

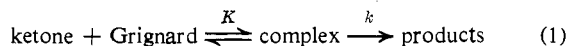
Kinetics and Mechanism of the Reaction of Grignard Reagents with Ketones¹

Stephen E. Rudolph, Larry F. Charbonneau, and Stanley G. Smith*

Contribution from the Department of Chemistry, University of Illinois, Urbana, Illinois 61801. Received August 22, 1972

Abstract: The kinetics of the reaction of 4-methylmercaptoacetophenone with cyclopentylmagnesium reagents, measured by stopped-flow uv and ir spectroscopy in the presence of excess organomagnesium reagent, indicate that, under these conditions, the reaction is first order in ketone, but that the kinetic order in organomagnesium approaches one in dilute solution and zero at high concentration, which corresponds to a mechanism involving complex formation between the reactants. Addition of MgBr₂ to 0.15 M dicyclopentylmagnesium depresses the observed first-order rate constant from 405 (0.002 M bromide) to 1.3 sec⁻¹ (0.84 M bromide). The kinetics and products are consistent with both (C₅H₉)₂Mg and C₅H₉MgBr contributing to the reactions, with a relative contribution which is a sensitive function of the concentration of magnesium bromide. The rate level with the deuterated reagent, 2,2,5,5-tetradeuteriocyclopentylmagnesium bromide, corresponds to a k_H/k_D of 2.0 for the reduction component of the reaction.

The reaction² of many ketones with Grignard³ reagents in diethyl ether seems to proceed through a rapidly formed complex^{4,5} between the reactants which subsequently rearranges to form products.^{6,7} The



products may, of course, involve simple addition to the carbonyl group, reduction when a β hydrogen is present in the Grignard reagent,⁸ and enolization if α protons are present in the ketone. If the structure of the ketone provides stabilization of an unpaired electron, ketyl formation^{9,10} resulting from single electron transfer from an organomagnesium compound may also contribute to the course of the reaction.

Since typical Grignard reagents are in equilibrium with the corresponding dialkylmagnesium species,^{11,12}

eq 2, reaction with a ketone could proceed through



RMgX, R₂Mg,¹³⁻¹⁶ or both of these organometallic compounds.^{10,17} Available data indicate that, in general, the dialkylmagnesium is substantially more reactive than the corresponding Grignard reagent.^{10,15-18} Convincing quantitative dissections^{19,20} of the contribution of R₂Mg and RMgX to the overall rate level and product composition are lacking, but it is clear that, in the case of methylmagnesium chloride addition to 4-methylmercaptoacetophenone,¹⁷ not all of the reaction goes through dimethylmagnesium.

The conceptually simple expedient of shifting the Schlenk equilibrium,^{11a} eq 2, in favor of RMgX by addition of MgX₂ is complicated by the formation of a complex between MgX₂ and the ketone, as evidenced by a new absorbance in the uv spectrum⁵ and by interaction between Grignard reagents and MgX₂, as judged by increased solubility of magnesium halides in ether solutions of Grignard reagents^{11b,21} and the isolation of mixed Grignard-magnesium halide species.^{22b}

Since Grignard reagents and magnesium halides are relatively polar, association^{11,22-24} is often observed in solvents such as diethyl ether, and apparent degrees of association, i , have been reported to range from near

(1) (a) This work was supported by the National Science Foundation; (b) S. G. Smith, S. E. Rudolph, L. Charbonneau, and J. Billet, presented in part at the 162nd National Meeting of the American Chemical Society, Washington, D. C., Sept 1971.

(2) For reviews see, e.g., (a) M. S. Kharasch and O. Reinmuth, "Grignard Reactions of Nonmetallic Substances," Prentice-Hall, New York, N. Y., 1954; (b) B. J. Wakefield, *Organometal. Chem. Rev.*, **1**, 131 (1966); (c) W. Tochtermann, *Angew. Chem.*, **5**, 351 (1966); (d) R. E. Dessy and W. Kitching, *Advan. Organometal. Chem.*, **4**, 280 (1966); (e) E. C. Ashby, *Quart. Rev.*, **Chem. Soc.**, **2**, 259 (1967).

(3) V. Grignard, *C. R. Acad. Sci.*, **130**, 1322 (1900).

(4) (a) D. O. Cowan and L. A. Dolak, *J. Org. Chem.*, **31**, 4296 (1966); (b) F. Strauss, *Justus Liebigs Ann. Chem.*, **393**, 235 (1912).

(5) S. G. Smith, *Tetrahedron Lett.*, 407 (1963).

(6) J. Meisenheimer and J. Casper, *Chem. Ber.*, **54B**, 1655 (1921).

(7) See S. G. Smith and G. Su, *J. Amer. Chem. Soc.*, **86**, 2750 (1964); S. G. Smith and G. Su, *ibid.*, **88**, 3995 (1966).

(8) (a) V. Grignard, *Ann. Chim. (Paris)*, **7**, 24, 433 (1901); (b) N. Iositch and J. Russ, *Phys. Chem. Soc.*, **36**, 443 (1904); (c) P. Sabatier and A. Mailhe, *Ann. Chim. (Paris)*, **8**, 10 (1907); (d) C. R. Noller, W. E. Crebe, and L. H. Knox, *J. Amer. Chem. Soc.*, **54**, 4690 (1932).

(9) (a) J. Schmidlin, *Chem. Ber.*, **39**, 4198 (1906); (b) G. A. Russel, E. G. Janzen, and E. T. Strom, *J. Amer. Chem. Soc.*, **86**, 1807 (1964); (c) K. Maruyama, *Bull. Chem. Soc. Jap.*, **37**, 897 (1964); (d) C. Blomberg and H. S. Mosher, *J. Organometal. Chem.*, **13**, 519 (1968); (e) E. C. Ashby, F. W. Walker, and H. M. Neumann, *Chem. Commun.*, **330** (1970); (f) H. R. Ward, R. G. Lawler, and T. A. Marzilli, *Tetrahedron Lett.*, 521 (1970).

(10) J. Billet and S. G. Smith, *J. Amer. Chem. Soc.*, **90**, 4108 (1968).

(11) (a) W. Schlenk, *Chem. Ber.*, **64B**, 734 (1931); (b) M. B. Smith and W. E. Becker, *Tetrahedron*, **23**, 4215 (1967); (c) M. B. Smith and W. E. Becker, *Tetrahedron Lett.*, 3843 (1965); (d) M. B. Smith and W. E. Becker, *Tetrahedron*, **22**, 3027 (1966); (e) R. Stewart and A. R. Ubbelohde, *J. Chem. Soc.*, 2649 (1949); (f) D. F. Evans and G. V. Fazakerly, *J. Chem. Soc. A*, 184 (1971); (g) D. F. Evans and M. S. Khan, *ibid.*, 1643 (1967).

(12) (a) G. E. Parris and E. C. Ashby, *J. Amer. Chem. Soc.*, **93**, 1206 (1971); (b) E. C. Ashby, G. Parris, and F. Walker, *Chem. Commun.*, 1464 (1970).

(13) C. Swain and W. E. Boyles, *J. Amer. Chem. Soc.*, **73**, 870 (1951).

(14) D. J. Cram, F. Elhafez, and H. Nyquist, *ibid.*, **76**, 22 (1954).

(15) (a) H. O. House and D. D. Traficante, *J. Org. Chem.*, **28**, 355 (1963); (b) H. O. House and J. E. Oliver, *ibid.*, **33**, 929 (1968).

(16) (a) T. Holm, *Acta Chem. Scand.*, **21**, 2753 (1967); (b) T. Holm, *Tetrahedron Lett.*, 3329 (1966); (c) *Acta Chem. Scand.*, **20**, 1139 (1966).

(17) J. Billet and S. G. Smith, *Tetrahedron Lett.*, 4467 (1969).

(18) (a) N. M. Bikales and E. I. Becker, *Can. J. Chem.*, **41**, 1329 (1963); (b) M. S. Singer, R. M. Salinger, and H. S. Mosher, *J. Org. Chem.*, **32**, 3821 (1967).

(19) S. G. Smith and G. Su, *Tetrahedron Lett.*, 4417 (1966).

(20) (a) E. C. Ashby, J. Laemmle, and H. M. Neumann, *J. Amer. Chem. Soc.*, **93**, 4601 (1971); (b) E. C. Ashby, J. Laemmle, and H. M. Neumann, *ibid.*, **94**, 5421 (1972).

(21) W. E. Doering and C. R. Noller, *ibid.*, **61**, 3436 (1939).

(22) (a) J. Toney and G. Stucky, *Chem. Commun.*, 1168 (1967); (b) J. Toney and G. Stucky, *J. Organometal. Chem.*, **28**, 5 (1971).

(23) (a) A. P. Terentjew, *Z. Anorg. Chem.*, **156**, 73 (1926); (b) J. Meisenheimer and W. Schlichenmaier, *Chem. Ber.*, **61**, 720 (1928); (c) A. D. Vreugdenhil and C. Blomberg, *Recl. Trav. Chim. Pays-Bas*, **84**, 39 (1965).

(24) (a) E. C. Ashby and M. B. Smith, *J. Amer. Chem. Soc.*, **86**, 4363 (1964); (b) E. C. Ashby and F. Walker, *J. Organometal. Chem.*, **7**, 17 (1967).

