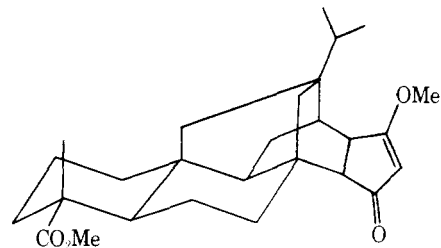
Introduction of substitution into the 16 position was a somewhat more complex matter and utilized the Favorskii rearrangement of epoxides of benzoquinone adducts which we developed earlier.^{3,7} Reaction of methyl levopimarate with methyl *p*-benzoquinone yielded the two isomeric adducts **7a** and **7b**, mp 160 and 195 $^\circ\text{C}$ (5:6 ratio), which were separated easily by fractional crystallization from acetone and methanol.



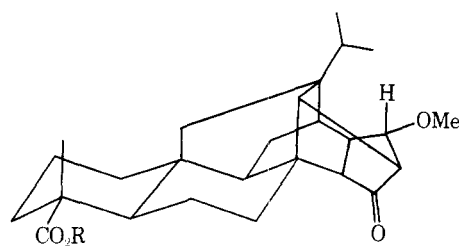
- 1a**, $R_1, R_2 = \text{H}$
b, $R_1 = \text{OMe}; R_2 = \text{H}$
c, $R_1 = \text{Me}; R_2 = \text{H}$
d, $R_1 = \text{Ph}; R_2 = \text{H}$
e, $R_1 = \text{H}; R_2 = \text{Me}$
f, $R_1, R_2 = \text{Me}$



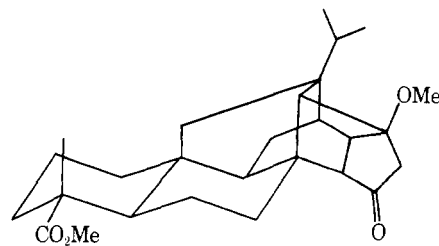
- 2a**, $R_1, R_2 = \text{H}$
b, $R_1 = \text{OMe}; R_2 = \text{H}$
c, $R_1 = \text{Me}; R_2 = \text{H}$
d, $R_1 = \text{H}; R_2 = \text{Me}$



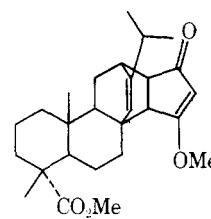
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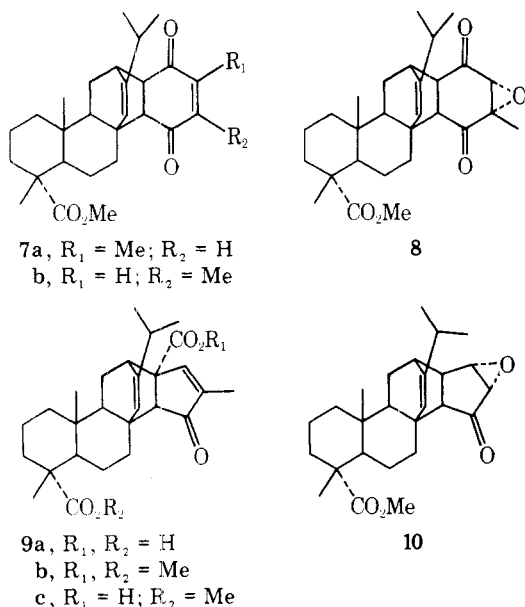
- 4a**, $R = \text{Me}$
b, $R = \text{H}$



5



6



Structure assignment rested on subsequent transformations. The conventional method of epoxidation (H₂O₂-NaOH) of both isomers resulted only in recovery of starting material. However, oxidation of **7b** in dioxane-THF at room temperature by slow addition of H₂O₂ in the presence of aqueous NaHCO₃ gave an excellent yield of an epoxide subsequently shown to be **8**.

Although it might have been expected that Favorskii rearrangement of **8** would produce a mixture, exposure of **8** to 10% aqueous NaOH in 95% ethanol resulted in isolation of only one rearranged γ -carboxy- α -methyl- α,β -unsaturated ketone (70% recrystallized yield) later shown to be **9c**. Apparently abstraction of H-14 by base encounters considerably more steric hindrance than abstraction of H-13. The NMR spectrum of the rearrangement product was compatible with an α,γ -disubstituted α,β -unsaturated ketone (β -vinyl proton at 7 ppm coupled allylically to a narrowly split vinyl methyl resonance). A singlet at 2.6 ppm could be attributed to H-14 and the presence of a carboxyl group was evident chemically and spectroscopically (IR spectrum; NMR resonance at 11.3 ppm exchangeable with D₂O).

Attempts to decarboxylate **9c** in the manner described for the lower homologue³ gave only the diester **9b**. Hydrolysis of **9b** gave **9a**. However, decarboxylation of **9c** was efficiently carried out by heating it to the melting point in a nitrogen atmosphere. This furnished **1e** in quantitative yield. The ORD curve of **1e** exhibited a negative Cotton effect like that of the lower homologue **1a**; a Δ^{15-17} ketone would have been expected to display a Cotton effect of opposite sign.³ Consequently, the product was indeed **1e** and its precursors **7b**, **8** and **9c**.

