General Method for Preparative Photolyses of 3a–c. A solution of **3** (2.9 or 5.0 mM) in water (180 mL) containing 1 mL of 1 N NaOH was irradiated internally in air with an unfiltered 300 W high-pressure mercury lamp (Eikosha P1H-300) for 180 or 150 min at ca. 30 °C. After irradiation, the precipitated products were filtered and separated by preparative TLC [silica gel PF_{254} (Merck), *n*-hexane] for the sulfonates **3a** and **3b**. For **3c**, the irradiated solution was extracted by $CHCl_3$ after acidification with dilute HCl, and the extract was analyzed on GLC [10% Silicone SE-GE-31 on Diasolid L (60–80 mesh) in a 2 m stainless steel column (inside diameter 2.5 mm), column temperature 212 °C, injection temperature 236 °C, carrier gas (N_2) 26.0 mL/min, sample 1 μL] and TLC [Silica gel PF_{254}-gilshaltig (Merck), 20 cm × 20 cm, thickness 2.2 mm, *n*-hexane] (see Table I).

Products were identified by comparisons of mp, IR, NMR, and/or retention times on GLC to those of the corresponding authentic samples (**4**, **5**, **7**, and **8**).

(21) L. F. Fieser and M. Fieser, "Reagents for Organic Syntheses", Vol. 1, Wiley, New York, 1967, p 302; E. S. Gould, "Mechanism and Structure in Organic Chemistry", Holt and Co., New York, 1959, p 103.

UV Spectra of the Irradiated Solutions: Detection of 6a and 6b in Vacuo. An aqueous solution of **3a** or **3b** (3.7 mM; 9 mL) containing 150 μL of 1 N KOH was degassed and then irradiated at 15 °C in a quartz cell. After 3 min of irradiation, the UV spectra of the solution were measured, λ_{max} (H_2O) for **3a** 435 nm (lit.[8] 435 nm). This maximum disappeared, and a maximum at 324 nm appeared on aeration, λ_{max} (H_2O) for **3b** 335 nm (sh) (authentic sample of **8b**, 335 nm).

Quenching with 1,3-Pentadiene. (a) Quenching of fluorescence of **3** in an aqueous solution (5.0 mM) with various concentrations of 1,3-pentadiene (distilled just before use) (1.3, 2.9, 5.2, 10.3, and 20.7 mM) was observed by the fluorometer at 25 °C. (b) Quenching of the products of desulfonylation and desulfonation from **3** in an aqueous solution (5.0 mM) with various concentrations of 1,3-pentadiene (1.3, 2.9, 5.2, 10.3, and 20.7 mM) in vacuo or in air was observed by UV and GLC. The $k_q\tau$ values were calculated from the slopes of the Stern–Volmer plots[16] (see Table II).

Registry No. 3a, 17213-01-3; **3b**, 85-47-2; **3c**, 65090-17-7; **4a**, 120-12-7; **4b**, 130-14-3; **4c**, 108-67-8; **5b**, 604-53-5; **7a**, 84-65-1; **7b**, 130-15-4; **8b**, 90-15-3; **8c**, 527-60-6; 9-nitroanthracene, 602-60-8; bimesitylene, 4482-03-5; mesitylenesulfonic acid, 3453-83-6.

Cationic Cyclizations. Cation Generation through Magnesium Alkoxide Thermolysis. Regioselective Indene Formation

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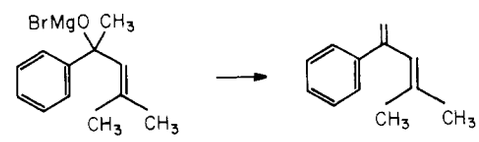
In contrast to the behavior of sodium or potassium alkoxides, magnesium alkoxides undergo heterolytic α cleavage to generate carbocations. Products resulting from such carbonium ions are mediated by their generation in strong base and exhibit remarkable purity and regioselectivity. Thus solid state thermolysis of magnesium salts of substituted 1-phenylallyl alcohols leads to efficient indene formation without the subsequent double bond migration characteristic of acid-mediated cyclizations. Compounds produced by such methods include 1-phenyl-3-methylindene, 1,3-diphenylindene, 1-phenyl-2-methylindene, and 1,1,3-trimethylindene. Similarly produced was 9-phenylfluorene. Magnesium alkoxide pyrolysis thus provides a method for trapping the kinetic product of rearrangement.