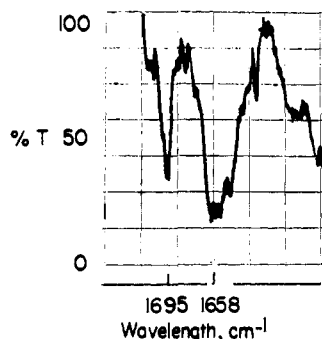
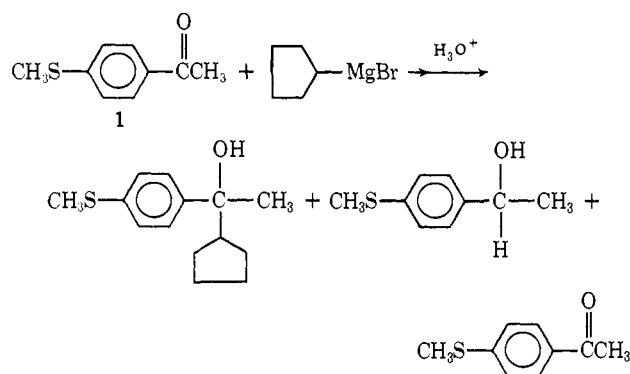


Figure 1. Plot of per cent transmission vs. wavelength for the reaction of *ca.* 0.1 *F* cyclopentylmagnesium bromide with 2×10^{-2} *M* 4-methylmercaptoacetophenone in diethyl ether observed *ca.* 0.001 sec after mixing. The single beam spectrum shows free ketone at 1695 cm^{-1} and complex absorption at 1658 cm^{-1} .

unity in dilute solution to, for example, 4 in 2 *M* ether solutions of phenylmagnesium bromide.²⁵ A complete description of the mechanism of reaction of ketones with Grignard reagents must include the role of such associated species.^{7, 10, 19}

In this work the reaction of dicyclopentylmagnesium and mixtures of dicyclopentylmagnesium and magnesium bromide with 4-methylmercaptoacetophenone in diethyl ether at 25.0° has been studied. The cyclopentyl moiety was selected because the reaction products consist of a mixture of addition, reduction, and enolization. Studies of the composition of the mixture as a function of MgBr_2 concentration provide supplemental data to the kinetic studies relating the contribution of dicyclopentylmagnesium and cyclopentylmagnesium bromide to the reaction. The ketone 1 has been used in previous studies.^{10, 17}



Results

Cyclopentylmagnesium Bromide. The infrared spectrum of ketone 1 and cyclopentylmagnesium bromide in ether, recorded *ca.* 0.001 sec after mixing of the reagents (Figure 1), shows the normal carbonyl stretching frequency at 1695 cm^{-1} and a new absorbance attributed to the complex between the carbonyl group and the Grignard reagent at 1658 cm^{-1} . This shift of the carbonyl absorption band to lower frequencies upon complex formation was noted earlier by Cowan⁴ for the fenchone-phenylmagnesium bromide complex (1740 to 1630 cm^{-1}). Holm¹⁶ has reported that the carbonyl absorption of acetone shifts from 1723 to 1695 cm^{-1} in the presence of butylmagnesium bromide.

(25) F. W. Walker and E. C. Ashby, *J. Amer. Chem. Soc.*, **91**, 3845 (1969).

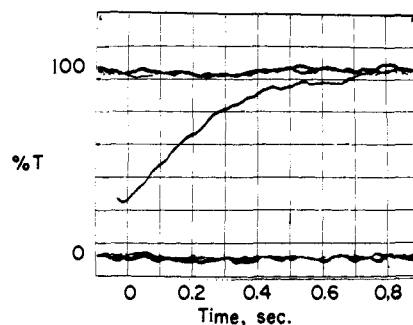


Figure 2. Plot of per cent transmission vs. time for the reaction of 0.02 *M* ketone 1 with 0.24 *F* cyclopentylmagnesium bromide in diethyl ether at 25.0° measured at 1658 cm^{-1} .

An apparent equilibrium constant for complex formation may be determined from the intensity of the carbonyl absorbance at 1695 cm^{-1} (ϵ 587), the initial ketone concentration, and the intensity of the absorbance attributed to the complex at 1658 cm^{-1} within 0.001 sec after mixing, since little reaction to form product has occurred. The data summarized in Table I for a range of Grignard concentrations from 0.055

Table I. Determination of Equilibrium Constant for Complex Formation between 4-Methylmercaptoacetophenone and Cyclopentylmagnesium Bromide (Base/Bromide = 0.83) in Diethyl Ether at 25.0°

Grignard, <i>M</i> ^a	10 ² ketone, <i>M</i> ^b	<i>A</i> at 1695 cm^{-1} ^c	<i>A</i> at 1658 cm^{-1} ^c	ϵ , complex ^d	<i>K</i> , ^e l./mol
0.055	2.27	0.760		389	13
0.076	2.27	0.662			12
0.066	2.01	0.577			15
0.087	2.01	0.506			14
0.212	2.27	0.311	0.640	368	14
0.240	2.01	0.255	0.527	334	14
0.260	2.01	0.226	0.583	358	15
0.284	3.06	0.351	0.757	308	13
0.350	2.01	0.205	0.638	384	12
0.360	3.06	0.292	0.839	328	13
0.362	3.06	0.247	0.837	317	16
0.476	3.06	0.173	0.789	285	18
0.53	2.55	0.177	0.763	339	13
0.59	2.55	0.148	0.845	379	14
0.59	2.01	0.142	0.538	304	14
0.62	2.55	0.153	0.718	312	13
				$\text{Av} = 339 \pm 1$	14 ± 1

^a Concentration expressed as total base. ^b Concentration of 4-methylmercaptoacetophenone in the ir cell at t_0 . ^c Measured absorbance in a 1.0-mm cell *ca.* 0.001 sec after mixing of reactants. ^d Calculated extinction coefficient for the complex assuming no reaction. ^e Equilibrium constant calculated on the basis of total concentration of magnesium. The value is 15 l./mol when expressed in terms of total base concentration.

to 0.62 *M* indicate that, with the reagent prepared from cyclopentyl bromide and magnesium in ether, which is characterized by a total base to bromide ratio of 0.83, the equilibrium constant for complex formation is 14 l./mol. Increasing the ratio of MgBr_2 to stoichiometric $\text{C}_5\text{H}_9\text{MgBr}$ so that base/bromide = 0.45 increases the fraction of the ketone complexed, the observed equilibrium constant being 19 ± 1 l./mol based on the total concentration of magnesium.

The kinetics of the disappearance of the carbonyl

absorbance at 1695 cm^{-1} and of the ketone-Grignard complex at 1658 cm^{-1} have been studied by following the absorbance at a fixed wavelength as a function of time with $(2\text{ to }3) \times 10^{-2}\text{ M}$ ketone and Grignard concentration ranging from 0.055 to 0.78 M . A representative plot of per cent transmission *vs.* time is illustrated in Figure 2. A digital analysis of the curve to yield the appropriate pseudo-first-order rate constant is summarized in Table II. As expected, the rate of disap-

Table II. Reaction of 0.020 M 4-Methylmercaptoacetophenone with 0.24 F Cyclopentylmagnesium Bromide (Base/Bromide = 0.83) in Diethyl Ether at 25° as Measured at 1658 cm^{-1}

Time, sec	Absorbance at 1658 cm^{-1}	$k_{\text{obsd}}, \text{sec}^{-1}$ (integrated)
0	0.525	
0.1	0.315	5.1
0.15	0.224	5.7
0.20	0.176	5.5
0.25	0.132	5.5
0.30	0.099	5.6
0.35	0.066	5.9
0.40	0.057	5.7
0.45	0.038	5.8
0.50	0.033	5.5
		$\text{Av} = 5.6 \pm 0.2$

pearance of the ketone absorbance is the same as that for the complex, Table III. The plot of the measured

Table III. Summary of the Rate of Reaction of Ketone 1 with Various Concentrations of Cyclopentylmagnesium Bromide in Diethyl Ether at 25.0° Measured by Infrared Stopped-flow Spectroscopy

Grignard, ^a <i>M</i>	10^2 ketone, <i>M</i>	Base/ bromide	$k_{\text{obsd}}, \text{sec}^{-1}$	
			Ketone ^b	Complex ^c
0.055	2.3	0.83	2.9	2.2
0.066	2.0	0.83	3.6	
0.087	2.0	0.83	4.1	
0.24	2.0	0.83	6.1	5.7
0.28	3.1	0.83	5.9	5.2
0.36	3.1	0.83	5.7	5.8
0.48	3.1	0.83	5.3	5.7
0.59	2.6	0.83	6.2	6.1
0.62	2.6	0.83	5.9	6.2
0.78	2.6	0.83	6.1	6.2
0.036	2.3	0.45	1.23	1.24
0.066	2.3	0.45	1.79	2.0
0.070	2.3	0.45	1.86	2.03
0.270	2.3	0.45	2.09	2.02
0.370	2.3	0.45	1.99	2.06
0.472	2.3	0.45		1.89
0.630	2.3	0.45		1.85

^a Concentration of base produced upon hydrolysis. ^b Measured at 1695 cm^{-1} . ^c Measured at 1658 cm^{-1} .

rate constant *vs.* $\text{C}_5\text{H}_9\text{MgBr}$ illustrated in Figure 3 indicates that at low concentration the reaction is first order in Grignard, but at high concentrations of cyclopentylmagnesium bromide the reaction order in $\text{C}_5\text{H}_9\text{MgBr}$ approaches zero as the fraction of the ketone which is complexed with the Grignard reagent approaches unity.^{26,28}

(26) See ref 27 for an alternative interpretation of the kinetic order of this reaction.

(27) E. C. Ashby, S. H. Yu, and P. V. Roling, *J. Org. Chem.*, **37**, 1918 (1972).