Photolyses. Irradiation of **1e** in methanol (Pyrex filter) by the procedures previously employed for **1a** and **1b** gave the [2 + 2] photocyclization product **2d** exclusively. The structure of the product was evident from the IR spectrum, which exhibited carbonyl absorption at 1770 (strained ketone) and 1720 cm⁻¹ (ester), in analogy with **2a** and **2b**, and the NMR spectrum, which was devoid of all low-field signals attributable to vinyl protons, but exhibited the required number of methyl resonances (methoxyl at 3.65 ppm, C-4 methyl and C-16 methyl superimposed at 1.15 ppm, unshielded C-10 methyl at 0.80 and isopropyl doublets centered at 0.92 ppm).

Irradiation of **1d** in methanol (Pyrex filter) for 24 h gave a complex mixture from which one pure substance was isolated in 30% yield. The NMR spectrum of this material indicated that the 18,19 double bond had been retained (broadened singlet at 5.20 ppm typical of H-19 and highly shielded methyl

Table I. ¹³C NMR Spectrum of **11**^a

C-1	38.5 t	C-15	104.9 d
C-2	17.2 t	C-16	59.6 d
C-3	36.9 t	C-17	27.4
C-4	47.3	C-18	89.7
C-5	49.9 d ^a	C-19	56.9 d
C-6	31.2 t	C-20	27.8 d
C-7	35.2 t	C-21	14.6 q ^e
C-8	31.4 ^b	C-22	20.4 q ^d
C-9	47.9 d ^a	C-23	179.0
C-10	35.5 ^b	C-24	17.2 q
C-11	20.2 t	C-25	16.5
C-12	32.9 d	C-26	51.6 q
C-13	24.3 d ^c	C-27	22.5 q ^d
C-14	23.3 d ^c	C-28	54.1 q

^a Run in CDCl₃ at 67.905 MHz on Bruker HX-270 MHz instrument in a microcell, using Me₄Si as internal standard. ^{b,c,d} Assignments may be interchanged. ^e Assignment based on shielding of corresponding proton resonance.

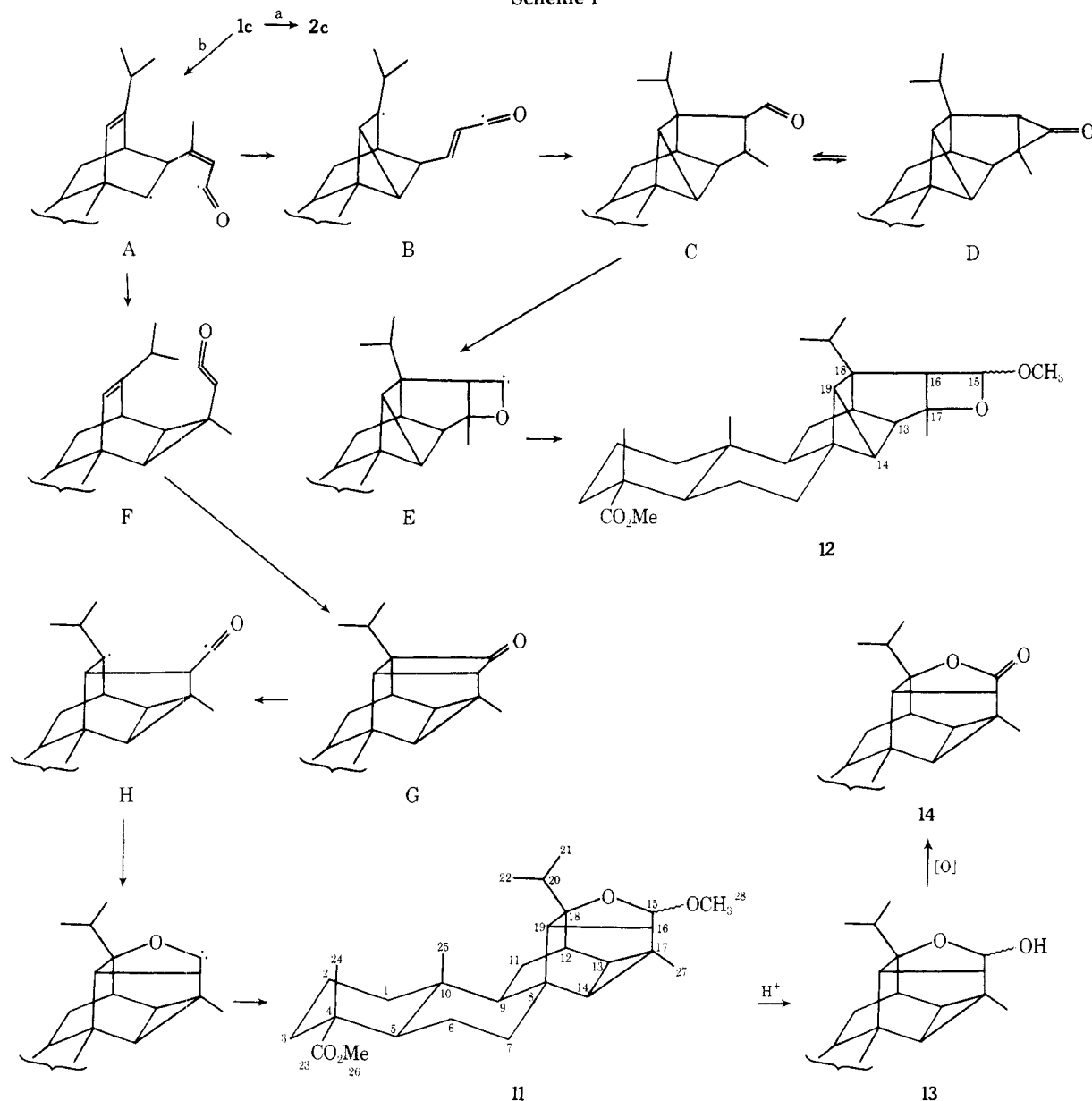
resonance at 0.5 ppm typical of C-10 methyl in normal Diels-Alder adducts). The remaining methyl groups (carbo-methoxyl at 3.60, C-4 methyl singlet at 1.10, and isopropyl doublets at 0.8 and 0.6 ppm) were also in evidence. The absence of other low-field signals and the presence of a sharp singlet at 2.8 ppm characteristic of a proton α to a carbonyl group in a cyclobutane ring indicated that the product was one of the four possible dimers of **1d**. This conclusion was supported by the high-resolution mass spectrum, which was superimposable on the high-resolution mass spectrum of the precursor **1d**, thus indicating extremely facile fragmentation of the dimer under electron impact even at low voltage. Work on the structure of the dimer is in progress.