Alkali metal alkoxides of certain tertiary alcohols readily undergo heterolytic β scission to generate ketones and carbanion derivatives in a reaction which is the reverse of the corresponding carbanion addition reaction (eq 1).[1]

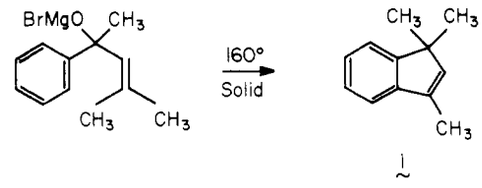
$$R_3C\text{–}O^- M^+ \rightarrow R^- M^+ + R_2C{=}O \qquad (1)$$

This reaction has been used in extensive mechanistic studies of carbanions. Until recently, the corresponding thermolyses of magnesium alkoxides have not been carried out.[2] We anticipated that the stronger magnesium–oxygen bond would have a pronounced effect upon the reactivity of such alkoxides, and we were intrigued by a report that the alkoxide generated by addition of phenylmagnesium bromide to 4-methyl-3-propen-2-one underwent facile 1,2 elimination to the olefin (Scheme I).[3] In the course of repeating that work, we observed the precipitation of the alkoxide from ether solution as a fluffy white solid and proceeded to investigate its chemistry directly by isolation

Scheme I



Scheme II



of the precipitate under inert atmosphere. When the dried powder was pyrolyzed at 160 °C under vacuum, a single liquid product was produced in high yield, 1,1,3-trimethylindene (Scheme II). The remarkable facility for indene formation prompted us to a further investigation of this reaction, not only with the anticipation that this would provide us with a single-step high-yield indene synthesis, but also with the expectation that mechanistic investigations would disclose the intermediates involved

(1) H. D. Zook, J. March, and D. F. Smith, *J. Am. Chem. Soc.*, 81, 1617 (1959).

(2) (a) During the preparation of this manuscript, the pyrolysis of magnesium alkoxides leading to elimination to olefins was reported. (b) E. C. Ashby, G. F. Willard, and Anil B. Goel, *J. Org. Chem.*, 44, 1221 (1979).

(3) V. I. Esafov, *Zh. Obsch. Khim.* 27, 2711 (1957).

0022-3263/79/1944-4584$01.00/0

Table I. Pyrolysis of Magnesium Phenylallyl Alkoxides

starting material	method	product (yield, %)	ref
$(CH_3)_2C{=}CHC(OMgBr)(CH_3)Ph$	A	1,1,3-trimethylindene (63)	7
$PhCH{=}CHC(OMgBr)Ph_2$	B	1,3-diphenylindene (55)	4
$Ph_2C{=}CHC(OMgBr)HPh$	B	1,3-diphenylindene (48)	4
trans-$PhCH{=}CHC(OMgBr)(CH_3)Ph$	B	3-methyl-1-phenylindene (45)	5, 6
cis-$PhCH{=}CHC(OMgBr)(CH_3)Ph$	B	3-methyl-1-phenylindene (62)	5, 6
$Ph(CH_3)C{=}C(OMgBr)HCHPh$	A	3-methyl-1-phenylindene (43)	5, 6
$PhCH{=}C(CH_3)C(OMgBr)HPh$	A	2-methyl-1-phenylindene (60)	
trans-$PhCH{=}CHC(OMgBr)HPh$	A	1,3-diphenylpropene (42)	
cis-$PhCH{=}CHC(OMgBr)HPh$	B	1,3-diphenylpropene (38)	

and the significance of the metal in determining the products. The experimental results which we now report strongly implicate cations as reactive intermediates but generated in such a way as to alter significantly the subsequent rearrangement steps. We suggest that magnesium alkoxides provide a new class of cation precursors in the presence of strong base which may have applications in further synthetic and mechanistic studies.

Methods. Our studies require the preparation of solid magnesium salts of 1-phenylallyl alcohols for pyrolysis. Where possible, the magnesium salts were prepared by direct addition of phenylmagnesium bromide to the appropriate α,β-unsaturated aldehyde or ketone (method A), using diethyl ether as solvent. In cases where conjugate addition was known to occur, method B was employed. This method employed phenyllithium addition to the aldehyde or ketone followed by treatment of the isolated alcohol with ethylmagnesium bromide, again in diethyl ether. In all cases except one, the unsaturated ketones or aldehydes were available commercially or by literature procedures. For the requisite β-methylcinnamaldehyde (3), we developed a one-step synthesis involving phenyllithium addition to the commercially available 4-methoxy-3-buten-2-one followed by hydrolysis–elimination upon workup. Of interest was the concurrent production of 2,4-diphenyl-3-buten-2-ol (eq 2) which arose either by an

$$CH_3OCH{=}CHCOCH_3 \xrightarrow[2.\ PhSO_2OH]{1.\ PhLi} Ph(CH_3)C{=}CHCHO + PhCCH_3(OH)CH{=}CHPh \quad (2)$$