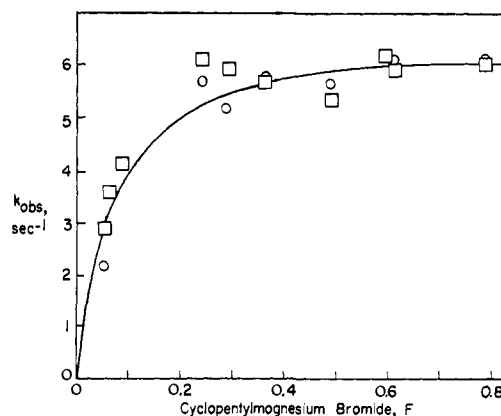


Figure 3. Plot of k_{obsd} *vs.* concentration of cyclopentylmagnesium bromide (base/bromide = 0.83) in diethyl ether at 25.0° . The line through the experimental points was calculated from eq 1, with $K = 15\text{ l./mol}$ and $k = 6.7\text{ sec}^{-1}$. Essentially the same line is obtained from eq 3. Points designated by \circ were measured at 1658 cm^{-1} and those indicated by \square were measured at 1695 cm^{-1} .

The line through the data points for this reaction of cyclopentylmagnesium bromide with ketone 1 was calculated from the simple mechanism, eq 1,³¹ involving rapid complex formation followed by rearrangement of the complex to product. In addition to the directly measured equilibrium constant, only a single parameter, the rate constant, 6.7 sec^{-1} , for conversion of complex to product, is required to describe quantitatively the reaction of ketone 1 with 0.055 to 0.78 M cyclopentylmagnesium bromide in diethyl ether at 25.0° .

At the concentrations used in these studies, the $\pi-\pi^*$ uv absorbance of uncomplexed ketone 1, $\lambda_{\text{max}} 308\text{ nm}$, is obscured by the absorption spectrum of solutions of cyclopentylmagnesium bromide in diethyl ether. However, solutions of the ketone in the presence of the Grignard reagents exhibit a new absorbance, $\lambda_{\text{max}} 343\text{ nm}$, which is present at the first spectroscopic observation, *ca.* 0.003 sec after mixing of the reagents. Based on studies with this same ketone and methylmagnesium bromide solution in which the spectrum of free ketone is not obscured,¹⁰ the new band at 343 nm is attributed primarily to a complex between ketone and the Grignard reagent. The uv spectrum of the complex, which was measured 38.4 times per second and was recorded 9.1 times per second, is illustrated in Figure 4.

The rate of disappearance of the band $\lambda_{\text{max}} 343\text{ nm}$ in the reaction of 4-methylmercaptoacetophenone with cyclopentylmagnesium bromide was studied by a stopped-flow, spectrophotometric technique in which the transmittance of a reacting solution was monitored at a single wavelength.

Measurement of the first-order rate constant for the disappearance of the long wavelength band in the uv spectrum associated with the complex did not yield ob-

(28) Since the observed reaction order²⁹ with respect to the Grignard reagent, present in excess, approaches unity in fairly dilute solution, the number of experimental points which describe a straight line is limited.^{20b} However, the deviation from unity provides substantial information about the complex and association of the reagent and should not be regarded^{20b} as a limitation of the experimental design.³⁰

(29) S. W. Benson, "The Foundation of Chemical Kinetics," McGraw-Hill, New York, N. Y., 1970, p 85.

(30) E. C. Ashby, H. M. Neumann, F. W. Walker, J. Laemmle, and L.-C. Chao, *J. Amer. Chem. Soc.*, **95**, 3330 (1973).

(31) L. P. Hammett, "Physical Organic Chemistry," 2nd ed, McGraw-Hill, New York, N. Y., 1970, p 85.

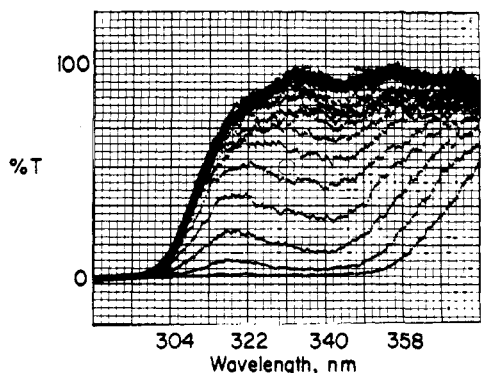


Figure 4. Transmission spectrum of $9.1 \times 10^{-4} M$ 4-methylmercaptoacetophenone in $0.148 M$ cyclopentylmagnesium bromide (base/bromide = ca. 0.80) in diethyl ether at 25.0° recorded 9.1 times per second. The first recorded spectrum was obtained under continuous flow conditions. The absorbance below ca. 315 nm is the base-line absorbance of excess cyclopentylmagnesium bromide.

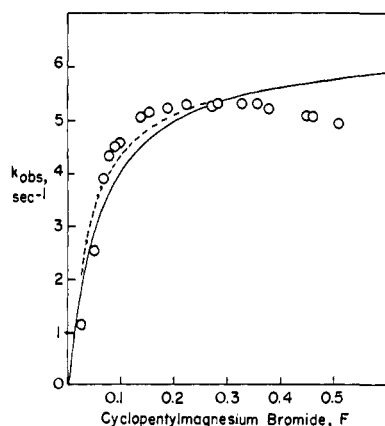


Figure 5. Plot of k_{obsd} vs. cyclopentylmagnesium bromide concentration for the reaction of cyclopentylmagnesium bromide (base/bromide = 0.83) with 4-methylmercaptoacetophenone in diethyl ether at 25.0° measured at 390 nm. The solid line was calculated excluding association data, and the dotted line was calculated assuming monomer was the only reactive component.

served first-order rate constants, k_{obsd} , that are independent of ketone concentration. Thus the observed rate constant for reaction of $0.322 M$ cyclopentylmagnesium bromide (base/bromide = 0.79), measured at 329 nm, decreases from 5.92 sec^{-1} at $0.05 \times 10^{-3} M$ ketone to 2.95 sec^{-1} at $8.35 \times 10^{-3} M$ ketone. In addition, kinetic data obtained at 329 nm generally exhibit infinity absorbances which tend to drift slowly to lower absorbance values, especially at higher Grignard reagent concentrations. Observed rate constants for reaction of cyclopentylmagnesium bromide with 4-methylmercaptoacetophenone at constant ketone concentration also showed a slight wavelength dependence when the rate of complex disappearance was measured at wavelengths near or below the recorded λ_{max} of the complex. Apparently, spectroscopic evaluation of rate constants for complex disappearance in the spectral region near the λ_{max} of the complex in the uv spectrum is complicated by the presence of one or more interfering absorbances.³²

(32) It has been reported that with 2-methylbenzophenone, the absorbance at 410 nm decreases²⁰ during the reaction with CH_3MgBr but increases³³ when the organometallic reagent is $(\text{CH}_3)_2\text{Mg}$.

(33) L. Laemmle, E. C. Ashby, and H. M. Neumann, *J. Amer. Chem. Soc.*, **93**, 5120 (1971).

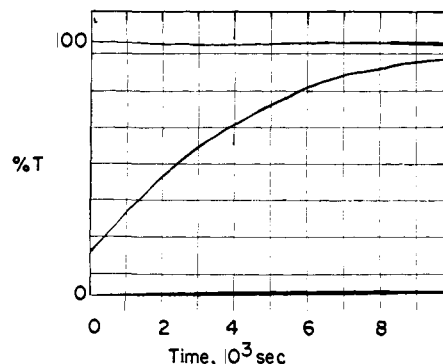


Figure 6. Oscillograph of per cent transmission at 390 nm vs. time for the reaction of $4.08 \times 10^{-3} M$ 4-methylmercaptoacetophenone with $0.161 M$ dicyclopentylmagnesium (base/bromide = 24) in diethyl ether at 25.0° (Table IV).

However, monitoring the reaction of cyclopentylmagnesium bromide (base/bromide = 0.79) with 4-methylmercaptoacetophenone at longer wavelengths, e.g., 390 nm, gives with this system pseudo-first-order rate constants independent of ketone concentration from 1.7×10^{-3} to $22.4 \times 10^{-3} M$ with a $0.281 M$ Grignard reagent. Rate constants are generally also independent of the wavelength used in the measurements for these reagents in the 370–390-nm region of the spectrum.

The observed pseudo-first-order rate constant measured at 390 nm for the reaction of cyclopentylmagnesium bromide (base/bromide = 0.83) with ca. $3 \times 10^{-3} M$ ketone increases from 1.14 to 5.20 sec^{-1} as the cyclopentylmagnesium bromide concentration increases from 0.026 to $0.200 M$ and remains approximately constant as the reagent concentration is further increased to $0.511 M$ (Figure 5). Comparison of the rate constants measured at 390 nm with those obtained at 1695 and 1658 cm^{-1} in the ir spectrum indicates that, except at the highest Grignard concentrations, these alternative criteria for determination of the reaction rate are in satisfactory agreement.

Mixtures of Dicyclopentylmagnesium, Cyclopentylmagnesium Bromide, and Magnesium Bromide. The reaction of dicyclopentylmagnesium with 4-methylmercaptoacetophenone (**1**) is considerably faster than that of the corresponding Grignard reagent and, because of current limitations in ir instrumentation, was studied only by uv stopped-flow spectroscopy. A typical run,³⁴ measured at 390 nm, is illustrated in Figure 6 and the integrated rate constants are shown in Table IV. Although the rate level is higher than the corresponding Grignard reagent by a factor of ca. 10^2 , the functional dependence of the measured first-order rate constant on the concentration of the organomagnesium species is similar, as may be seen by comparing the shape of Figure 7 with that of Figure 3. The curve illustrated in Figure 7 is quantitatively described by an equilibrium constant of 8.2 l./mol and an apparent rate constant for product formation of 690 sec^{-1} . The apparent reaction rate level as measured at 390 nm is also independent of the ketone concentration from 1 to $23 \times 10^{-3} M$ with $0.13 M$ dicyclopentylmagnesium in diethyl ether at 25.0° .

