Structures of Isomeric Grignard Compounds Derived from 2,2-Diphenylethyl 2,4,6-Trimethylphenyl Ketone and Their Corresponding Enol Benzoates[1]

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Enol benzoates I and II formed from reactions of magnesium enolates I and II with benzoyl chloride are determined to have *E* and *Z* configurations, respectively. The configurations are established using the vinyl substituent shielding constants of Pascual et al.[7] and Tobey.[8] The corresponding magnesium enolates, I and II, likewise have *E* and *Z* configurations. Magnesium enolate I is formed from the reaction of benzalacetomesitylene (1) and phenylmagnesium bromide; magnesium enolate II is formed from the reaction of 2,2-diphenylethyl 2,4,6-trimethylphenyl ketone (2) and ethylmagnesium bromide. Cryoscopic studies in naphthalene show that magnesium enolates I and II are both monomeric; this together with other evidence indicates that they contain tricoordinate magnesium analogous to the Grignard compound derived from isopropyl mesityl ketone.[6] Ir spectra confirm the enolic nature of the magnesium compounds, I and II.

In 1935 Kohler, Tishler, and Potter[3] reported the preparation of the bromomagnesium derivative of 2,2-diphenylethyl 2,4,6-trimethylphenyl ketone (2) by three routes (Scheme I): (A) 1,4 addition of phenylmagnesium bromide to benzalacetomesitylene (1); (B) action of Grignard reagent on 2,2-diphenylethyl 2,4,6-trimethylphenyl ketone (2); (C) action of Grignard reagent on 2,2-diphenyl-1-bromoethyl 2,4,6-trimethylphenyl ketone (3). They noted that the magnesium compounds prepared by route A vs. those from routes B and C formed stereoisomeric (cis–trans) enol benzoates (4) in high yield (ca. 96%) on reaction with benzoyl chloride. A high-melting benzoate (162°) was formed by the first method and a lower melting benzoate (142°) by the other two methods (Scheme II). They reasoned that the magnesium compounds were the corresponding magnesium enolates.

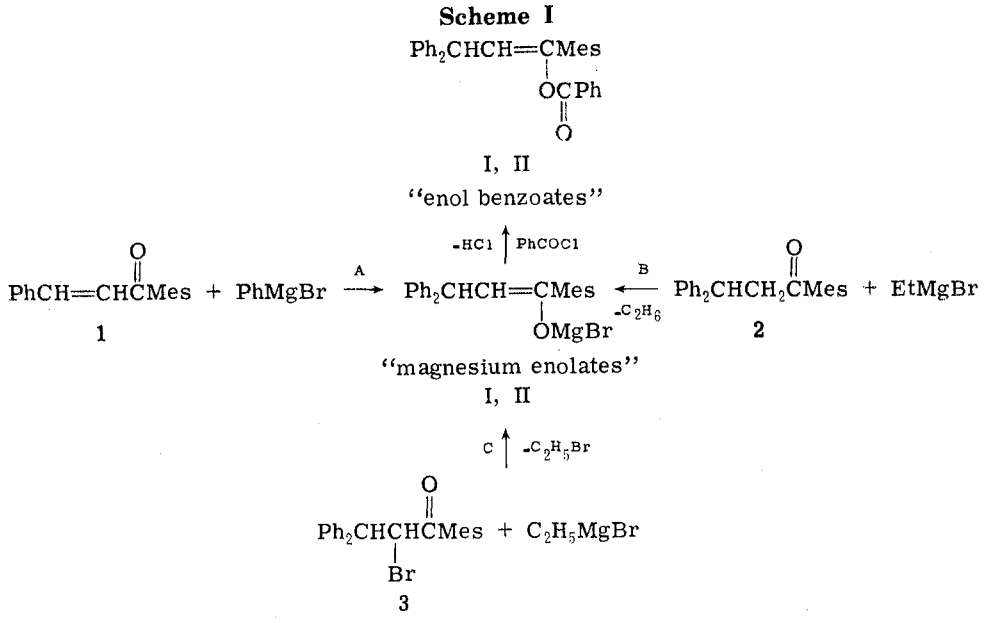
Nesmeyanov, Sazonova, and Landor[4] characterized the isomeric enol benzoates and bromomagnesium derivatives from routes A and B by elemental analysis, which showed that the latter each contained one molecule of ether. (The benzoates were also previously analyzed by Kohler et al.[3]) The compound from route A was about ten times as soluble in benzene as that from route B and only the former compound was oxidized to peroxide by atmospheric oxygen. Both isomers formed the same ketone quantitatively on hydrolysis. The authors concluded that solubility of the magnesium compounds in benzene as well as absence of interconversion excluded consideration of mesomeric anionic forms. However, neither the Nesmeyanov group nor the earlier Kohler group were able to assign cis–trans structures to the isomeric magnesium enolates or enol benzoates and the molecular states of aggregation of the former were not determined.