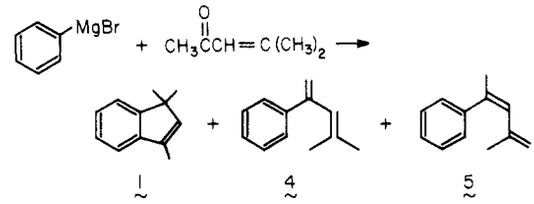
initial 1,4 addition to the ketone or by a base-catalyzed isomerization of the initial 1,2 adduct followed by elimination of lithium methoxide. We did not investigate this result further.

Using either method A or method B, we observed that the magnesium salt precipitated when ca. 80% of an equivalent of Grignard reagent had been added; the addition was continued to 100%. Addition of further amounts caused the precipitate to resolubilize and reduced the yield. The precipitate was removed by filtration under argon and then pyrolyzed at 160 °C in vacuo, and the product(s) were collected in an ice trap.

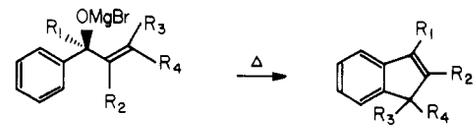
The importance of obtaining dry crystalline magnesium salts cannot be overemphasized. When filtration was omitted, or when no precipitate formed and the solvent was removed by evaporation, products were reduced in yield and complicated by side products. For instance, the thermolysis of crystalline 1,3-dimethyl-1-phenyl-2-butene 1-oxide magnesium bromide produced 1,1,3-trimethylindene (1), 98% pure (GC analysis), while the thermolysis of a sticky glassy solid obtained from direct ether evaporation gave three products in approximately equal amounts (Scheme III).

Scope and Generality. Indenes are conventionally synthesized from dehydration of indanols obtained from reduction of or addition to the corresponding indanones. The ease of trimethylindene formation suggested that

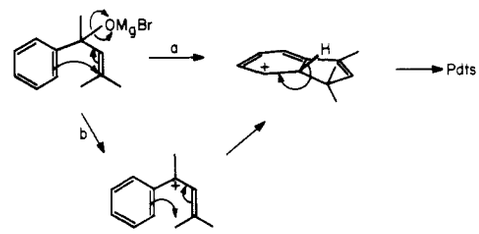
Scheme III



Scheme IV



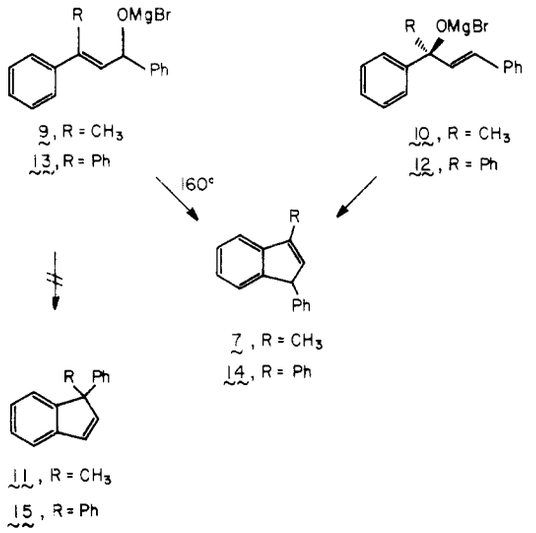
Scheme V



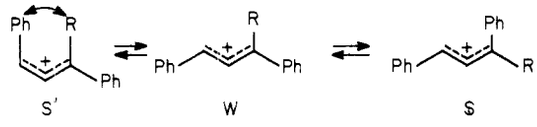
pyrolysis of substituted magnesium 1-phenylallyl alkoxides could provide a facile one-pot synthesis of substituted indenes according to Scheme IV. Accordingly, we examined the products resulting from thermolysis of magnesium 1-phenylallyl alkoxides substituted with hydrogen, methyl, and phenyl. The thermolysis at 160 °C of the crystalline powders produced in almost every case an indene. Although yields were modest, the products were characterized by exceptional purity, including 1,3-diphenylindene, which crystallized spontaneously despite reports of its reluctant crystallinity.[4] The one requirement for the efficacy of the reaction appeared to be the presence of two substituents in addition to the requisite phenyl group. Thus the alkoxide derived from 1-phenyl-2-methyl-2-propen-2-ol produced a complex mixture of products, and that derived from 1,3-diphenylpropenol produced the product of hydride abstraction, 1,3-diphenylpropene (6). The precursors and indene products produced are shown in Table I. Especially noteworthy is the production of 1-phenyl-3-methylindene (7) without the double bond migration characteristic of acid conditions.[5,6] Also produced was the previously unreported 1-phenyl-2-methylindene (8).