(34) Although these and data reported earlier^{7,10,17} appear to give acceptable first-order behavior, there has been a report of a related system which does not display a constant kinetic order within a run.³⁶

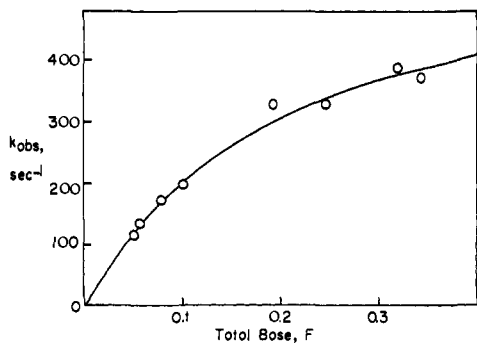


Figure 7. Plot of k_{obsd} measured at 390 nm vs. total base concentration for reaction of 4×10^{-3} M 4-methylmercaptoacetophenone with dicyclopentylmagnesium (base/bromide = 24) in diethyl ether at 25.0°.

Table IV. Reaction of 0.161 M Dicyclopentylmagnesium (Base/Bromide = 24) with 4.08×10^{-3} M 4-Methylmercaptoacetophenone in Diethyl Ether at 25.0°

Time, sec	Rel A (390 nm)	k_{obsd} , sec ⁻¹ (integrated)
0.0000	0.460	
0.0010	0.308	400
0.0015	0.258	390
0.0020	0.212	390
0.0030	0.149	380
0.0040	0.100	380
0.0050	0.065	390
0.0060	0.041	400
0.0070	0.027	410
0.0080	0.019	400
0.0090	0.015	380

$\bar{A}_v = 390 \pm 10$

The addition of excess magnesium bromide to cyclopentylmagnesium bromide serves not only to depress the overall rate level, measured at 390 nm, but results in a change in the shape of plots of k_{obsd} vs. concentration of C_5H_9MgBr . In the example illustrated in Figure 8 in which sufficient $MgBr_2$ has been added to give a base to bromide ratio of 0.46, there is more of a tendency for k_{obsd} to level off at lower Grignard concentrations than in the absence of excess halide and then to fall slightly with further increases in concentrations.

The overall effect of bromide on the rate level for the reaction of ketone 1 with cyclopentylmagnesium reagents may be obtained by studying the rate as a function of concentration, as illustrated in Figures 3, 5, and 7 for a series of reagents ranging from essentially pure dicyclopentylmagnesium to cyclopentylmagnesium bromide solutions which are saturated with respect to magnesium bromide. Then by selecting a common reagent concentration, represented as titratable base, from each curve a plot of k_{obsd} vs. bromide concentration may be constructed. Such a plot, constructed from several hundred kinetic measurements, for reagents corresponding to 0.30 M total base and $ca. 4 \times 10^{-3}$ M ketone 1 is illustrated in Figure 9. Some of the data on which Figure 9 is based are summarized in Table V. In this example the measured rate constant increases from 1.3 to 405 sec⁻¹ as the bromide content of a 0.3 M cyclopentylmagnesium reagent (expressed as total base) decreases from 0.839 to 0.002 M. The enlarged portion of Figure 9 showing the high bromide

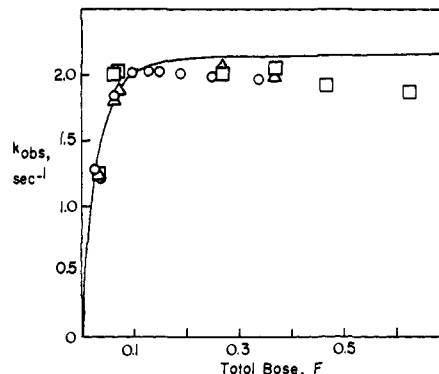


Figure 8. Plot of k_{obsd} vs. total base for reaction of 4-methylmercaptoacetophenone with a cyclopentylmagnesium bromide-magnesium bromide mixture (base/bromide = 0.46) in diethyl ether at 25.0°: (O) measured at 390 nm (Table V); (Δ) measured at 1695 cm⁻¹; (\square) measured at 1658 cm⁻¹ (Table III).

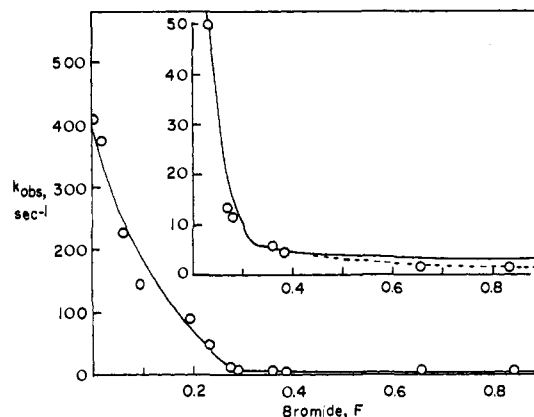


Figure 9. Plot of k_{obsd} measured at 390 nm vs. bromide concentration for the reaction of $ca. 4 \times 10^{-3}$ M 4-methylmercaptoacetophenone with cyclopentylmagnesium reagents of 0.30 M total base concentrations in diethyl ether at 25°. The solid line was calculated from eq 3, and the dotted line was calculated including contributions from a magnesium bromide coordinated cyclopentylmagnesium species.

region as an insert in the figure indicates that the rate level has not been depressed to a constant value.

Kinetics of the Reaction of 2,2,5,5-Tetradeuteriocyclopentylmagnesium Bromide with 4-Methylmercaptoacetophenone. The cyclopentylmagnesium analog deuterated in the β positions, 2,2,5,5-tetradeuteriocyclopentylmagnesium bromide, was prepared from cyclopentanone, which had been successively exchanged with portions of D_2O in the presence of base. The exchanged cyclopentanone, containing 3.92 deuterium atoms per molecule by mass spectral analysis, was converted to 2,2,5,5-tetradeuteriocyclopentanol by reduction with lithium aluminum hydride at $ca. -78^\circ$.³⁵ Conversion of the alcohol to the 2,2,5,5-tetradeuteriocyclopentyl bromide was accomplished with triphenylphosphine and bromine in dimethylformamide.³⁶ Mass spectral analysis of the deuterated cyclopentyl bromide indicated 3.88 deuterium atoms per molecule. The Grignard reagent, 2,2,5,5-tetradeuteriocyclopentylmagnesium bromide, was made from the deuterated cyclopentyl bromide by the usual procedure.

(35) A. Streitwieser, Jr., R. H. Jagow, R. C. Fahey, and S. Suzuki, *J. Amer. Chem. Soc.*, **80**, 2326 (1958).

(36) G. A. Wiley, R. L. Hershowitz, B. M. Rein, and B. C. Chung, *ibid.*, **86**, 964 (1964).

Table V. Summary of Rate Constants for the Reaction of Cyclopentylmagnesium Reagents with $ca. 4 \times 10^{-3} M$ 4-Methylmercaptoacetophenone in Diethyl Ether at 25.0° Measured at 390 nm

Grignard, ^a <i>M</i>	Base/ halide	k_{obsd} , sec ⁻¹ ^b	Grignard, ^a <i>M</i>	Base/ halide	k_{obsd} , sec ⁻¹ ^b
0.052	24	115	0.059	1.11	7.6
0.060		135	0.061		6.2
0.062		132	0.122		9.6
0.080		172	0.137		9.7
0.104		199	0.138		11.1
0.194		327	0.175		11.2
0.246		329	0.226		12.1
0.322		392	0.246		12.6
0.342		376	0.255		12.7
0.054	5.0	81	0.026	0.83	1.14
0.095		141	0.052		2.51
0.109		160	0.068		3.87
0.170		202	0.080		4.30
0.194		210	0.089		4.50
0.224		218	0.101		4.55
0.294		234	0.137		5.02
0.030	3.1	33	0.155		5.15
0.072		76	0.191		5.18
0.106		107	0.225		5.24
0.149		123	0.274		5.22
0.182		134	0.282		5.29
0.220		152	0.359		5.27
0.255		162	0.372		5.15
0.284		169	0.449		5.07
0.048	1.3	19.1	0.459		5.04
0.051		18.9	0.511		4.89
0.123		38.0	0.022	0.46	1.27
0.132		40.0	0.025		1.20
0.243		47.7	0.056		1.84
0.269		49.1	0.097		2.09
0.309		51.8	0.124		2.04
			0.150		2.07
			0.171		2.01
			0.240		1.99
			0.275		1.90

^a Expressed as the amount of base generated upon hydrolysis.

^b Each run is the average of more than three independent kinetic runs.

The kinetics of the reaction of 2,2,5,5-tetradeuterio-cyclopentylmagnesium bromide with 4-methylmercaptoacetophenone was examined by the same techniques used for the nondeuterated reagents. The observed rate constants for the reaction of 2,2,5,5-tetradeuterio-cyclopentylmagnesium bromide (base/bromide = 0.90) with 4-methylmercaptoacetophenone are independent of ketone concentration from 0.91×10^{-3} to $13.35 \times 10^{-3} M$ and the observed pseudo-first-order rate constant for reaction with $3 \times 10^{-3} M$ 4-methylmercaptoacetophenone increases from 2.59 to 3.96 sec⁻¹ as the concentration of 2,2,5,5-tetradeuteriocyclopentylmagnesium bromide increases from 0.055 to 0.218 *M*. First-order rate constants obtained for several concentrations of 2,2,5,5-tetradeuteriocyclopentylmagnesium bromide are summarized in Table VI.

