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CRYSTAL STRUCTURE OF 2,2-DIPHENYLETHYL 2,4,6-TRIMETHYLPHENYL KETONE:* KOHLER'S KETONE. MECHANISM OF STEREOSPECIFIC ENOLIZATION REACTION WITH GRIGNARD REAGENTS.

A. G. PINKUS*, D. F. MULLICA*, W. O. MILLIGAN†, D. A. GROSSIE AND P. W. HURD
Department of Chemistry, Baylor University, Waco, Texas 76798

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Abstract - The title compound crystallizes in the monoclinic space group $P2_1/n$ with a = 10.875(2), b = 6.039(5), c= 29.015(8)A, and β = 91.29(2)°. The observed density for Z = 4 is 1.14(1) Mgm^{-3} (D_c = 1.155 Mgm^{-3}). The reliability factors for 1127 unique reflections are R = 0.066 and R_w = 0.064.The dihedral angle between the mesityl ring and the carbonyl to α-carbon plane is 114.4° in contrast to an angle of 89.9° reported earlier for a substituted t-butyl mesityl ketone. A mechanism is proposed for the formation of an E-magnesium enolate from the reaction of Kohler's ketone with Grignard reagents.

Most unhindered and some hindered ketones undergo 1,2-addition with Grignard reagents to yield tert. alcohols after hydrolysis. Mechanisms of this reaction[1] and that of reduction[2] have been thoroughly investigated. For ketones that have one or more hydrogens alpha to the carbonyl group, formation of magnesium enolate is a competing reaction. Numerous studies[3] have been carried out to determine competitive addition/enolization/reduction ratios and competive rates as dependent on ketone structure, Grignard component, and other conditions. In the case of acetomesitylene (methyl 2,4,6-trimethylphenyl ketone) and other related alkyl mesityl ketones (mesityl = 2,4,6-trimethylphenyl), only the enolization reaction occurred[4] even with methylmagnesium halides as evidenced by quantitative methane evolution with no detectable 1,2-addition. Rate studies[5] of a series of alkyl mesityl ketones with alkylmagnesium bromides are in accord with a cyclic mechanism for the reaction. A crystal structure study of at least one of these alkyl mesityl ketones would be desirable in order to determine the solid state conformation which might be related to solution structures[5,6]. Unfortunately, none of these ketones are solids and x-ray crystallographic studies of alkyl aryl ketones are rare[7]. The title compound is a key compound in the formation of magnesium enolates. Kohler and his students[8] showed that the enol benzoate from the reaction of the magnesium enolate of the title compound with benzoyl chloride differed in melting point from that obtained from the corresponding reaction of the magnesium enolate from 1,4-addition of phenylmagnesium bromide to benzalacetomesitylene. The former enol benzoate was shown[9] to have an E and the latter a Z configuration which correspond to their respective magnesium enolates, since reaction occurs at the Mg-O bond. These observations are significant because (1) they show conclusively that the magnesium to oxygen bond is of a covalent nature, since the isomeric magnesium enolates do not interconvert; and (2) the magnesium enolates may be the first published examples of tricoordinate magnesium compounds[10]; and (3) the results are useful in explaining why an E configuration is obtained in the enolization reaction with Grignard reagents.

*Also named systematically as 3,3-diphenyl-1-(2,4,6-methylphenyl)propane-1-one. The trivial name, Kohler's ketone, will be used in this article for brevity.
†Deceased Feb. 18, 1984.

EXPERIMENTAL

The title ketone was prepared by published procedures[8,9] in 45% yield after recrystallization from absolute ethanol mp 80-81°C (lit[8] 82°). Single crystals for structural studies were obtained by slow evaporation of absolute ethanol solutions.

A single crystal of dimensions 0.337 x 0.260 x 0.223 mm. was mounted on an Enraf-Nonius CAD-4F automated diffractometer. Cell constants were derived from the setting angles of 23 reflections. Intensity data was collected using the ω-2θ scan technique with graphite monochromatized MoKα radiation, a variable scan rate of 0.38 to 3.35° min^{-1} and a Si(Li) energy dispersive detector. Two reflections (4,2,2 and 1,1,2) were measured every two hours and revealed only random deviations (<1.2%) from mean intensities. Lorentz and polarization corrections were applied to the 2552 unique reflections (3°<2θ<50°) and the 1127 with $I > 2\sigma(I)$ were used in the refinement of the structure. The direct methods program[11] MULTAN 11/82 was used to solve the structure. Phases for the largest E values were calculated and the phase set with the highest combined figure of merit produced an E map which revealed the positions of all non-hydrogen atoms. Table 1 presents a summary of experimental and statistical data for the title compound.