(4) L. L. Miller and R. F. Boyer, *J. Am. Chem. Soc.*, **93**, 650 (1971).
(5) A. R. Taylor, G. W. Keen, and E. J. Eisenbraun, *J. Org. Chem.*, **42**, 3477 (1977).
(6) (a) W. G. Miller and C. U. Pittman, Jr., *J. Org. Chem.*, **39**, 1955 (1974); (b) C. U. Pittman, Jr., and W. G. Miller, *J. Am. Chem. Soc.*, **95**, 2947 (1973).
(7) R. M. Roberts and M. B. Abdel-Baset, *J. Org. Chem.* **41**, 1698 (1976).

Scheme VI



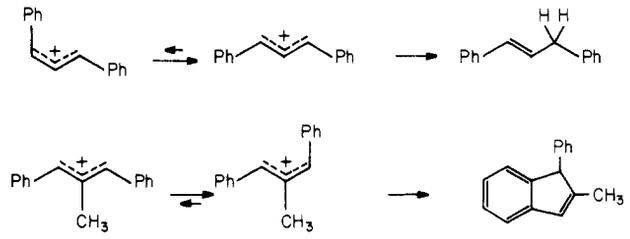
Scheme VII



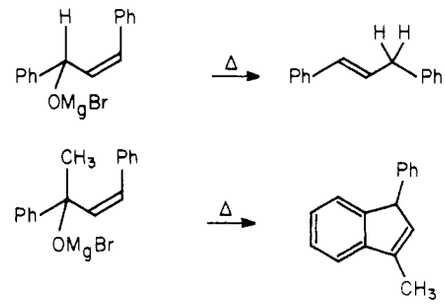
Results. Regiospecificity vs. Regioselectivity. The purity and specificity of products obtained despite the intrinsic possibility of additional isomers suggested that the first mechanistic consideration should be whether the reaction was regiospecific or regioselective. Specifically, if the reaction involved concerted elimination of magnesium oxide (step a of Scheme V), then the product should reflect the position of the oxymagnesium moiety in the starting material, i.e., the reaction should be *regiospecific*. However, if the mechanism involved breaking the carbon–oxygen bond as a first step (step b of Scheme V), then an allyl cation would be formed which should produce the same product regardless of the regioisomer used, i.e., the reaction should be *regioselective*. To distinguish between these two possibilities, the alkoxides of 1,3-diphenyl-2-buten-1-ol (**9**) and its regioisomer 2,4-diphenyl-3-buten-2-ol (**10**) were thermolyzed. In each case, the same indene was produced, namely, 1-phenyl-3-methylindene (**7**). No detectable amounts (NMR analysis) of 1-phenyl-1-methylindene (**11**) were produced. Similarily, the magnesium alkoxides of 1,1,3-triphenyl-2-propen-1-ol (**12**) and 1,3,3-triphenyl-2-propen-1-ol (**13**) both produced 1,3-diphenylindene (**14**) (Scheme VI). Control reactions to 50% conversion and analysis of the remaining alkoxide demonstrated that preisomerization did not occur. Thus we conclude that the reaction is regioselective, that a common intermediate is involved, and that the intermediate is a carbonium ion by analogy with independently produced carbocations.[6]

The next mechanistic consideration we faced was determining the origin of the regioselectivity, i.e., what determined the predisposition of the 1,3-diphenyl-1-methylallyl cation to cyclize to indene **7** at the expense of indene **11**. This problem has been alluded to by Pittman and co-workers,[6] who suggested that the selectivity effect could in principle be rationalized by (1) a conformational preference or (2) an intrinsically greater rate constant for electrophilic attack by the less stabilized end of the allylic system. The conditions utilized for the studies reported here, which circumvent the formation of indanyl cations, as well as further examples of cyclizations, convincingly