Comparison of k_{obsd} values for deuterated and nondeuterated reagents reacting with 4-methylmercaptoacetophenone indicates that the introduction of deuterium into the β positions of the Grignard reagent has the effect of lowering the rate level for reaction with 4-methylmercaptoacetophenone. A cyclopentylmagnesium bromide reagent having base/bromide = 0.90 and at 0.2 *M* concentration would be expected to have a k_{obsd} value of 6.2 sec⁻¹. The corresponding value for 2,2,5,5-tetradeuteriocyclopentylmagnesium bromide is

Table VI. Reaction of 2,2,5,5-Tetradeuteriocyclopentylmagnesium Bromide (Base/Bromide = 0.90) with $3 \times 10^{-3} M$ 4-Methylmercaptoacetophenone in Diethyl Ether at 25.0°

$C_5H_3D_3MgBr$, ^a <i>M</i>	k_{obsd} , sec ⁻¹ (390 nm)
0.055	2.59
0.089	3.28
0.139	3.74
0.178	3.87
0.218	3.96

^a Base titration.

3.9 sec⁻¹, which gives an overall observed kinetic isotope effect of 1.58.

Products of the Reactions of Cyclopentylmagnesium Reagents with 4-Methylmercaptoacetophenone. The products of reactions of cyclopentylmagnesium reagents with 4-methylmercaptoacetophenone were examined under the same conditions as those used to obtain the kinetic data. Typically, excess cyclopentylmagnesium reagent was mixed with 4-methylmercaptoacetophenone in the stopped-flow apparatus at concentrations similar to those used in kinetic studies. The reacted solutions were quenched in ice water and worked up after the basic salts had been neutralized with dilute sulfuric acid. Analyses were accomplished by quantitative vapor phase chromatography. Tests for 2,3-bis(4-methylmercaptohenyl)-2,3-butanediol, which was not eluted from the glpc column, were accomplished by thin layer chromatography. In no case was a detectable amount of this pinacol found, placing the upper limit for its presence in the product mixtures at *ca.* 5%.

The product distributions for reactions of several concentrations of cyclopentylmagnesium bromide-dicyclopentylmagnesium mixture with 4-methylmercaptoacetophenone are outlined in Table VII. The

Table VII. Products from Reaction of a Cyclopentylmagnesium Reagent with 4-Methylmercaptoacetophenone in Diethyl Ether at 25.0°

Base, <i>M</i>	Base/ bromide	10 ³ ketone, <i>M</i>	Yield, % ^a		
			Red. ^b	Add. ^c	Enol ^d
0.039	4.5	2.87	64.9	17.8	17.3
0.074	4.5	2.77	65.5	17.4	17.1
0.118	4.5	2.81	67.7	18.4	13.9
0.220	4.5	2.83	66.9	21.1	12.0
0.424	4.5	2.77	70.5	21.8	7.7
0.106	0.83	2.95	79.0	9.4	11.6
0.140	0.83	2.98	80.1	8.5	11.4
0.177	0.83	2.85	80.7	12.0	7.3
0.343	0.83	2.68	78.5	15.0	6.5
0.503	0.83	2.59	79.6	14.7	5.7
0.045	0.38	2.86	86.3	6.3	7.4
0.114	0.38	2.89	88.2	5.7	6.1
0.144	0.38	2.89	87.5	6.9	5.6
0.223	0.38	2.72	86.0	9.5	4.5
0.324	0.38	2.84	83.4	12.8	3.8

^a Determined by quantitative vpc. Yields are normalized to 100%. ^b 1-(4-Methylmercaptohenyl)ethanol. ^c 1-Cyclopentyl-1-(4-methylmercaptohenyl)ethanol. ^d 4-Methylmercaptoacetophenone.

data indicate that a 0.22 *M* solution of dicyclopentylmagnesium upon reaction with ketone 1 would give 67% reduction, 21% addition, and 12% enolization

products. However, there is a slight dependence of the composition of the products on the concentration of the organomagnesium reagent.

Addition of magnesium bromide not only depresses the rate level but changes the composition of the product mixture as well. As summarized in Table VII, a reagent with a base to bromide ratio of 0.38 gives a larger fraction of reduction than is observed with reagents reacting predominantly by way of dicyclopentylmagnesium. At the 0.22 *M* level with excess bromide (base/bromide = 0.38), 86% reduction, 10% addition, and 5% enolization were observed. The ratio of addition to enolization also seems to be a function of the absolute concentration of the organomagnesium reagent.

Products of the Reaction of 2,2,5,5-Tetradeuteriocyclopentylmagnesium Bromide with 4-Methylmercaptoacetophenone. The products of the reaction of 2,2,5,5-tetradeuteriocyclopentylmagnesium bromide with 4-methylmercaptoacetophenone were examined by the same techniques used for the corresponding non-deuterated reagents. Table VIII lists the product

Table VIII. Products from Reaction of 2,2,5,5-Tetradeuteriocyclopentylmagnesium Bromide (Base/Bromide = 0.90) with 4-Methylmercaptoacetophenone in Diethyl Ether at 25.0°

$C_5D_4H_3MgBr$, <i>M</i> ^a	10 ³ ketone, <i>M</i>	Yield, % ^b		
		Red. ^c	Add. ^d	Enol ^e
0.055	2.94	58	19	23
0.089	2.94	56	22	22
0.139	3.02	57	26	17
0.178	3.02	60	22	18
(0.200) ^f		(59) ^f	(22) ^f	(19) ^f
0.218	2.97	60	24	16
0.222	0.92	72	19	9
0.222	13.35	56	29	15

^a Base titration. ^b Determined by vpc. No internal standard used and yields are assumed to total to 100%. ^c 1-Deuterio-1-(4-methylmercapto(phenyl)ethanol and 1-(4-methylmercapto(phenyl)ethanol. ^d 1-(2,2,5,5-Tetradeuteriocyclopentyl)-1-(4-methylmercapto(phenyl)ethanol. ^e 4-Methylmercaptoacetophenone. ^f Products calculated from nondeuterated reaction and kinetic isotope effects.

compositions observed for reaction of various concentrations of 2,2,5,5-tetradeuteriocyclopentylmagnesium bromide (base/bromide = 0.90) with 4-methylmercaptoacetophenone. As noted for the corresponding non-deuterated reagents, there is a slight concentration dependence on the relative yields of addition and enolization products for reaction with *ca.* 3×10^{-3} *M* 4-methylmercaptoacetophenone. Comparison of the product distributions from reaction of 2,2,5,5-tetradeuteriocyclopentylmagnesium bromide and cyclopentylmagnesium bromide with 4-methylmercaptoacetophenone shows that the deuterated reagent gives less reduction and more addition and enolization products than the non-deuterated reagent. Thus the product distribution from reaction of 0.2 *M* 2,2,5,5-tetradeuteriocyclopentylmagnesium bromide with *ca.* 3×10^{-3} *M* ketone is 59% reduction, 24% addition, and 17% enolization, while the expected products for reaction of a 0.2 *M* cyclopentylmagnesium bromide reagent of the same composition (base/bromide = 0.90) are 76% reduction, 14% addition, and 10% enolization.

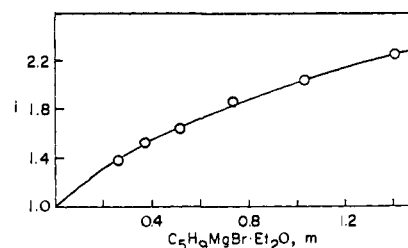


Figure 10. Plot association, *i*, vs. molality of cyclopentylmagnesium bromide (base/bromide = 0.80) in diethyl ether at 0°. The line was calculated for a polymerization model with $K = 2.1 m^{-1}$.

Reagent Association. The apparent molecular weight of cyclopentylmagnesium (base/bromide = 0.8) was studied by differential vapor pressure techniques.³⁷ As illustrated in Figure 10, the apparent degree of association (*i*) extrapolates to 1 at infinite dilution but increases to greater than 2 in a 0.7 *F* solution of the Grignard reagent. The data are adequately described by a simple picture of monomeric Grignard in equilibrium with aggregates containing 1, 2, 3, . . . *n* RMgX units with the equilibrium constant of 2.1 *m* for addition of each RMgX unit.³⁸

Although the line in Figure 10, which fits the data, was calculated on this basis, it is clear that many alternative schemes could describe the data and that adequately accounting for activity effects might substantially alter the apparent degree of association at high concentrations of Grignard reagent.

Discussion

The data for the reaction of 4-methylmercaptoacetophenone with excess cyclopentylmagnesium reagents in diethyl ether solvent at 25.0° may be represented conceptually as the surface, Figure 11, resulting from a three-dimensional plot of the measured parameters, k_{obsd} , base generated upon hydrolysis, and total bromide content of the solution. Increasing the concentration of the organometallic, measured as total base, from 0.01 to 0.5 *M* causes k_{obsd} to increase rapidly at low concentration followed by a tendency to approach a limiting rate level at *ca.* 0.3 to 0.5 *M*, and addition of bromide, as $MgBr_2$, depresses k_{obsd} . A quantitative description of the mechanism of the reaction should represent this surface in terms of the nature of the species in the base-halide plane as a function of the base-halide ratio, total concentration, and the contribution of each species to k_{obsd} .^{39, 40}

Apparently addition of up to a stoichiometric amount of $MgBr_2$ to R_2Mg favors formation of a substantial amount of RMgX at equilibrium, eq 2, for many dialkylmagnesium compounds. Estimates of values for K_s range from *ca.* 15 for phenylmagnesium iodide^{11b}

(37) D. P. Novak and T. L. Brown, *ibid.*, **94**, 3793 (1972).