Table 1. Experimental and Statistical Data for 3,3-Diphenyl-1-(2,4,6-trimethylphenyl)propan-1-one.

a(A)	10.875(2)	T(K)	291
b	6.039(5)	F(000)	716
c	29.015(8)	Max. 2θ(°)	50
β(°)	91.29(2)	Unique Reflections	2551
V(A^3)	1095.1(25)	R(int)	0.011
Z	4	$I>2\sigma(I)$	1127
Crystal form	monoclinic	L.S. Parameters	227
Space Group	$P2_1/n$	R	0.066
Dm (Mg m^{-3})	1.14(1)	Rw	0.064
Dx (Mg M^{-3})	1.155	Goodness of Fit	1.99
M.W.	331.24	g (e x 10^{-6})	3.93(6)
μ (mm^{-1})	0.064	Residual (e A^{-3})	0.21(5)

The structure was refined using a Full-Matrix least-squares refinement program. At the latter stages of refinement, a difference Fourier map revealed the positions of the 12 aliphatic hydrogens. These hydrogen positions in

Table 2. Atomic Positional Parameters (x 10^4) and Equivalent Isotropic Thermal Parameters (x 10^3) for 3,3-Diphenyl-1-(2,4,6-trimethylphenyl)propan-1-one.

Atom	x	y	z	Ueq*
O(1)	7517(4)	-2236(8)	-843(2)	72(2)
C(1)	7273(6)	-520(11)	-648(2)	49(2)
C(2)	6472(6)	1250(11)	-864(2)	49(2)
C(3)	6242(6)	979(10)	-1374(2)	46(2)
C(11)	7679(6)	-214(10)	-152(2)	42(2)
C(12)	8587(5)	1483(11)	-44(2)	51(2)
C(13)	8909(5)	1740(11)	433(2)	51(2)
C(14)	8421(6)	454(12)	773(2)	57(2)
C(15)	7554(6)	-1145(11)	654(2)	54(2)
C(16)	7186(5)	-1514(11)	199(2)	46(2)
C(17)	9170(6)	2871(11)	-407(2)	50(2)
C(18)	8816(7)	728(12)	1269(2)	75(3)
C(19)	6280(6)	-3300(12)	81(2)	68(3)
C(21)	5181(6)	2417(11)	-1539(2)	45(2)
C(22)	4955(6)	4508(12)	-1356(2)	57(2)
C(23)	3939(6)	5718(12)	-1501(2)	66(3)
C(24)	3133(6)	4897(14)	-1833(2)	76(3)
C(25)	3351(7)	2882(14)	-2030(3)	82(3)
C(26)	4371(6)	1660(12)	-1876(2)	65(3)
C(31)	7385(6)	1431(11)	-1660(2)	46(2)
C(32)	7795(6)	-154(12)	-1964(2)	61(2)
C(33)	8818(6)	220(13)	-2228(2)	76(3)
C(34)	9453(7)	2195(14)	-2195(2)	80(3)
C(35)	9038(6)	3740(12)	-1893(2)	73(3)
C(36)	8034(6)	3412(11)	-1631(2)	55(2)

*Ueq is defined as one third the trace of the U(i,j) matrix.

addition to the 13 calculated aromatic hydrogen positions were used in structure factor calculations but were not refined. Refinement was terminated when the weighted R-factor became stationary and the maximum shift/error was less than 0.01. The function minimized in the refinement was $\Sigma w(|F_o| - |F_c|)^2$, where $w = \sigma^{-2}(Fo)$ with $\sigma(Fo) = [Ip + Ib + (0.02(Ip - Ib))^2]^{1/2}$ where Ip and Ib are the peak and background intensities. Final R, Rw and Goodness of Fit for the structure are 0.066, 0.064, and 1.99, respectively. Scattering factors and anomalous dispersion terms were taken from the International Tables for X-Ray Crystallography[12]. All computer programs used were locally written or part of the Enraf-Nonius VAX structure determination package[13]. Final atomic positions and equivalent isotropic thermal parameters with their estimated standard deviations (e.s.d.'s) are listed in Table 2.

RESULTS AND DISCUSSION

Crystal structure*. All pertinent bond distances and angles are given in Tables 3 and 4, respectively. It is noted that all carbon-carbon bond distances for both of the unsubstituted phenyl rings (C^{21-26} and C^{31-36}) are quite normal, the average C-C bond length is 1.38A. Further, the average C-C bond distance of the tetra-substituted phenyl ring is 1.40A. All other C-C bonds lengths are reasonable, range 1.495 to 1.535A. The carbonyl bond length of 1.212A is an ideal standard value.