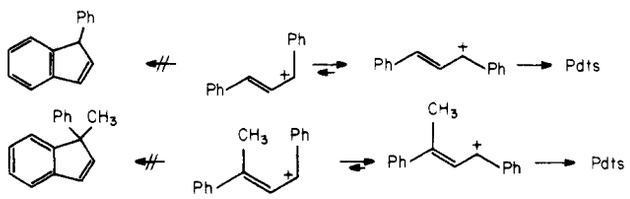
Scheme VIII



Scheme IX



Scheme X



demonstrate that the former is the more compelling argument. This rationale can be outlined in the following way: For the substituted 1,3-diphenylallyl cations, three conformations may be presumed to exist in equilibrium, an extended *E,E* ("W") conformation and two *E,Z* ("S") conformations (Scheme VII). We note that the *Z,Z* ("U") conformation is too severely hindered to play a controlling role. Only the S conformations can lead to indene product, and we see that conformation S leads to the observed product while conformation S′ leads to the unobserved product. Moreover, the severe flagpole interaction present in conformer S′ decreases its concentration markedly over that of the conformer S, and the product reflects the relative concentrations. This rationale is confirmed by the products from the 1,3-diphenylallyl cation itself and the 1,3-diphenyl-2-methylallyl cation. In the first case no indene product is observed, but rather the hydride abstraction product, 1,3-diphenylpropene. In contrast, the 2-methyl-substituted cation produces the anticipated 1-phenyl-2-methylindene product. If the lack of stabilization at the end of the allyl system were the controlling factor, both cations should lead to parallel results. Again, the relative populations of the cation conformers control the reaction, the central methyl group facilitating the population of the S conformer leading to indene product. In the absence of this effect, the S conformer is not populated and hydride abstraction from the W confirmation intervenes (Scheme VIII).

We attempted to test this effect by producing the unobserved S′ conformers directly. Thus the magnesium alkoxides of *cis*-1,3-diphenyl-2-propen-1-ol and *cis*-2,4-diphenyl-3-buten-2-ol were thermolyzed. In each case, the products were identical with those observed from the trans isomers (Scheme IX). We conclude that isomerization to the W conformation is faster than cyclization to the indene, so that the stereochemical integrity of the S conformer is

Table II. Pyrolysis of Substituted Magnesium Diphenyl Methoxides

starting material	product (yield, %)
$Ph_3COMgBr$	Ph_3CH (50) + 9-phenylfluorene (32)
$Ph_2CHOMgBr$	Ph_2CH_2 (65)
$Ph_2C(CH_3)OMgBr$	$Ph_2C{=}CH_2$ (75)

lost, resulting in the previously described products.

A New Substituted Fluorene Synthesis. If the double bond of the 1-phenylallyl alcohol is replaced by a benzene ring, the same process leading to indene formation should lead to fluorene formation. This result was in fact obtained for the alkoxide of triphenylmethanol, which produced 9-phenylfluorene in 32% yield. However, the dominant product was that of hydride abstraction, triphenylmethane. In contrast, the magnesium derivative of benzhydrol produced exclusively the product of hydride abstraction, diphenylmethane, while magnesium 1,1-diphenyl ethoxide produced the elimination product, 1,1-diphenylethylene (see Table II). Again, the products are reminiscent of a cationic mechanism and correspond in at least one case to the products resulting from treatment of the alcohol with concentrated sulfuric acid.[8]

Conclusions. Thermolysis of magnesium alkoxides of 1-phenylallyl alcohols provides a synthesis of substituted indenes without the experimental and mechanistic complications of strong acid solutions,[6] despite the intervention of carbocations. The obvious extension to acid-labile functional groups has not been carried out. Magnesium oxide constitutes a novel leaving group which may have significant applications in organic synthesis.[9]

The contrasting behavior of sodium and magnesium alkoxides dramatically illustrates the principle of microscopic reversibility. In the case of the sodium alkoxides, the reaction observed is the reverse of the nucleophilic addition of an organosodium compound to a ketone. In the case of the magnesium alkoxides, the products reflect a different process. Nucleophilic attack of organomagnesium compounds on ketones is thought to involve an electron transfer step.[10] In other words, at some point on the energy surface corresponding to nucleophilic attack, electron demotion occurs to a state corresponding to a geminate radical pair. Thus β cleavage from magnesium alkoxides cannot occur as it does for sodium alkoxides because the state corresponding to this process is an excited state. The reacting species follows the lowest energy pathway available, which under the constraints discussed here leads most generally to indene formation.

Experimental Section

All NMR spectra were recorded on a Varian T-60 spectrometer, and chemical shifts are reported in δ units. Galbraith Laboratories, Inc. of Knoxville, Tenn., performed elemental analyses. Melting points were measured on a hotstage apparatus and are uncorrected. Argon was deoxygenated and dried using an Ace-Burlitch inert atmosphere system.