(38) (a) E. E. Schrier, *J. Chem. Educ.*, **45**, 176 (1968); (b) P. O. P. Ts'o, I. S. Melvin, and A. C. Olson, *J. Amer. Chem. Soc.*, **85**, 1289 (1963); (c) M. Davies and D. K. Thomas, *J. Phys. Chem.*, **60**, 763, 767 (1956).

(39) Examination of limited regions of such a surface can be misleading since mechanistic proposals may not prove to be sufficiently general to describe the reaction under a different set of conditions. Mechanisms ranging from slow complex formation²³ to rate limiting formation of dialkylmagnesium^{9e, 15a, 16a, 40} have been proposed for the reaction of Grignard reagents with ketones.

(40) An alternative analysis which is not applicable to all of our data has recently been proposed.^{20b}

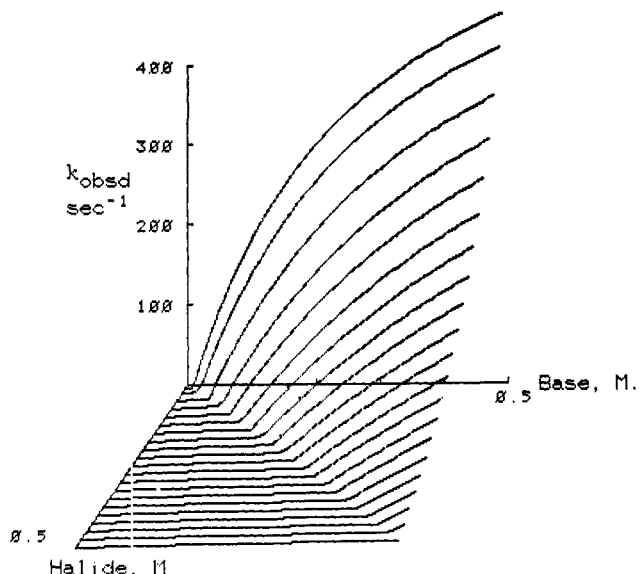
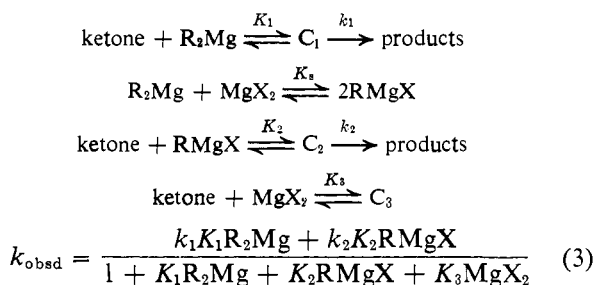


Figure 11. Computer-generated three-dimensional plot of the measured parameters k_{obsd} , concentration of organometallic represented as base-generated upon hydrolysis, and bromide for the reaction of cyclopentylmagnesium reagents with 4-methylmercaptoacetophenone in diethyl ether at 25.0°.

to 10^4 for butylmagnesium bromide in diethyl ether.¹⁶ However, the association measurements^{11,22-24} indicate that the monomeric formulation RMgX is an oversimplification except at low concentrations. Addition of more than one equivalent of MgBr_2 to R_2Mg further depresses k_{obsd} and changes the shape of a plot of k_{obsd} vs. total base.¹⁹ Unfortunately, a quantitative description of the species present in cyclopentylmagnesium bromide solutions containing excess MgBr_2 and the changes in degree of association with concentration are not available.

It is of interest to impose the simple scheme^{6,7,10} in eq 3 on the available kinetic data without regard to



the apparent complexities arising from associations. In this scheme K_1 is the equilibrium constant for complex formation, C_1 , between ketone and dicyclopentylmagnesium. The constant K_2 represents complexation with cyclopentylmagnesium bromide and the products are represented as arising from C_1 and C_2 by first-order rate constants k_1 and k_2 . Apparent values of K_1 and k_1 may be determined in regions of high base/bromide ratio by plotting $1/k_{\text{obsd}}$ vs. $1/(\text{C}_5\text{H}_9)_2\text{Mg}$, since for the scheme, eq 1, $1/k_{\text{obsd}} = 1/kKG + 1/k$. Such a plot for base/bromide = 24 is illustrated in Figure 12. Evaluation of the slope and intercept gives an equilibrium constant of 8.2 l./mol and a rate constant of 690 sec^{-1} . These values are not necessarily unique, however, since they are very sensitive to the slope of the $1/k_{\text{obsd}}$ vs. $1/\text{R}_2\text{Mg}$ plot. Since these parameters are

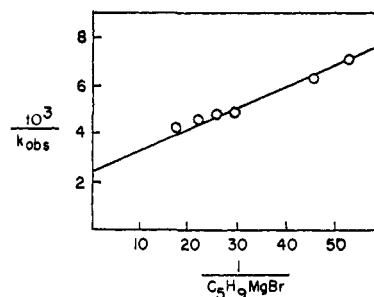


Figure 12. Plot of $1/k_{\text{obsd}}$ vs. $1/\text{cyclopentylmagnesium bromide concentration}$ for the reaction of 4-methylmercaptoacetophenone with a cyclopentylmagnesium bromide-dicyclopentylmagnesium mixture (base/bromide = 5.0) in diethyl ether at 25.0°.

based on a solution which is not pure dicyclopentylmagnesium (base/bromide = 24), a better description of the reaction of halide-free reagent may be obtained by assuming that the equilibrium constant, 8.2 l./mol, is correct but extrapolating derived rate constants, which are very sensitive to halide, to zero bromide. This approach gives a rate constant for conversion of complex, C_1 , to product of 740 sec^{-1} .

If it is assumed that the equilibrium constant directly measured by fast-infrared techniques on a solution with base/bromide = 0.83 is representative of K_2 , the equilibrium constant for formation of a complex between ketone 1 and cyclopentylmagnesium bromide C_2 , then the addition of the parameter, k_1 , the rate constant for conversion of C_2 to product, and the Schlenk equilibrium constant, K_s , should describe all of the data relating k_{obsd} to organomagnesium and halide concentrations in the region where MgBr_2 is not present in excess if the simplified scheme in eq 3 is applicable to this system. The constant K_3 representing complex formation between ketone 1 and free MgBr_2 , measured in an independent experiment, is ca. 20 l./mol in diethyl ether.

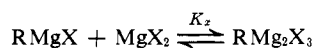
Imposing a value of about 7 sec^{-1} for the rate constant for conversion of the cyclopentylmagnesium bromide-ketone 1 complex to products, a value for the Schlenk equilibrium constant K_s of ca. 10^4 , and the directly measured values for K_1 , k_1 , K_2 , and K_3 on eq 3 result in a reasonable description of the effect of MgBr_2 on rate levels as well as the functional dependence of k_{obsd} on organomagnesium concentration for base/bromide ratios ranging from essentially pure dicyclopentylmagnesium to ca. 0.8. The lines through the data points in Figures 3, 5, 7, and 9 were calculated with these parameters. However, at a base/bromide ratio of 0.45 the calculated rate constant from eq 3 is higher than observed by a factor of 1.4 to 1.8.

To the extent that this simplified scheme which neglects association is representative of the dynamics of the reaction, at base/halide ratios greater than 1.3 more than 90% of the reaction with ketone 1 proceeds through dicyclopentylmagnesium. The reagent directly prepared from cyclopentyl bromide and magnesium in diethyl ether (base/halide = ~ 0.8) reacts predominantly ca. 95%, by way of cyclopentylmagnesium bromide. The variation of the fraction of the reaction yielding addition, reduction, and enolization as a function of the base to halide ratio, Table VII, provides added support for the concept of reaction proceeding predominantly by way of dicyclopentylmagnesium at high base to halide ratios and with an important con-

tribution from another species, *e.g.*, cyclopentylmagnesium bromide, in solution which analyzes for base to bromide ratios of *ca.* 0.82 or less. Of course, the ratio of reactivity of dialkylmagnesium to alkylmagnesium halide is a function of the nature of the alkyl group, ketone, solvent, temperature, etc.

A better description of the observed rate levels at relatively high magnesium bromide levels is obtained by recognition of the possibility of specific coordination between a Grignard reagent and magnesium bromide.^{41,42}

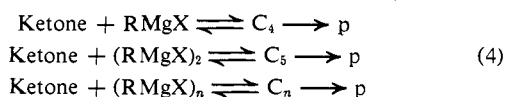
Justification for such a formulation rests on isolation and X-ray structure proof^{22b} of the related compound $(\text{EtMgCl} \cdot \text{MgCl}_2)_2$ and on the enhanced solubility^{19,21} of



magnesium bromide in a solution of cyclopentylmagnesium bromide compared with pure ether. For example, at *ca.* 25° a saturated solution of MgBr_2 in ether is about 0.2 *M*. However, 1 *M* cyclopentylmagnesium bromide solutions containing the formal equivalent of 0.6 *M* MgBr_2 have been prepared in this work.