Irradiation of **1c** in methanol (Pyrex filter) for 24 h gave equal amounts of two noncrystalline products (total yield quantitative) which were separated by preparative TLC. The less polar substance was the [2 + 2] photocyclization product **2c** whose structure was deduced by the same criteria previously employed for **2c** [IR bands at 1770 (strained ketone) and 1720 cm⁻¹ (ester), NMR spectrum devoid of signals downfield from the methoxyl at 3.7 ppm]. The C-10 methyl signal occurred at a normal frequency of 0.8 ppm since it was no longer deshielded by a 17,18 double bond.

Analysis and high-resolution mass spectrum of the noncrystalline, more polar product demonstrated the empirical formula C₂₈H₄₂O₄, i.e., the inclusion of an extra molecule of methanol. Its spectral properties (ester band at 1720 cm⁻¹, absence of hydroxyl absorption or ketone bands, the latter confirmed by CD measurements which showed complete transparency in the 250-375-nm region, NMR signals at 4.82 singlet, 3.80 methoxyl of ester, 3.30 methoxyl of ether as the result of incorporation of a molecule of methanol, C-4 methyl and C-10 methyl signals at 1.18 and 0.80 ppm) indicated a structure entirely different from the previous photoproducts. Especially noteworthy was the remarkable great chemical shift difference between the methyl signals of the isopropyl group at 0.90 and 0.45 ppm and the conversion of the C-16 methyl group of **1c** to a singlet.

These data and the noise-decoupled ¹³C NMR spectrum of the unknown photolysis product (see Table I), which exhibited the requisite 28 signals (six singlets, nine doublets, six triplets, and seven quartets), confirmed the absence of a ketone group, showed the absence of vinyl carbons, displayed a doublet at 104.8 ppm in the range of acetal or ketal carbons consonant with the proton singlet at 4.82 ppm and a singlet at 89.7 ppm attributable to the other terminus of the acetal which must be quaternary, as well as the quartet of a methoxyl group at 54.1 ppm, led to the conclusion that formation of the

Scheme I



second product must have initially involved a type I cleavage of 1c, and, at some subsequent stage, reaction of an oxycarbene with methanol 9. Of the two possible structures 11 and 12 (Scheme I), which satisfied the spectral data given so far,^{10,13} 11 was shown to be correct as follows.