In connection with our interest in the structures of Grignard compounds derived from methyl[5] and isopropyl[6] mesityl ketones, it was thought that the characterization and assignments of the isomeric structures of the magnesium enolates and corresponding enol benzoates would aid in the determination of the structures of Grignard compounds derived from alkyl mesityl ketones which were under investigation at the time.

Results and Discussion

Configuration of Enol Benzoates. Enol benzoates I and II were prepared by treating magnesium enolates I and II with benzoyl chloride according to the procedure of Kohler et al.[3] as modified by Nesmeyanov et al.[4] (The designations I and II by the latter group are retained in the present paper in order to maintain continuity with the previous workers.) The relationships are outlined in Schemes I and

Scheme I

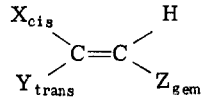


Scheme II

"magnesium enolate I" ⟶ "enol benzoate I" (mp 162°) (via route A)

"magnesium enolate II" ⟶ "enol benzoate II" (mp 142°) (via routes B and C)

II. The configurations were established mainly from ^{1}H NMR data. The principal feature was the chemical shift of the vinyl proton which was compared with the values calculated by using the concept of additivity of vinyl substituent shielding constants as developed by Pascual et al.[7] and Tobey.[8] The chemical shift of the vinyl proton can be calculated from eq 1 where −5.27 represents the value for unsubstituted ethylene. The substituent shielding constants in Table I taken from the literature were used. Since no values for the diphenylmethyl group have been reported, the value for the benzyl group was used.[9] The calculations for *Z* and *E* configurations are shown. These values check



$$\delta_{ppm} = -5.27 + \sigma_{cisX} + \sigma_{transY} + \sigma_{gemZ} \quad (1)$$

Z: $\delta_{ppm} = -5.27 + 0.11 + 0.51 - 1.05 = -5.70$

E: $\delta_{ppm} = -5.27 + 0.10 - 0.15 - 1.05 = -6.37$

very well with those observed for the vinyl protons of enol benzoate I at −5.75, establishing it as having the *Z* configuration, and enol benzoate II at −6.35, which indicates the *E* isomer. From molecular models, the vinyl proton of the *Z* isomer is apparently in the shielding zone of the mesityl ring, this being in accord with observations. The other ^{1}H NMR assignments are clear-cut and are given in the Experimental Section.

Magnesium Enolates. A. Molecular Weight Determinations. The two enolates were prepared by the Kohler[3] and Nesmeyanov[4] procedures. As reported, the magnesium enolate obtained as a precipitate from the reaction of phenylmagnesium bromide and benzalacetomesitylene (1) in diethyl ether was soluble in dry benzene at room temperature to the extent of 10–15 wt % and was recrystallized from this solvent. This is designated "magnesium enolate I". "Magnesium enolate II", obtained as a precipitate from the reaction of ethylmagnesium bromide and 2,2-diphenylethyl 2,4,6-trimethylphenyl ketone (2), was only soluble to the extent of 1–2 wt % in benzene. The molecular weights of these samples were determined by a cryoscopic method[10] using naphthalene. The results obtained show a molecular weight of 521 ± 26 (average of four runs with four to six determinations per run) for magnesium enolate I and 501 ± 5 (average of two runs with six determinations per run) for magnesium enolate II. The calculated molecular weight for the formula $C_{28}H_{33}O_2MgBr$ is 506 so the respective *i* values are 1.03 for enolate I and 0.990 for enolate II. (*i* values are defined[11] as the degree of association = *i* = experimental mol wt/theoretical mol wt.) These results show that each enolate is coordinated with one molecule of ether and is monomeric in naphthalene. Thus, these two enolates can be added to the examples in which magnesium is tricoordinate.[6]