Table 3. Bond Distances (A) for 3,3-Diphenyl-1-(2,4,6-trimethylphenyl)propan-1-one.

Atom1	Atom2	Distance	Atom1	Atom2	Distance
O(1)	C(1)	1.212(5)	C(16)	C(19)	1.495(7)
C(1)	C(2)	1.505(7)	C(21)	C(22)	1.394(7)
C(1)	C(11)	1.508(6)	C(21)	C(26)	1.380(6)
C(2)	C(3)	1.504(6)	C(22)	C(23)	1.382(7)
C(3)	C(21)	1.513(6)	C(23)	C(24)	1.380(7)
C(3)	C(31)	1.535(6)	C(24)	C(25)	1.367(8)
C(11)	C(12)	1.452(6)	C(25)	C(26)	1.396(7)
C(11)	C(16)	1.403(6)	C(31)	C(32)	1.382(7)
C(12)	C(13)	1.426(6)	C(31)	C(36)	1.390(6)
C(12)	C(17)	1.499(6)	C(32)	C(33)	1.384(7)
C(13)	C(14)	1.373(6)	C(33)	C(34)	1.376(8)
C(14)	C(15)	1.388(7)	C(34)	C(35)	1.367(8)
C(14)	C(18)	1.501(7)	C(35)	C(36)	1.359(7)
C(15)	C(16)	1.387(6)			

The observed torsional angle ($O^1C^1C^{11}C^{12}$) of 114.4° for the carbonyl-to-carbon/mesityl ring planes can be compared with the corresponding one reported by Bear et al.[7] for the t-butyl ketone of 89.9°. The latter torsional angle was attributed[7] to the extreme restriction of rotation of the t-butyl group by the ortho methyl groups. In the present case, the α-carbon (C^2) is bonded to two hydrogen atoms in addition to the diphenylmethyl group. Because of the two hydrogen atoms positioned α to the carbonyl group, less interference with the ortho methyl groups results in the wider observed torsional angle of 114.4°.

*Calculated and observed structure factors, anisotropic thermal parameters and hydrogen atom coordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

Table 4. Bond Angles (°) for 3,3-Diphenyl-1-(2,4,6-trimethylphenyl)propan-1-one.

Atom1	Atom2	Atom3	Angle	Atom1	Atom2	Atom3	Angle
O(1)	C(1)	C(2)	122.9(5)	C(11)	C(16)	C(19)	119.8(5)
O(1)	C(1)	C(11)	119.1(5)	C(15)	C(16)	C(19)	120.6(5)
C(2)	C(1)	C(11)	117.7(5)	C(3)	C(21)	C(22)	122.6(5)
C(1)	C(2)	C(3)	114.5(4)	C(3)	C(21)	C(26)	120.3(6)
C(2)	C(3)	C(21)	111.0(4)	C(22)	C(21)	C(26)	117.0(6)
C(2)	C(3)	C(31)	113.2(4)	C(21)	C(22)	C(23)	120.7(6)
C(21)	C(3)	C(31)	110.4(4)	C(22)	C(23)	C(24)	120.9(6)
C(1)	C(11)	C(12)	118.4(5)	C(23)	C(24)	C(25)	119.8(7)
C(1)	C(11)	C(16)	121.1(5)	C(24)	C(25)	C(26)	118.8(6)
C(12)	C(11)	C(16)	120.4(5)	C(21)	C(26)	C(25)	122.8(6)
C(11)	C(12)	C(13)	115.9(5)	C(3)	C(31)	C(32)	119.9(6)
C(11)	C(12)	C(17)	122.5(5)	C(3)	C(31)	C(36)	122.4(5)
C(13)	C(12)	C(17)	121.5(5)	C(32)	C(31)	C(36)	117.7(5)
C(12)	C(13)	C(14)	123.0(5)	C(31)	C(32)	C(33)	121.0(6)
C(13)	C(14)	C(15)	119.0(6)	C(32)	C(33)	C(34)	120.7(6)
C(13)	C(14)	C(18)	121.3(6)	C(33)	C(34)	C(35)	117.7(6)
C(15)	C(14)	C(18)	119.7(6)	C(34)	C(35)	C(36)	122.6(6)
C(14)	C(15)	C(16)	122.0(5)	C(31)	C(36)	C(35)	120.3(6)
C(11)	C(16)	C(15)	119.6(5)				

Figure 1 is an ORTEP II[14] steroscopic presentation with ellipsoids of 50% thermal probability and with the numbering scheme adopted throughout the structural analysis of the title compound which is found at a general site within the monoclinic system. The two unsubstituted phenyl rings (C^{21-26} and C^{31-36}) are quite planar having a maximum deviation out of the mean least-squares planes of 0.008 and 0.001A, respectively. The mesityl ring is also planar with all six atoms of the phenyl ring and the three attached methyl carbon atoms being within 0.03A of planarity (mean deviation, 0.017A). A stereoscopic packing diagram displaying the contents of the unit cell with 20% equiprobability ellipsoids represented, is shown in Figure 2. The previous discussion relating to the torsional angle (114.4°) of atoms $O^1C^1C^{11}C^{12}$ is substantiated by the packing diagram.