Serendipitously, it was discovered that the photoproduct underwent hydrolysis on silica during attempts at purification by TLC. Hydrolysis on a preparative scale ($\text{CHCl}_3\text{-HCl}$) resulted in irreversible formation of a hemiacetal (IR band at 3600 cm^{-1}) whose NMR spectrum was identical with that of the photoproduct except for the absence of the methoxyl resonance and a slight downfield shift (to 4.95 ppm) of H-15. This was more in keeping with structure 11 than with 12, which because of the strain inherent in the four-membered ring of 12 would have been expected to form a hemiketal less spontaneously after hydrolysis. Lastly oxidation of the hemiketal with Jones reagent resulted in quantitative conversion to a γ -lactone 14 which exhibited IR bands at 1770 (γ -lactone) and 1720 cm^{-1} (ester) and no NMR signals downfield from the methoxyl resonance at 3.62 ppm. Thus the polar photolysis product of 1c was 11. The path from 1c to 11 is outlined in Scheme I. Path b is the typical type I photochemical cleavage of cyclic ketones. Formation of B from A leading eventually to the discarded possibility 12 would involve participation of

the 18,19 double bond analogous to reactions involved in somewhat simpler bicyclo[2.2.2]octene systems which in turn would result in another radical C. The latter could stabilize itself by forming a cyclopropane D, which, however, would be expected to react further with solvent methanol, or form oxycarbene E which would add methanol to give 12.

Apparently, however, the preferred mode of reaction of A is intramolecular attack by C-14 on C-17 to form ketene F which adds to the 18,19 double bond to give cyclobutanone G.¹⁴ Cyclobutanones have been shown to undergo photolytic rearrangement to ketals of type 11 by irradiation in hydroxylic solvents, presumably by way of type I cleavage to H and rearrangement to oxocarbenes.^{8,9} However, although each step in the formation of 11 has precedent, the concatenation of steps as the result of the proximity of the 18,19 double bond is highly unusual.

That one of the isopropyl methyls resonates at unusually high field is in agreement with 11 since the formula requires that it be sterically compressed and shielded by the acetal oxygen. Such pronounced shielding of one of the isopropyl methyls has been observed previously in derivatives of Diels-Alder adducts where an oxygen is attached to C-18.¹⁵ Moreover, the formation of the five-membered alicyclic ring of C by attack of the keto radical in B on C-18 would be highly

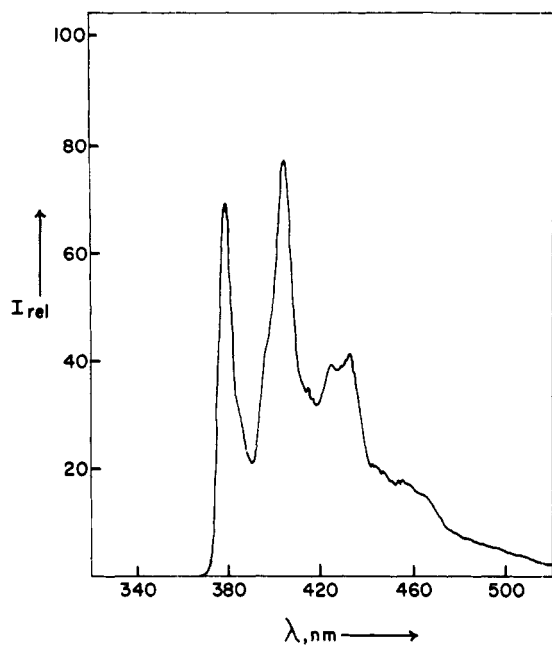


Figure 1. Phosphorescence spectrum of 1c at 77 K in EPA.

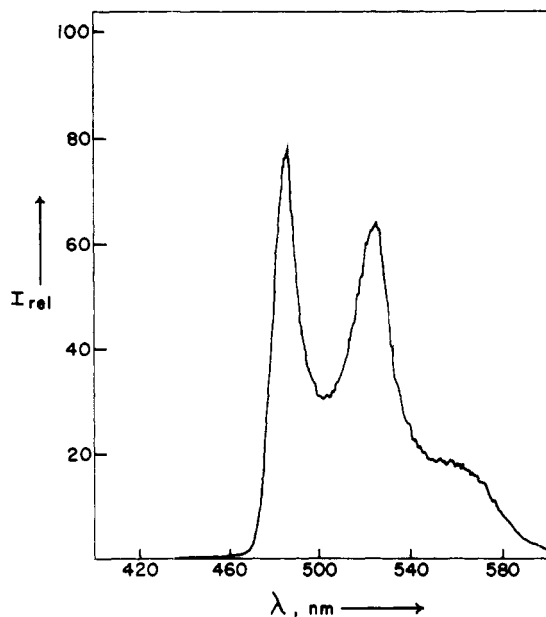


Figure 2. Phosphorescence spectrum of 1d at 77 K in EPA.

unusual, whereas cyclopropane formation by attack of the carbon β to the carbonyl in A on C-14 has been observed previously.¹⁶

Conclusions

Thus, although the products formed on photolysis of 1c, 1d, and 1e differed from compound to compound, the photolyses resembled that of 1a and differed from that of 1b in that no products resulting from intramolecular energy transfer to the isolated double bond were isolated. A possible explanation for this is provided by the phosphorescence emission spectra in EPA shown in Figures 1, 2, and 3.¹⁷ These indicate that the lowest emitting triplets of 1c and 1e, like that of 1a whose phosphorescence emission spectrum they resemble,⁵ are $n-\pi^*$, as the vibrational spacing between the O-0 and the O-1 band corresponds to the stretching frequency of the ketone group. That they do not yield products resulting from intramolecular energy transfer like 1d which has a low-lying $\pi-\pi^*$ triplet is