The following points can be made concerning the possibility of solute association at higher concentrations. Enolate I was measured over a concentration range of 8–12.2 wt % and no trend in values with concentration was discernible. Enolate II was measured at a lower concentration of 1.8–2.0 wt % because of its lower solubility. However, at concentrations of 2–3%, the Grignard compound derived from methyl mesityl ketone was found[5] to be a dimer, showing that no dissociation occurred at a low concentration under similar conditions, whereas the corresponding compound derived from isopropyl mesityl ketone was a monomer[6] at comparable concentrations. The molecular weights for both of these compounds were also determined at comparable concentrations by cryoscopy in benzene with comparable results, showing no appreciable effects of temperature or solvent changes.

Table I
^{1}H NMR Substituent Shielding Constants[e] for Some Vinylic Substituents

Substituent	σ_{cis}	σ_{trans}	σ_{gem}	Ref
$PhCO_2$	+0.10	+0.51	−2.46	*a*
2,4,6-Me_3Ph	+0.11	−0.15	−1.36	*b*
$ArCH_2$	+0.29	+0.32	−1.05	*c*
XMgO	+0.86	+1.11		*d*

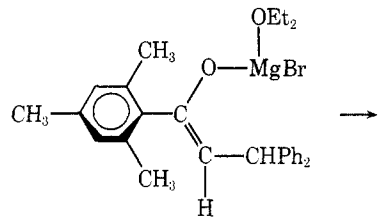
[a] P. D. Kaplan and M. Orchin, *Inorg. Chem.*, 6, 1096 (1967); ref 7. [b] Average of values from Gurudata, J. B. Stothers, and J. D. Talman, *Can. J. Chem.*, 45, 731 (1967); L. M. Jackman and R. H. Wiley, *J. Chem. Soc.*, 2881 (1960); R. E. Mayo and J. H. Goldstein, *J. Mol. Spectrosc.*, 14, 173 (1964); H. Rottendorf, S. Sternhell, and J. R. Wilmshurst, *Aust. J. Chem.*, 18, 1789 (1965); ref 7; M. Schlosser and V. Ladenberger, *Chem. Ber.*, 100, 3901 (1967); R. van der Linde, O. Korver, P. K. Korver, P. J. van der Haak, J. U. Veenland, and T. J. de Boer, *Spectrochim. Acta*, 21, 1893 (1965); E. S. Huyser and L. Kim, *J. Org. Chem.*, 33, 1243 (1968). [c] Reference 7. [d] Average of values from K. B. Wiberg and B. J. Nist, *J. Am. Chem. Soc.*, 83, 1226 (1961); G. Stork and P. F. Hudrlik, *ibid.*, 90, 4464 (1968); Gurudata et al., footnote *b*. [e] In parts per million.

Concerning the assignment of the two magnesium enolates of the present work as having tricoordinate magnesium, this is based on the following considerations. The elemental analyses and molecular weight determinations clearly establish that the compounds are monoetherates and not dietherates. For monomeric dietherates, the molecular weight would have deviated by about 15% from the value found, and the elemental analyses also by a substantial amount. Since the compounds are monoetherates, there are only three atoms bound to magnesium, since the possibility of forming a dimer was excluded. The reason for the inability to dimerize in the present cases is apparently the same as that suggested for the isopropyl case,[6] that is, steric crowding by the diphenylmethyl group preventing cyclization which results in dimer formation.

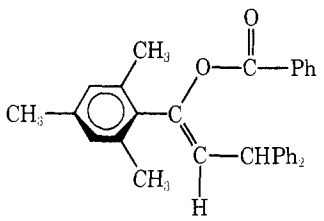
B. Structural Considerations. The infrared spectra of the magnesium enolates both show C=C stretching bands as a doublet at 1658 and 1650 cm^{-1}, in excellent agreement with those observed[5,6] for magnesium enolates derived from alkyl mesityl ketones. This establishes the enolate nature of these compounds.