Materials. Chalcone, cinnamaldehyde, 3-phenylcinnamaldehyde, 2-methylcinnamaldehyde, mesityl oxide, fluorenone, and benzophenone were commercial samples and were used without further purification, except for mesityl oxide, which was distilled.

cis-Chalcone was prepared by UV irradiation of *trans*-chalcone, according to the method of Wasserman.[11] The cis isomer was separated from the trans isomer by silica gel chromatography, although a more convenient method involved carrying both isomers through the next step, e.g., methyllithium addition, and chromatographing the resulting cis and trans alcohols.

cis-Diphenyl-2-propen-1-ol was prepared by lithium aluminum hydride reduction of *cis*-chalcone by the published method.[12]

3-Methylcinnamaldehyde. A 10.35-g portion (0.103 mol) of 4-methoxy-3-buten-2-one (Aldrich) in 10 mL of ether was cooled in an ice bath and treated with 75 mL of 1.5 M phenyllithium in ether. After 30 min, the mixture was quenched with water, ether extracted, the solvent removed in vacuo, and the residue taken up in 50 mL of benzene to which a few crystals of *p*-toluenesulfonic acid had been added. The solution was stirred for 30 min, taken up in 200 mL of ether, and washed successively with 10% sodium bicarbonate and water. The residue upon drying and concentrating was vacuum distilled to yield 4.10 g (28.1 mmol, 27%) of a 3:1 *E*/*Z* mixture of pure 3-methylcinnamaldehyde with spectra corresponding to those reported.[13] NMR and TLC analysis of the residue showed the major component to be 2,4-diphenyl-3-buten-2-ol.[6b]

***cis*-2,4-Diphenyl-3-butenol.** A 5.86-g portion of a 2:1 cis/trans mixture of chalcone was treated in 50 mL of anhydrous ether with 13.4 mL of 2.1 M methyllithium in hexane. The solution was stirred for 30 min, quenched with water, and ether extracted. The concentrated extracts were chromatographed on a 2.5 × 40 cm column of silica gel, using 20% ether–hexane as eluent. Fraction 3 (500-mL fractions) yielded 1.234 g (5.56 mmol, 20%) of pure *cis*-2,4-diphenyl-3-butenol. The NMR spectrum was as follows: ($CDCl_3$) δ 1.59 (s, 3 H), 2.56 (2, 1 H), 6.12 (d, J = 14 Hz, 1 H), 6.62 (d, J = 14 Hz, 1 H), 7.14–7.70 (m, 10 H).

Preparation of Magnesium Alkoxides. Method A. A solution of 10.0 mmol of the requisite unsaturated carbonyl compound in 10 mL of anhydrous ether was treated at 0 °C with 10 mmol of phenylmagnesium bromide (ca. 1.0 M, titrated) in anhydrous ether. The slurry was allowed to stir for 30 min, and the solvent was removed by inserting a filter stick and pressurizing the flask with argon. The remaining solvent was removed in vacuo, and the pyrolysis was carried out as indicated below.

Preparation of Magnesium Alkoxides. Method B. The requisite allylic alcohol was prepared by phenyllithium or methyllithium addition to the α,β-unsaturated carbonyl compound. The alcohol was isolated by ether extraction and dried under vacuum, then 10.0 mmol were redissolved in 10 mL of ether. To this solution was added dropwise at 0 °C 10 mmol of freshly prepared ethylmagnesium bromide in 10 mL of ether. The solvent was removed and the white solid isolated as above.

Pyrolysis of Magnesium Alkoxides. The bulb containing the solid dry magnesium alkoxide prepared as above was placed in an Aldrich Kugelrohr oven and attached to an elongated U-tube immersed in a dry ice bath. The bulb was evacuated, and the oven was heated gradually to a temperature of 160 °C, where it was maintained until no further product evolved (ca. 2 h). The products generally crystallized immediately, although in some instances the presence of a slight yellowish impurity necessitated silica gel chromatography. Products prepared in this manner are reported in Tables I and II. The physical properties are as reported except for 1-phenyl-3-methylindene, whose corrected[5] NMR spectrum is as follows: NMR ($CDCl_3$) δ 2.13 (t, J = 1.5 Hz, 3 H), 4.43 (m, 1 H), 6.07 (m, 1 H), 7.0–7.6 m (m, 9 H).