The molecules are oriented in the unit cell in a layered structure parallel to the ab face. The layers are bounded by the unsubstituted phenyl rings above and below. All molecules within a layer lie with the mesityl ring parallel to the mesityl ring of its neighbors.

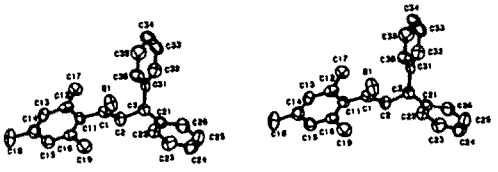


Fig. 1. Stereo drawing of 3,3-Diphenyl-1-(2,4,6-trimethylphenyl)propan-1-one.

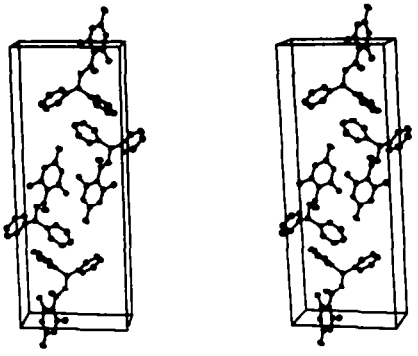
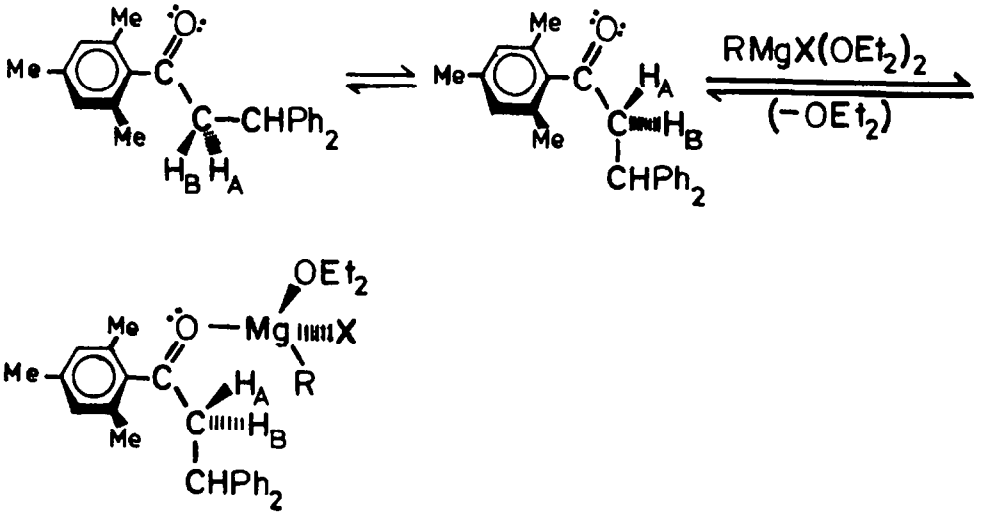


Fig. 2. Stereoscopic unit cell drawing of 3,3-diphenyl-1-(2,4,6-trimethylphenyl)propan-1-one.

Mechanism. The following mechanism (Schemes 1 and 2) is proposed to explain the formation of the E-magnesium enolate from the reaction of Grignard reagents with Kohler's ketone. If the lowest energy conformation of Kohler's ketone in solution is the same as the solid state crystal structure, then a rotation about the carbonyl to methylene bond (C^1 to C^2) is postulated to occur first. Observation of a scale molecular model shows that this rotation can occur without any interference from ortho methyl groups and therefore the conformation could easily be formed in solution even though it might be of slightly higher energy than the solution conformation assumed from the crystal structure. This conformation allows complexation of the magnesium of the Grignard reagent with carbonyl oxygen with less interference from the diphenylmethyl group and also places the methylene hydrogens into position for the cyclic elimination step. In the rate-determining elimination step (formation of R-H alkane) a slight rotation of the C=O to α-C bond brings one of the α-hydrogens (H_A) into position for bond formation with the R electrons (bonded to Mg).