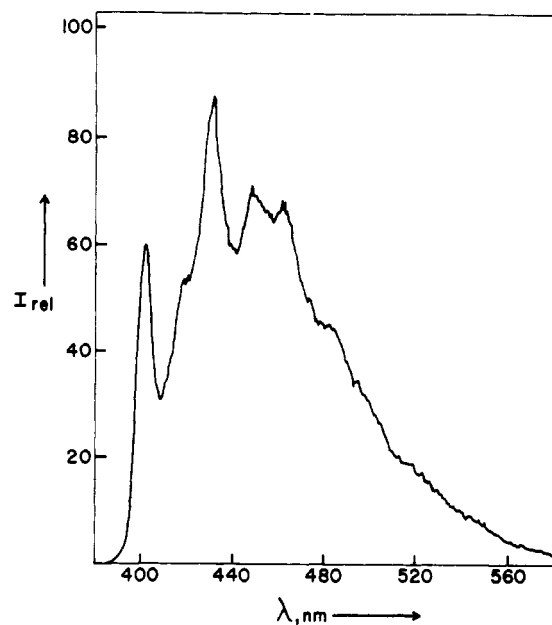


Figure 3. Phosphorescence spectrum of 1e at 77 K in EPA.

therefore understandable in the light of our earlier discussion.⁵

The energies of the triplets of 1a, 1c, and 1e are 72,⁵ 75, and 72 kcal/mol, respectively. Since the triplet energy of 1e is the same as that of 1a it is not surprising that [2 + 2] photocyclization is the only photolytic reaction observed. As for 1c, it is unusual for a β -alkyl α,β -unsaturated cyclopentenone to have a triplet energy as high as that of saturated ketones, which range from 75–80 kcal/mol and characteristically exhibit Norrish type I cleavage. Consequently, the high triplet energy of 1c may be responsible for the type I cleavage which initiates the complex series of steps terminating in the oxycarbene rearrangement of Scheme I and competes with the normal [2 + 2] photocycloaddition characteristic of endo Diels–Alder adducts. Parenthetically we note that 2-methyl substitution has not had the effect of altering the characteristics of the phosphorescence spectrum to the extent observed in other rigid cyclopentenones;¹⁸ in view of this, it would be interesting to study the phosphorescence emission spectrum and photochemical behavior of the yet unknown compound 1f.

The situation with respect to 1d is somewhat different. Although its phosphorescence spectrum is quite structured, its energy (59 kcal) indicates that it is a perturbed styrene and that the lowest triplet should be $\pi-\pi^*$. Localization of excitation in the styrene unit may be responsible for the circumstance that it undergoes dimerization rather than intramolecular cyclization.

Experimental Section²²

Preparation of 1c. To a solution of 1 g of 6³ in 20 mL of ether immersed in a dry ice–acetone bath (nitrogen atmosphere) was added with stirring 4 mL of a 0.2 M solution of methyl lithium. After 15 min the reaction was quenched by addition of 20 mL of 5% H₂SO₄. The ether layer was separated, washed, dried, and evaporated to furnish 1c, which crystallized on addition of hexane: yield 0.9 g; mp (after recrystallization from ethyl acetate–hexane) 170 °C; IR bands at 1720 (ester), 1680 and 1620 cm⁻¹ (conjugated cyclopentenone); NMR signals at 5.2 br (H-19), 5.7 br (H-16), 3.51 (methoxyl), 1.85 (vinyl methyl), 1.00 (C-4 methyl), 0.80d $J = 7$ Hz (isopropyl methyls), and 0.50 ppm d ($J = 7$ Hz, C-10 methyl); UV λ_{max} (cyclohexane) 238, 323 nm (ϵ 12 100, 62); ORD curve [α]₂₄₀ –2860.

Anal. Calcd for C₂₇H₃₈O₃: C, 78.98; H, 9.33; O, 11.69. Found: C, 78.72; H, 9.53; O, 11.70.

Preparation of 1d. The procedure was that employed in the previous section, using phenyllithium in place of methyl lithium. The

yield of crude product was quantitative; after recrystallization from ethyl acetate-hexane it melted at 186 °C; IR bands at 1720, 1685, and 1625 cm^{-1} ; NMR signals at 7.5 c (5 phenyl protons), 6.38 (H-16), 5.35 br (H-19), 3.8 (methoxyl), 1.18 (C-4 methyl), 0.70 d ($J = 7$ Hz, isopropyl methyls) and 0.6 ppm (C-10 methyl); UV (cyclohexane) λ_{max} 275, 340 nm (ϵ 19 400, 97).

Anal. Calcd for $\text{C}_{32}\text{H}_{40}\text{O}_3$: C, 81.32; H, 8.53; O, 10.15. Found: C, 81.34; H, 8.41; O, 10.06.