2-Methyl-1-phenylindene. A solution of 15.1 g (103 mmol) of 2-methylcinnamaldehyde in 50 mL of ether was treated at 0 °C with 100 mmol of 1.0 M phenylmagnesium bromide in ether, and the resulting precipitate was isolated and pyrolyzed at 160 °C as described above. The resulting crystalline solid was recrystallized from methanol to yield 12.3 g (59.7 mmol, 60%) of colorless needles, mp 47.5–49.0 °C. The spectral data were as

(8) F. Bergmann and S. Israelashwili, *J. Am. Chem. Soc.*, 68, 1 (1946).

(9) The eliminations reported by Ashby[2b] provide dramatic, if contrasting, support for this statement. We rationalize the difference in elimination vs. cyclization as the result of increased cation stability for phenylallyl systems. That these reactions are *not* Lewis acid catalyzed cyclizations of olefins formed by 1,2 elimination is indicated by the failure of such olefins to cyclize under the pyrolytic conditions. Finally, we note that in cases of reduced substitution on the allyl system elimination begins to compete.

(10) See I. G. Lopp, J. D. Buhler, and E. C. Ashby, *J. Am. Chem. Soc.*, 97, 4966 (1975), and references contained therein.

(11) H. H. Wasserman and N. E. Aubrey, *J. Am. Chem. Soc.*, 77, 590 (1955).

(12) R. E. Lutz and J. O. Weiss, *J. Am. Chem. Soc.*, 77, 590 (1955).

(13) G. Quinkert, M. Hintzmann, P. Michaelis, P. Jürges, Helmut Appelt, and U. Krüger, *Justus Liebigs Ann. Chem.*, 748, 38 (1971).

follows: NMR ($CDCl_3$) δ 1.86 (br s, 3 H), 4.24 (br s, 1 H), 6.50 (m, 1 H), 6.90–7.60 (m, 9 H); IR (KBr) 3000, 1600, 1450, 1432, 741, 729, 692 μm.

Anal. Calcd for $C_{16}H_{14}$: C, 93.15; H, 6.85. Found: C, 92,84; H, 6.83.

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Registry No. 1, 2177-45-9; (*E*)-3, 21866-70-6; (*Z*)-3, 21878-52-4; 6, 3412-44-0; 7, 22360-63-0; 8, 37634-53-0; 9, 71831-93-1; *trans*-10, 71831-94-2; *cis*-10, 71831-95-3; 12, 71831-96-4; 13, 71831-97-5; 14, 4467-88-3; 1,3-dimethyl-1-phenyl-2-butene 1-oxide magnesium bromide, 71831-98-6; 2-methyl-1,3-diphenyl-2-propene 1-oxide magnesium bromide, 71831-99-7; *trans*-1,3-diphenyl-2-propene 1-oxide magnesium bromide, 71832-00-3; *cis*-1,3-diphenyl-2-propene 1-oxide magnesium bromide, 71832-01-4; 4-methyl-3-penten-2-one, 141-79-7; *trans*-1,3-diphenyl-2-propen-1-one, 614-47-1; 3,3-diphenyl-2-propenaldehyde, 1210-39-5; *cis*-chalcone, 614-46-0; 2-methylcinnamaldehyde, 101-39-3; *trans*-cinnamaldehyde, 14371-10-9; *cis*-cinnamaldehyde, 57194-69-1; *trans*-1,1,3-triphenyl-2-propen-1-ol, 71832-02-5; 1,3,3-triphenyl-2-propen-1-ol, 21711-85-3; *trans*-2,4-diphenyl-3-buten-2-ol, 56763-56-5; *cis*-2,4-diphenyl-3-buten-2-ol, 71832-03-6; *cis*-1,3-diphenyl-2-propen-1-ol, 62839-70-7; 4-methoxy-3-buten-2-one, 4652-27-1; triphenylmethane 1-oxide magnesium bromide, 71832-04-7; diphenylmethane 1-oxide magnesium bromide, 36233-75-7; methyldiphenylmethane 1-oxide magnesium bromide, 68986-36-7; triphenylmethane, 519-73-3; 9-phenylfluorene, 789-24-2; diphenylmethane, 101-81-5; 1,1-diphenylethene, 530-48-3.