Assuming formation of a species such as RMg_2X_3 with an equilibrium constant in the range of 1–10 l./mol and a relatively low reactivity toward ketone **1** result in a scheme which represents the observed rate as a function of reagent concentration for base to halide ratios of *ca.* 0.45, Figure 8. However, improving the fit of a complex kinetic scheme by the introduction of two additional parameters does not constitute proof of the correctness of the concept.⁴³

The molecular weight studies indicate that the apparent degree of association, *i*, for a reagent with base/bromide = 0.83 increases from unity at low concentration to about 2 in a 1 *M* solution. Since the kinetic analysis indicates that a reagent with this composition reacts predominantly by way of $\text{C}_5\text{H}_9\text{MgBr}$, the effect of concentration and association on the observed rate level may be approximated by the scheme in eq 4, where



RMgX represents the monomeric reagent $(\text{RMgX})_2$, a dimeric Grignard reagent, etc. Calculations of the observed rate level as a function of concentration made by assuming that only monomeric RMgX complexes and reacts with ketone **1** are represented by the dotted line in Figure 5. The difference in the precision of the fit of the calculated rate levels to the experimental data for the assumption of reaction only by way of monomeric reagent compared with assuming rate levels which depend only on the stoichiometric concentration of the Grignard reagent, Figure 5, does not allow definitive conclusions to be drawn regarding relative reactivities of the monomeric reagent compared with various higher aggregates.^{41,44} However, to the extent that activity

(41) (a) A. Tuulmets, *Reakts. Sposobnost Org. Soedin.*, **6**, 854 (1969); (b) J. Loit, M. Luuk, and A. Tuulmets, *ibid.*, **8**, 237 (1971).

(42) J. H. Wotiz, C. A. Hollingsworth, and R. E. Dessy, *J. Org. Chem.*, **21**, 1063 (1956).

(43) With complex kinetic schemes, it is highly probable that several alternative mathematical models can be derived which describe the available data. The availability of such alternative descriptions does not^{20b} however, reflect on the validity of the experimental kinetic data.

(44) The experimental basis of the recent assertion²⁷ that the addition of Grignard reagents to ketones involves only monomeric RMgX is not clear.

and medium effects⁴⁵ for cyclopentylmagnesium bromide and methylmagnesium bromide can be equated, the tendency of rate levels with CH_3MgBr to continue to increase^{7,10} above about 0.3 *M* while cyclopentylmagnesium bromide solutions approach a limiting rate level as all of the ketone becomes complexed suggests that at least in the case of methylmagnesium bromide, species such as $(\text{CH}_3\text{MgBr})_2$ may be more reactive than the monomeric form.

By combining kinetic and product data from the reaction of both deuterated and nondeuterated cyclopentylmagnesium bromide, it is possible to estimate the kinetic isotope effect for the reduction reaction. If the kinetic order is the same for addition, reduction, and enolization, then the observed rate constant may be written as a sum of individual rate constants, k_a , k_r , and k_e , for each of three component reactions. For the reaction of the nondeuterated cyclopentylmagnesium bromide, this is written as eq 5, where k_r^H represents the rate con-

$$k_{\text{obsd}} = k_a + k_r + k_e$$

$$k_{\text{obsd}}^H = k_a + k_r^H + k_e = 6.12 \text{ sec}^{-1} \quad (5)$$

stant for hydrogen transfer in the reduction reaction and 6.12 sec^{-1} is the expected rate constant for reaction of a 0.2 *M* cyclopentylmagnesium reagent of composition base/bromide = 0.90 (estimate based on Figure 9). The expected products from reaction of this reagent are 76% reduction, 14% addition, and 10% enolization (estimate based on data from Table VII). Use of these data in conjunction with eq 5 indicates that k_{obsd} may be factored into k_a , k_r , and k_e , with values of 0.87, 4.7, and 0.62 sec^{-1} , respectively.

For the reaction of 2,2,5,5-tetradeuteriocyclopentylmagnesium bromide (base/bromide = 0.90), the observed rate constant for a 0.2 *M* reagent was 3.9 sec^{-1} . The assumption that there is no isotope effect on addition or enolization allows calculation of a rate constant for deuterium transfer in the reduction reaction, eq 6,

$$k_{\text{obsd}}^D = k_a + k_r^{D+H} + k_e = 3.9 \text{ sec}^{-1}$$

$$k_r^{D+H} = 3.9 \text{ sec}^{-1} - 0.87 \text{ sec}^{-1} -$$

$$0.62 \text{ sec}^{-1} = 2.41 \text{ sec}^{-1} \quad (6)$$

where k_r^{D+H} represents a value that contains a slight contribution from proton transfer since the Grignard reagent used was only 97% deuterated. Correcting k_r^{D+H} for the small amount of nondeuterated reagent present yields a value for the primary kinetic isotope effect on the reduction reaction⁴⁶ of 2.0, a value commensurate with other known values based only on product composition.⁴⁷ The derived rate constants may be used to calculate the composition of the product mixture that reaction of 0.2 *M* 2,2,5,5-tetradeuteriocyclopentylmagnesium bromide (base/bromide = 0.90) would be expected to give. The results summarized in Table VIII are within experimental error of measured yields.

A related study by Holm⁴⁷ was not successful in de-

(45) The possibility that medium effects can affect rate levels at high reagent concentrations in the relatively nonpolar solvent diethyl ether is not easily discounted and has been invoked in other studies: ref 20b.

(46) (a) G. E. Dunn and J. Warkentin, *Can. J. Chem.*, **34**, 75 (1956); (b) T. C. Morrison and R. W. Ridgeway, *J. Amer. Chem. Soc.*, **91**, 4601 (1969); (c) G. Chauviere and Z. Welvart, *Bull. Soc. Chim. Fr.*, 765 (1970); (d) T. Holm, *J. Organometal. Chem.*, **29**, C45 (1971).

(47) T. Holm and I. Crossland, *Acta Chem. Scand.*, **25**, 59 (1971).

tecting isotope effects on the rate constants for reactions of several reagents with benzophenone, although the isotope effects were observed in the product distributions. This result was explained in terms of a mechanism for these reactions involving a biradical intermediate and separate rate-determining and product-determining steps. Clearly the mechanism and conclusions of Holm⁴⁷ are not applicable to the data presented here.

Experimental Section

Cyclopentylmagnesium Reagents. All cyclopentylmagnesium reagents were prepared in an all-glass, grease-free apparatus which was dried under vacuum prior to use and kept under positive pressure of argon gas during all operations. The magnesium used was Dow singly sublimed magnesium, cut to size with carbide tools, washed with ether, and dried under vacuum prior to use. Reagent ether was freshly distilled from a *ca.* 0.5 *M* preparation of refluxed *n*-butylmagnesium bromide through a 10-in. Vigreux column into the vessel used for preparation of the cyclopentylmagnesium reagents. Argon was Linde high-purity argon further purified by being passed through a tower of Linde 4-A molecular sieves.

Cyclopentyl bromide (Aldrich) was purified by fractional distillation through a 2-ft glass helices packed column and kept cold in dark bottles prior to use. Cyclopentyl bromide was degassed by repeated evacuations at *ca.* -78° followed by refilling with argon immediately prior to reagent preparation.

In general, a Grignard reagent was prepared by slow addition of cyclopentyl bromide to a stirred mixture of *ca.* 300 ml of anhydrous diethyl ether and at least a 2 *M* excess of magnesium. After the reaction was complete, reagents were generally allowed to stand overnight. Reagents were then filtered twice through sintered glass disks and delivered into silicone rubber serum-capped vessels. If desired, reagents were diluted directly in these vessels by addition of freshly distilled ether.

Dicyclopentylmagnesium and cyclopentylmagnesium bromide-dicyclopentylmagnesium mixtures were prepared by the removal of magnesium bromide from cyclopentylmagnesium bromide solutions by precipitation with purified and degassed dioxane.

Where cyclopentylmagnesium bromide reagents containing excess magnesium bromide were desired, preparation was achieved by slow addition of a degassed mixture of cyclopentyl bromide and 1,2-dibromoethane to excess magnesium in ether. The reagents so prepared were filtered and delivered into silicone rubber serum-capped vessels as usual. Magnesium bromide was found to be soluble in cyclopentylmagnesium bromide to the extent that homogeneous reagents of base/bromide composition as low as 0.38 could be prepared. Attempts to prepare reagents having higher bromide content resulted in the formation of a two-phase system.

The preparation of the deuterated cyclopentylmagnesium bromide analog, 2,2,5,5-tetradeuteriocyclopentylmagnesium bromide, was accomplished by the same techniques used for cyclopentylmagnesium bromide.

Reagent Analysis. The organomagnesium reagents used in these studies were analyzed for total base and halide titers. Total base titers⁴⁸ were obtained by injecting a syringe aliquot of reagent into a known excess of hydrochloric acid in aqueous ethanol and back titrating with standard sodium methoxide. Bromide titers were accomplished by the Volhard method in aqueous ethanol. The precision of duplicate analyses by both methods was *ca.* ±2%.

4-Methylmercaptoacetophenone. The preparation of this ketone has been described.⁴⁹

2,2,5,5-Tetradeuteriocyclopentanone was prepared by a method similar to that described in the literature.⁵⁰ The nmr spectrum (neat, nmr-1) has one absorption only, corresponding to the protons on the carbon atoms not adjacent to the carbonyl group. The infrared spectrum (neat) showed no peak at 1407 cm⁻¹, characteristic of the methylene hydrogens adjacent to the carbonyl group. The mass spectrum had peaks at *m/e* 88 (93%) and *m/e* 87 (7%), corresponding to 98% deuterium incorporation or *ca.* 3.92 deuterium atoms per molecule.