Reaction of Methyl Levopimarate with Methyl *p*-Benzoquinone. (This reaction was originally carried out by Dr. M. G. Nair.) A solution of 40 g of methyl levopimarate in 60 mL of benzene was allowed to stand at room temperature with 14 g of methyl *p*-benzoquinone in 30 mL of benzene for 24 h and evaporated. The resulting mixture was separated by fractional crystallization from acetone-methanol to yield 20 g of **7a**, mp 160 °C, and 24 g of **7b**, mp 195 °C. Both substances exhibited IR bands at 1720 (ester), 1690, and 1620 cm^{-1} (α,β -unsaturated cyclohexenone) and NMR signals at 6.4 br (α proton on α,β -unsaturated ketone), 5.35 br (vinyl proton of bridge), 3.6 (methoxyl), 1.9 d ($J = 2$ Hz, vinyl methyl), 1.18 (C-4 methyl), 1.00 d ($J = 7$ Hz, isopropyl methyls), and 0.60 ppm (C-10 methyl).

Anal. Calcd for $\text{C}_{28}\text{H}_{38}\text{O}_4$: C, 76.67; H, 8.73; O, 14.59. Found for **7a**: C, 76.61; H, 8.33; O, 15.02. Found for **7b**: C, 76.83; H, 8.61; O, 14.75.

Epoxidation of 7b. To a solution of 4 g of **7b** in 30 mL of dioxane-tetrahydrofuran was added slowly with stirring at room temperature 10 mL of 10% sodium carbonate solution and 20 mL of 30% H_2O_2 . After the yellow color had disappeared, the reaction mixture was worked up in the usual fashion. The product **8** was recrystallized from methanol: yield 3 g; mp 138 °C; IR bands at 1720 cm^{-1} (broad, ester and ketones); NMR signals at 5.6 br (vinyl proton of bridge), 3.7 (methoxyl), 3.4 (H-17), 3.2 br (H-13 and H-14), 1.50 (C-16 methyl), 1.20 (C-4 methyl), 1.00 d ($J = 7$ Hz, isopropyl methyls), and 0.65 ppm (C-10 methyl).

Anal. Calcd for $\text{C}_{28}\text{H}_{38}\text{O}_8$: C, 73.98; H, 8.43; O, 17.60. Found: C, 74.23; H, 8.45; O, 17.47.

Under these conditions, the isomeric unsaturated ketone **7a** could not be epoxidized.

Favorskii Rearrangement of 8. To a solution of 1 g of **8** in 50 mL of ethanol was added with stirring 10 mL of aqueous 10% sodium hydroxide, the mixture being kept at 50 °C. After 1 h, the solvent was evaporated and the residue diluted with 20 mL of water. The aqueous portion was acidified and extracted with ether. The washed and dried ether extracts were evaporated. Trituration of the remaining gum with methanol-hexane resulted in crystallization of **9c** which was recrystallized from methanol: yield 0.7 g; mp 260 °C; IR bands at 3500 (-OH), 1720 (broad, ester and carboxyl), 1680 and 1620 cm^{-1} (cyclopentenone); NMR signals at 11.3 (carboxyl OH, exchangeable with D_2O), 7.00 br (β -H on cyclopentenone), 3.7 (methoxyl), 2.60 (H-14), 1.68 d ($J = 2$ Hz, vinyl methyl), 1.18 (C-4 methyl), 1.00 ($J = 7$ Hz, isopropyl methyls), 0.6 ppm (C-10 methyl).

Anal. Calcd for $\text{C}_{28}\text{H}_{38}\text{O}_5$: C, 73.98; H, 8.43; O, 17.60. Found: C, 73.99; H, 8.38; O, 17.62.

The dimethyl ester **9b** was obtained from **9c** by refluxing with methanol-sulfuric acid under the condition described for successful decarboxylation of the lower homologue.³ Hydrolysis of the diester gave the dibasic acid **9a**.

Preparation of 1e. A two-neck flask containing 0.2 g of **9c** was swept with a stream of N_2 , heated slowly by means of an electrically heated oil bath to 260 °C, and maintained at this temperature for 15 min. Decarboxylation proceeded smoothly at the melting point. After cooling, the product (**1e**) was recrystallized from hexane: yield 0.18 g; mp 148-149 °C; IR bands at 1720 (ester), 1690 and 1620 cm^{-1} (cyclopentenone); NMR signals similar to those of **9c** except for absence of the carboxyl -OH; uv λ_{max} (cyclohexane) 235, 324 nm (ϵ 11 800, 67); ORD curve $[\alpha]_{240} -2860$.

Anal. Calcd for $\text{C}_{27}\text{H}_{38}\text{O}_3$: C, 78.98; H, 9.33; O, 11.69. Found: C, 79.11; H, 9.10; O, 11.93.

Photolysis of 1e. Irradiation of **1e** (0.01 M solution in methanol, Pyrex filter, 24 h) and evaporation of the solvent gave a gum which was chromatographed over alumina. The chloroform eluate furnished **2d** as a gum in 95% yield; IR bands at 1770 (strained cyclopentanone) and 1720 cm^{-1} (ester); NMR signals at 3.65 (methoxyl), 1.15 br (superimposed C-4 and C-16 methyl), 0.92d ($J = 7$ Hz, isopropyl methyls), and 0.80 ppm (C-10 methyl).