Since enol benzoate I, obtained in high yield from reaction of magnesium enolate I with benzoyl chloride, was shown to have different physical properties from enol benzoate II, which was obtained in high yield in the same manner from magnesium enolate II, the configurations of the magnesium enolates are retained and are directly related to the configurations of the enol benzoates. Since reaction must necessarily occur at the O–Mg bond, magnesium enolate I must have the *Z* configuration and magnesium enolate II the *E* configuration. The correlations between the benzoates and the magnesium enolates are in Scheme III. If isomerization had occurred during the reaction, a mixture of enol benzoates would have been obtained, or the same

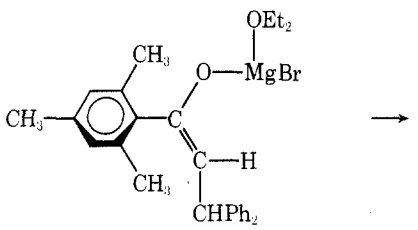
Scheme III



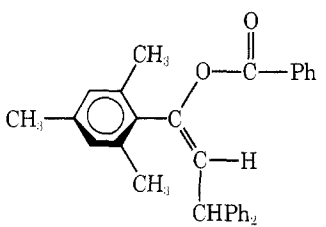
"magnesium enolate I"
(via route A) *Z* configuration



"enol benzoate I"
(*Z*)-(1-mesityl-2-diphenylmethyl)vinyl benzoate



"magnesium enolate II"
(via routes B and C) *E* configuration



"enol benzoate II"
(*E*)-(1-mesityl-2-diphenylmethyl)vinyl benzoate

isomer would be obtained from both reactions (depending on whether or not equilibrium was attained).

Experimental Section

2-Phenylvinyl 2,4,6-trimethylphenyl ketone (benzalacetomesitylene, 1) was prepared by (a) sodium hydroxide catalyzed condensation of acetomesitylene and freshly distilled benzaldehyde according to the procedure of Kohler and Barnes[12] in 97.4% crude yield, mp 60.5–61.5° after recrystallization from petroleum ether (bp 30–60°) (lit.[13] mp 63°) [the recrystallized product showed a single spot, R_f 0.56, on a thin layer chromatogram [80% chloroform–20% carbon tetrachloride mixture on silica gel–poly(ethylene terephthalate); Eastman Chromatogram type K301R]]; (b) Friedel–Crafts aluminum chloride catalyzed acylation of mesitylene with cinnamoyl chloride in carbon disulfide using a modification of the procedures of Kohler[14] and Nesmeyanov and Sazonova,[13] 82% yield, mp 62.5–63.0° after recrystallization from petroleum ether.

Ir and ^{1}H NMR spectra showed that the same trans product was obtained from the two different methods of preparation. A trans or *E* configuration is assigned on the basis[15] of the coupling constant ($J_{H_\alpha H_\beta}$) of 16.5 Hz for the vinyl protons at δ 6.82 and 7.18, respectively, for H_α and H_β. The other ^{1}H NMR assignments (CCl_4) are: δ 2.14 (*o*-CH_3), 2.28 (*p*-CH_3), 6.88 (two ArH on Mes), 7.41 m (C_6H_5). Ir (CCl_4) 1681 sh, 1650 s (C=O), 1629 s, 1610 s, 1582 cm^{-1} m (C=C stretch, aliphatic). The two carbonyl bands and C=C stretching bands result from s-cis–s-trans isomerism of the conjugated enone system.[16]

2,2-Diphenylethyl 2,4,6-trimethylphenyl ketone (2) was prepared by the hydrolysis of the bromomagnesium compound obtained from the reaction of phenylmagnesium bromide and benzalacetomesitylene (1) according to the method of Kohler et al.[3] A yield of 95% (lit.[4] quantitative) was obtained after three recrystallizations from absolute ethanol: mp 80–82° (lit.[3,4] mp 82°); ^{1}H NMR ($CDCl_3$) δ 1.89 (*o*-CH_3), 2.22 (*p*-CH_3), 3.46 (d, J_{CH_2CH} = 7.2 Hz), 4.80 (t, CH), 6.75 (two ArH on Mes), 7.24 (m, Ph_2); ir (mineral oil) 1689 cm^{-1} s (C=O).