Microbial Stereodifferentiating Reduction of the Carbonyl Groups Located on the C_2 Axes of Gyrochiral Molecules[1]

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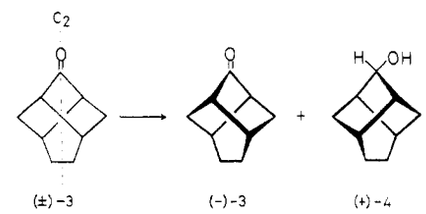
The enantiomer selectivity of *Curvularia lunata* and *Rhodotorula rubra* with respect to some C_2 ketone substrates having the C_2 axis coincident with the carbonyl axis has been examined. Both microbes were found to exhibit a marked stereodifferentiation between enantiomers of (±)-9-*twist*-brendanone (**3**), (±)-2-brexanone (**5**), (±)-D_3-trishomocubanone (**8**), (±)-bisnoradamantanone (**10**), (±)-biphenyl (**14**), and (±)-α-binaphthyl (**16**) bridged ketones, selectively reducing the *P*-C_2 ketone enantiomers (**2**).

Flanking a carbonyl group with substituents degenerates the C_{2v} symmetry inherent to the original carbonyl group to give C_s, C_2, and C_1 ketones.[2] The molecular environment around the carbonyl group of these ketones can readily be visualized when the ketones are oriented in a three-dimensional system (Figure 1). The faces around the carbonyl group are enantiotopic[3] in a C_s ketone and diastereotopic[3] in a C_1 ketone, and microbial stereodifferentiation between these faces has been well documented.[4]

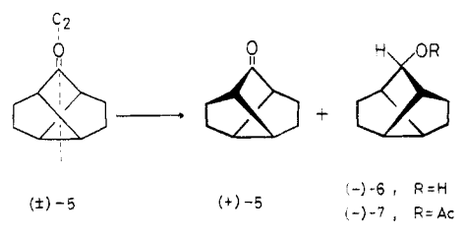
In a C_2 ketone with two identical chiral substituents flanking the carbonyl group, the faces are homotopic[3] in an internal comparison, and the only stereochemical distinction is that between enantiotopic faces in each enantiomer in an external comparison.

Our continuing interest in gyrochiral[5] cage-shaped molecules[6] has led us to study microbial stereodifferentiation between the enantiotopic faces of *M*-C_2 ketone **1**

Scheme I



Scheme II



and *P*-C_2 ketone **2**[7] (Figure 2) on which there has been no investigation reported, and this paper reports our results with *Curvularia lunata* and *Rhodotorula rubra*.

Results

Microbial Stereodifferentiating Reduction of Cage-Shaped C_2 Ketones. (±)-Tricyclo[4.3.0.0^{3,8}]nonan-9-one ("9-*twist*-Brendanone", 3) (Scheme I).[9] Monitoring the process with gas chromatography indicated that 40 h of incubation with *C. lunata* at 29 °C was enough

(1) Presented at the 26th IUPAC Congress, Sept 8, 1977, Tokyo, Japan, Abstracts p 63. For a preliminary account of this work see: Nakazaki, M.; Chikamatsu, H.; Naemura, K.; Nishino, M.; Murakami, H.; Asao, M. *J. Chem. Soc., Chem. Commun.* **1978**, 667–8. For a review summarizing our studies on stereodifferentiating microbial reduction see: Nakazaki, M.; Chikamatsu, H. *Kagaku No Ryoiki* **1977**, *31*, 819–33.

(2) In this paper, ketones are conveniently classified according to their symmetry: C_s ketones belong to the C_s point group and have the plane of symmetry coincident with the carbonyl plane; C_2 ketones belong to the C_2 point group and have the C_2 axis coincident with the carbonyl axis; C_1 ketones have no symmetry element passing through the carbonyl axis.

(3) Mislow, K.; Raban, M. *Top. Stereochem.* **1967**, *1*, 1–38.

(4) Concise reviews can be found in: (a) Bentley, R. "Molecular Asymmetry in Biology"; Academic Press: New York, 1970; Vol. 2, pp 41–50. (b) Sih, C. J.; Rosazza, J. P. "Applications of Biochemical Systems in Organic Chemistry"; Jones, J. B., Sih, C. J., Perlman, D., Eds.; Wiley: New York, 1976; Part 1, Chapter 3. (c) Kieslich, K. *Synthesis* **1969**, *1*, 147–57.

(5) This name is proposed to describe the symmetry of a shape which is chiral but not asymmetric; cf.: Nakazaki, M.; Naemura, K.; Yoshihara, H. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 3278–84.

(6) For a review see: Nakazaki, M.; Naemura, K. *Yuki Gosei Kagaku Kyokai Shi* **1977**, *35*, 883–96.

(7) An inspection of the quadrant projection formula (Figure 2) should support the adequacy of our adopting *M* and *P* helicity[8] to describe these chiralities.

(8) Cahn, R. S.; Ingold, C. K.; Prelog, V. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 385–415.

(9) All structural formulas in this paper are presented in their absolute configurations.

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