Anal. Calcd for $\text{C}_{27}\text{H}_{38}\text{O}_3$: mol wt, 410.2820. Found: mol wt (MS), 410.2819.

Photolysis of 1c. A 0.01 M solution of **1c** in methanol was irradiated for 24 h in a quartz immersion well (Pyrex filter) with the usual source (Hanovia 679-A-36 lamp). Evaporation of methanol furnished a gum (quantitative yield) which consisted of a 1:1 mixture of **2c** and **11**. The mixture was separated by preparative TLC; the less polar

substance, a gum, being **2c**, IR bands at 1770 (strained cyclopentanone) and 1720 cm^{-1} (ester); NMR signals at 3.7 (methoxyl), 1.10 (superimposed C-4 methyl and methyl on cyclobutane ring), 1.00 ppm d ($J = 7$ Hz, two isopropyl methyls).

Anal. Calcd for $\text{C}_{27}\text{H}_{38}\text{O}_3$: C, 78.98; H, 9.33; O, 11.69. Found: C, 78.69; H, 9.15; O, 11.86.

The more polar product **11** was also a gum: IR band at 1720 cm^{-1} (ester); NMR signals at 4.82 (proton under methoxyl), 3.8 (ester methoxyl), 3.3 (ether methoxyl), 1.32 (methyl on cyclopropane), 1.18 (C-4 methyl), 0.9 d, 0.45 d ($J = 7$ Hz, isopropyl methyls), and 0.8 ppm (C-10 methyl). The ^{13}C NMR spectrum is given in Table I.

Anal. Calcd for $\text{C}_{28}\text{H}_{42}\text{O}_4$: C, 75.98; H, 9.56; O, 14.46; mol wt, 442.3082. Found: C, 75.69; H, 9.61; O, 14.20; mol wt (MS), 442.3074.

A solution of 0.1 g of **11** in 20 mL of CHCl_3 and a few drops of acetic acid was allowed to stand at room temperature overnight, washed with water, dried, and evaporated. The residue **13** crystallized on trituration with hexane and was recrystallized from ethyl acetate-hexane: mp 173 °C; IR bands at 3600 (-OH) and 1720 cm^{-1} (ester); NMR spectrum superimposable on that of **11** except for the absence of the methoxyl signal at 3.3 ppm which was replaced by a sharp one-proton singlet at 4.95 ppm.

To a solution of 50 mg of **13** in 10 mL of acetone was added dropwise with stirring Jones reagent until the solution became yellow. After 3 h the solution was worked up in the usual fashion; trituration of the product with hexane afforded **14** in quantitative yield. Recrystallization from methanol gave material of mp 183-185 °C; IR bands at 1770 (γ -lactone) and 1720 cm^{-1} ; NMR spectrum identical with that of **11** except for the absence of the ether methoxyl singlet.

Anal. Calcd for $\text{C}_{27}\text{H}_{38}\text{O}_4$: mol wt, 426.2768. Found: mol wt (MS), 426.2758.

Photolysis of 1d. Irradiation of a 0.01 M solution of **1d** in methanol for 24 h (Pyrex filter) followed by evaporation of solvent and addition of ether resulted in formation of a crystalline dimer which was filtered and recrystallized from CHCl_3 -ether: yield 30%; mp 195 °C; $[\alpha]_{\text{CHCl}_3}^{\text{D}}$ +142°; IR bands at 1720 cm^{-1} (esters and ketones); NMR signals at 7.0 c (phenyl protons), 5.2 br (vinyl proton of bridge), 3.6 (methoxyl), 2.80 (H-16), 1.1 (C-4 methyl), 0.70 d ($J = 7$ Hz, isopropyl methyls), and 0.5 ppm (C-10 methyl). The high-resolution mass spectrum was superimposable on that of **1d**.

Epoxidation of 1a. To a solution of a 0.5 g of **1a** in 20 mL of acetone was added with stirring 1 mL of 10% sodium hydroxide solution and 5 mL of 30% hydrogen peroxide. Stirring was continued for 30 min and the mixture worked up as usual. The product (**10**), obtained in quantitative yield, was recrystallized from heptane: mp 170 °C; IR bands at 1720 and 1710 cm^{-1} (ester and ketone); NMR signals at 5.35 br (H-19), 3.5 m (H-17), 3.6 (methoxyl), 3.1 d ($J = 3$ Hz, H-16), 1.15 (C-4 methyl), 1.05 d ($J = 7$ Hz, isopropyl methyls), and 0.55 ppm (C-10 methyl).

Anal. Calcd for $\text{C}_{26}\text{H}_{36}\text{O}_4$: C, 75.69; H, 8.81; O, 15.51. Found: C, 75.86; H, 8.81; O, 15.30.