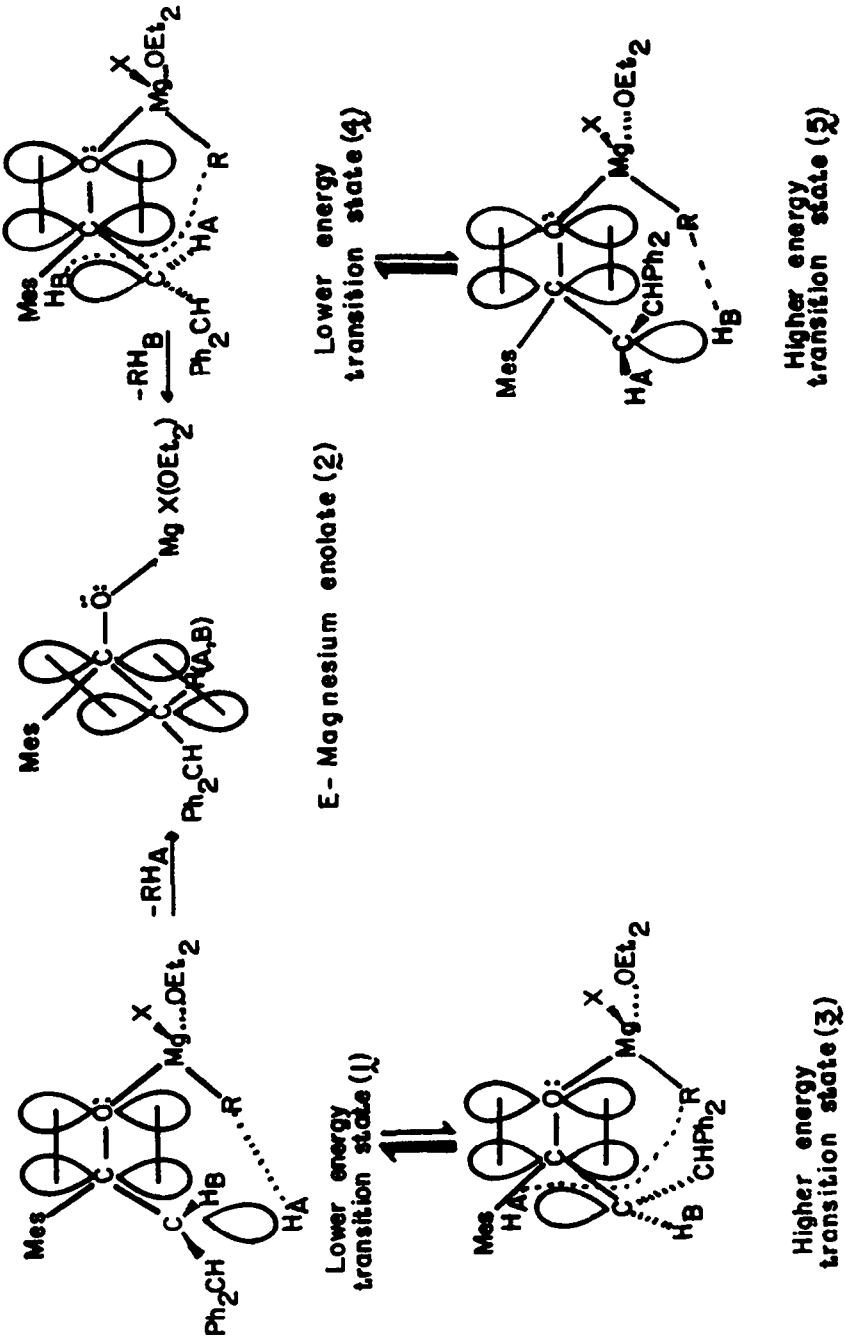
Making use of stereoelectronic control for the elimination mechanism

SCHEME I



(Scheme 2), conformation (1) in which the H_A-C sp^3 sigma orbital is parallel with the carbonyl π orbitals is favored for H_A removal and leads to the observed E-magnesium enolate (2). The transition state for this conformation is of lower energy than the one for H_A removal from conformation (3) in which there is steric interaction between the largest grouping[15] (the magnesium attached to halogen, an R group, and a bulky diethyl ether) and the diphenylmethyl grouping. Similarly for H_B the lower energy transition state conformation (4) is more favorable for formation of the E-magnesium enolate than that for the other conformation (5) which would result in formation of Z-enolate. It is evident

SCHEME 2



from molecular models (though not in the drawing) that the distance from R to the hydrogen being eliminated (H_A or H_B) is the same in 3 and 4 as in 1 and 5.

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