2,2,5,5-Tetradeuteriocyclopentanol. Preparation of 2,2,5,5-tetradeuteriocyclopentanol was carried out by lithium aluminum

hydride reduction of 2,2,5,5-tetradeuteriocyclopentanone in 72% yield.

Products of reactions of cyclopentylmagnesium reagents with 4-methylmercaptoacetophenone were examined under conditions designed to approximate as closely as possible the conditions of the kinetic measurements. In a typical run, 50 ml of 0.686 *M* cyclopentylmagnesium bromide (base/bromide = 0.84) (3.43×10^{-3} mol) was mixed with 50 ml of 5.36×10^{-3} *M* 4-methylmercaptoacetophenone (2.68×10^{-3} mol) in the stopped-flow apparatus at 25.0°. Portions, *ca.* 10 ml, of mixed solution were collected in the stop syringe, allowed sufficient time to completely react, and then quenched in ice water, the process being repeated until the 100-ml total volume of reacted solution had been so treated. The product mixture was then neutralized with dilute sulfuric acid added by an automatic buret⁵⁰ which adjusted the pH to 6. The aqueous phase was washed twice with ether and the combined organic portions were washed twice with saturated Na₂CO₃ and twice with water. The ether was carefully removed under vacuum. Quantitative vapor phase chromatography, using a 4-ft column of 10% Apiezon M and 5% Carbowax 20 M on base-washed Chromosorb P at 205°, calibrated with authentic materials and using biphenyl as an internal standard, indicated the products to be 78.5% 1-(4-methylmercaptophenyl)ethanol (retention time 5 min), 15.0% 1-cyclopentyl-1-(4-methylmercaptophenyl)ethanol (23 min), and 6.5% 4-methylmercaptoacetophenone (4 min). Yields are normalized to 100%; the actual observed total yield for this run was 108%. Precision of the chromatographic analysis is *ca.* ±5%. Small peaks at retention times of 2 and 10 min on this column, apparently due to some dehydration of reduction and addition alcohols, respectively, were observed for both authentic materials and for the product mixture and were included in the integrations of the appropriate alcohol peaks. A test for the presence of 2,3-bis(4-methylmercaptophenyl)-2,3-butanediol, the expected product if coupling of the ketyl of 4-methylmercaptoacetophenone occurs, was carried out in 9:1 pentane:ether on Gelman ITLC Type SA. No evidence for the presence of the pinacol was found by this method, which has a limit of sensitivity of *ca.* 5%.

The same procedure was used for examining the products from reaction of 4-methylmercaptoacetophenone with several other concentrations of this reagent and for examining the products from reaction of this ketone with various concentrations of reagents of base/bromide composition 0.38, 0.93, and 4.5.

The products from reaction of 4-methylmercaptoacetophenone with 2,2,5,5-tetradeuteriocyclopentylmagnesium bromide were also examined in the same way. However, no internal standard was used for the vapor phase chromatographic analyses and the yields were assumed to total 100%. Mass spectral analyses were obtained on material collected from the vapor phase chromatograph corresponding to the reduction products from reaction of 0.222 *M* 2,2,5,5-tetradeuteriocyclopentylmagnesium bromide (base/bromide = 0.90) with both 0.92×10^{-3} and 13.35×10^{-3} *M* 4-methylmercaptoacetophenone. The mass spectrum for the reduction product from reaction at lower ketone concentration showed peaks at *m/e* 169 (91%) and *m/e* 168 (9%) corresponding to the deuterated reduction product, 1-deuterio-1-(4-methylmercaptophenyl)ethanol, and the nondeuterated reduction product, 1-(4-methylmercaptophenyl)ethanol, respectively. For the reduction product from reaction at the higher ketone concentration the results were essentially the same, the mass spectrum showing peaks at *m/e* 169 (90%) and at *m/e* 168 (10%).

Kinetics and Spectroscopy. Stopped-flow uv equipment has been described previously.^{49,51}

The infrared stopped-flow spectrometer consists of a pair of 0.75-in. stainless steel drive syringes equipped with spring loaded Teflon V packings. Syringe barrels are further sealed to exclude air from the chambers and operated under a positive pressure of purified argon. Gibson-Chance type stainless steel mixers are connected to the drive syringes by Tomco S90A 580 wt solenoid operated valves. The calcium fluoride flow-through type ir cells have a 1-mm path length.

Drive and stop syringes are positioned by a solenoid controlled hydraulic system operated at 400 psi. Estimated time between mixing and observation is 1 msec.

All valve openings and syringe movements are controlled by a relay operated digital logic system. The entire system is submerged in a thermostated ethylene glycol-water bath.

(48) H. Gilman, E. A. Zoeller, and J. B. Dickey, *J. Amer. Chem. Soc.*, **51**, 1576 (1929).

(49) S. G. Smith and J. Billet, *ibid.*, **89**, 6948 (1967).

(50) S. G. Smith and D. J. W. Goon, *J. Org. Chem.*, **34**, 3127 (1969).

(51) S. G. Smith, L. F. Charbonneau, D. P. Novak, and T. L. Brown, *J. Amer. Chem. Soc.*, in press.

The image of the ir source element (P.E. 137-0032) on the cell, chopped at 5 kHz, is focused by a NaCl lens and spherical front surface mirrors on a Jarrell Ash 0.25-m monochromator containing a 148 g/mm, 5.0 μ blaze grating. The band pass filter output (P.E. 237-1202) is focussed on a Philco-Ford Type GPC201 detector. A tuned preamplifier coupled with a phase-sensitive detector system provides a signal proportional to % T to a storage oscilloscope. Analysis of photographs of oscillographs of % T vs. time was performed with an analog computer as previously described.⁴⁹

Association Measurements. The vapor pressure of ether solu-

tions of cyclopentylmagnesium bromide (base/bromide = 0.8) relative to pure ether at 0° was measured as previously described.⁵¹

Calculations of the fit of various models of the reaction to the experimental data were performed on the PLATO IV computer-based teaching system.⁵² This computer system provides essentially instantaneous interaction with the mathematical model of the system and represents the data with two-dimensional graphics.

(52) D. Alpert and D. L. Bitzer, *Science*, **167**, 1582 (1970).

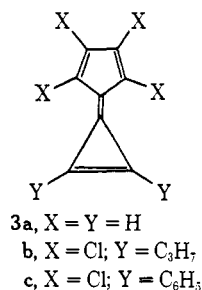
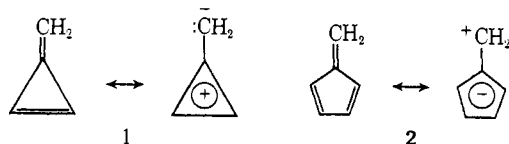
Structures of, and Charge Separation in, 2,3-Diphenyl-4,4-dicyanotriafulvene and 2,3-Diphenylcyclopropenone

Herman L. Ammon

Contribution from the Department of Chemistry, University of Maryland, College Park, Maryland 20742. Received April 6, 1973

Abstract: The crystal structures of 2,3-diphenyl-4,4-dicyanotriafulvene (CYANOF) and 2,3-diphenylcyclopropenone (PROPEN) have been determined with Mo K X-ray diffraction data. CYANOF crystallizes in the monoclinic space group $A2/a$, with cell parameters of $a = 9.5800$, $b = 10.0791$, $c = 14.2918$ Å, and $\beta = 106.546^\circ$ and $Z = 4$. PROPEN crystallizes as the monohydrate in the orthorhombic space group $Pbca$ with cell parameters of $a = 9.291$, $b = 20.658$, and $c = 25.081$ Å and $Z = 16$. The final R factors were 0.035 for CYANOF and 0.043 for PROPEN after full-matrix least-squares structure refinement. Four least-squares minimization functions were tested with the CYANOF data. CNDO/2 calculations have been carried out to obtain charge density and bond order information. The O charge magnitudes in cyclopropenones are 0.12–0.14 e larger than the corresponding charges in saturated ketones. There is a larger negative charge on O in PROPEN (-0.387) than on the $C(CN)_2$ group in CYANOF (-0.366), but the positive charge distributions in the remainder of the molecules place more of the charge on the CYANOF phenyl than on the PROPEN phenyl. This result is in accord with the relative ^{19}F nmr chemical shifts of 2,3-di(*p*-fluorophenyl)-4,4-dicyanotriafulvene and 2,3-di(*p*-fluorophenyl)cyclopropenone.

The fulvenes are nonalternant hydrocarbons which can formally reach Hückel aromatic status by the shift of a π -electron pair either toward, or away from, an unsaturated ring. Mesomeric structures such as the two π -electron cyclopropenium form of triafulvene (1)¹ and the six π -electron cyclopentadienide form of



pentafulvene (2)¹ have intrigued chemists for years with the promise of pseudoaromatic character. The three-ring donor and five-ring acceptor can be joined

(1) The "Chemical Abstracts" names of these compounds are cyclopropenyliidene methane for 1 and cyclopentadienyliidene methane for 2.

to form a fulvalene, an example of which is pentatriafulvene (3a, calicene).

Many attempts have been made to increase the ground state dipolarities of these compounds by the substitution of electron withdrawing groups for H (a) on the rings of acceptor fulvenes and (b) on the methylene carbons exocyclic to the rings of donor fulvenes. As part of a program to identify the structural consequences of charge separation, the structure of a compound of type b, *viz.*, 2,3-diphenyl-4,4-dicyanotriafulvene (4) (CYANOF; 2,3-diphenyl-2-cyclopropene- $\Delta^{1,\alpha}$ -malononitrile), and the structure of the corresponding ketone (5) (PROPEN, 2,3-diphenylcyclopropenone) have been investigated. The pair of struc-