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Registry No.—**1a**, 21727-58-2; **1c**, 61570-46-5; **1d**, 61570-44-3; **1d** dimer, 61570-45-4; **1e**, 61570-47-6; **2c**, 61570-48-7; **2d**, 61570-49-8; **6**, 21727-52-6; **7a**, 61570-50-1; **7b**, 61570-51-2; **8**, 61570-52-3; **9c**, 61570-53-4; **10**, 61570-54-5; **11**, 61570-55-6; **13**, 61570-56-7; **14**, 61570-57-8; methylolithium, 917-54-4; phenyllithium, 591-51-5; methyl levopimarate, 3513-69-7; methyl *p*-benzoquinone, 553-97-9.

References and Notes

- (1) Research supported in part by grants from the National Science Foundation (GP-12582) and from the donors of the Petroleum Research Fund, administered by the American Chemical Society.
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Asymmetric Reduction with Chiral Reagents from Lithium Aluminum Hydride and (S)-(-)-N-(o-Substituted benzyl)- α -phenylethylamines

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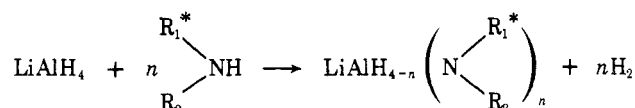
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Asymmetric reduction of carbonyl compounds with chiral hydride reagents modified by (S)-(-)-N-(o-substituted benzyl)- α -phenylethylamines (**3-8**) in toluene was investigated in order to clarify the role of the functional group in the amine ligands on the stereoselectivity. Of all the functional groups in the chiral secondary amines tested, the NMe_2 group exerted a remarkable effect on the asymmetric reduction of ketones (toluene solvent) affording fairly good optical yields [PhCH(OH)CH₃, 43% ee; PhCH(OH)Et, 52% ee; and PhCH(OH)Bu-*t*, 47% ee]. The presence of additives such as 1,2-dimethoxyethane or *N,N,N',N'*-tetramethylethylenediamine in the reaction mixture caused a dramatic decrease in the stereoselectivity, while that of 1,2-dimethylmercaptoethane did not. These observations strongly suggest that chelate ring formation in the chiral hydride reagent is one of the essential factors for the high observed stereoselectivities.

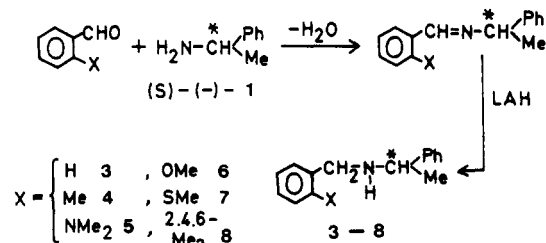
Reduction of an achiral carbonyl compound by a chiral reducing agent to give unequal amounts of the enantiomeric secondary carbinol has been the subject of much study. Most of such studies have been carried out by use of $LiAlH_4$ derivatives modified by the various chiral ligands.¹ One of the prerequisites for a useful chiral ligand is that it be readily available in optically pure form and that it can be easily recovered from the reaction mixture without any loss of optical purity. So far, various naturally occurring chiral carbinols and their derivatives, such as alkaloids,² monosaccharides,³ terpene alcohols,⁴ and tartaric acid derivatives,⁵ have been so employed. Recently, synthetic chiral ligands such as (+)-(2*S*,3*R*)-4-dimethylamino-3-methyl-1,2-diphenyl-2-butanol,^{6,7} oxazoline derivatives⁸ and amino carbinols⁹ have been used for the formation of $LiAlH_4$ complexes which provided substantial stereoselectivity.

These hydride reagents employed so far mostly have been limited to the chiral carbinol or amino carbinol complexes and little is known¹⁰ concerning the stereoselectivity of carbonyl reductions with chiral amine- $LiAlH_4$ complexes. A systematic study of the effect of functional group substituents on the chiral amine ligands should afford a better understanding of the mechanism of these asymmetric reductions as well as the necessary information for the design of a more effective chiral amine- $LiAlH_4$ reagent. We have begun such a study using various chiral secondary amines (**3-8**) for the reaction with $LiAlH_4$ in various molar ratios. The effect of three achiral

complexing additives also has been studied. The chiral reducing agent can be represented by the following scheme.



Ortho-substituted benzaldehydes were condensed with (S)-(-)- α -phenylethylamine (**1**) to give the corresponding Schiff bases which were in turn reduced with excess $LiAlH_4$ in boiling ether. The (S)-(-)-N-(o-substituted benzyl)- α -phenylethylamines (**3-8**) thus obtained were purified by



fractional distillation under reduced pressure. These chiral amines are tabulated in Table I.

It was shown conclusively that there was no racemization during the synthesis of amine **3**. The NMR spectrum of *dl* amine **2** in the presence of the chiral shift reagent $\text{Eu}(\text{hfc})_3$, tris[3-(heptafluoropropyl)hydroxymethylene-*d*-campho-