Preparation of "Magnesium Enolate I" [Bromo Grignard Compound from Reaction of Phenylmagnesium Bromide and Benzalacetomesitylene (1)]. The general procedures of Kohler et al.[3] and Nesmeyanov et al.[4] were followed. The initial precipitate was recrystallized from dry benzene, the crystals forming after standing for several days in a nitrogen-filled drybox: ir (mineral oil) 1658, 1650 (C=C stretch, aliphatic), 1613 cm^{-1} (C=C stretch, aromatic).

Preparation of "Magnesium Enolate II" [Bromo Grignard Compound from Reaction of Ethylmagnesium Bromide and 2,2-Diphenylethyl 2,4,6-Trimethylphenyl Ketone (2)]. The general procedures of Kohler et al.[3] and Nesmeyanov et al.[4] were followed. The precipitated "enolate" was collected by vacuum filtration and washed with anhydrous ether: yield 73%; ir (mineral oil) 1658, 1650 (C=C stretch, aliphatic), 1613 cm^{-1} (C=C stretch, aromatic).

"Enol benzoate I" was prepared by the reaction of "magnesium enolate I" with benzoyl chloride according to the general procedure of Kohler et al.[3] and Nesmeyanov et al.[4] The initial crude product was recrystallized twice from acetone: mp 162–163° (lit. mp 161°,[3] 162°[3,4]); ^{1}H NMR ($CDCl_3$) δ 2.24 (*o*-Me), 2.41 (*p*-Me), 5.23 (d, CH, $J_{CH,CH=}$ = 10.1 Hz), 5.75 (d, CH=), 6.82 (*m*-Mes-H), 7.23 (Ph_2), 7.41 (m, *m*- + *p*-C_6H_5C=O); ir (mineral oil) 1736 (C=O stretch), 1689 (C=C stretch, aliphatic), 1613 cm^{-1} (C=C stretch, aromatic).

"Enol benzoate II" was prepared by the reaction of "magnesium enolate II" with benzoyl chloride following the general procedure of Kohler et al.[3] and Nesmeyanov et al.[4] The initial product was recrystallized twice from acetone, mp 143–145° (lit. mp 142°,[3] 145°[4]). (The 148° value also given in the Kohler paper is apparently in error.) The melting point range of a 1:1 mixture of enol benzoates I and II was 126–134°: ^{1}H NMR ($CDCl_3$) δ 2.29 (*o*-Me), 2.25 (*p*-Me), 4.48 (d, –CH–, $J_{CH,CH=}$ = 11.0 Hz), 6.35 (d, CH=), 6.88 (*m*-MesH_2), 7.19 (Ph_2), 7.41 (m, *m*- + *p*-C_6H_5C=O), 8.01 (m, *o*-C_6H_5C=O); ir (mineral oil) 1733 (C=O stretch), 1689 (C=C stretch, 8.01, aliphatic), 1615 cm^{-1} (C=C stretch, aromatic).

Instruments and Methods. Reactions and operations using moisture- and oxygen-sensitive compounds were carried out in a nitrogen-filled drybox. Phosphorus pentoxide spread on vermiculite was used as a desiccant in the drybox and as part of a drying train for the nitrogen. Traces of oxygen were removed by bubbling through Fieser's solution.[17]

Ir spectra were taken on a Perkin-Elmer Model 337 grating spectrophotometer. Band positions were calibrated against polystyrene film.

^{1}H NMR spectra were taken with Varian Associates Models DP-60 or A56/60A spectrometers on samples having concentrations of 10–15% w/v, Me_4Si internal reference.

Melting points were determined with a modified Thiele apparatus using a calibrated thermometer.

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Registry No.—1, 55800-30-1; 2, 55800-31-2; magnesium enolate I, 55869-68-6; magnesium enolate II, 55800-34-5; enol benzoate I, 55800-32-3; enol benzoate II, 55800-33-4; acetomesitylene, 1667-01-2; benzaldehyde, 100-52-7; mesitylene, 108-67-8; cinnamoyl chloride, 102-92-1; benzoyl chloride, 98-88-4.

References and Notes

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A Low-Pressure, Palladium-Catalyzed *N,N'*-Diarylurea Synthesis from Nitro Compounds, Amines, and Carbon Monoxide

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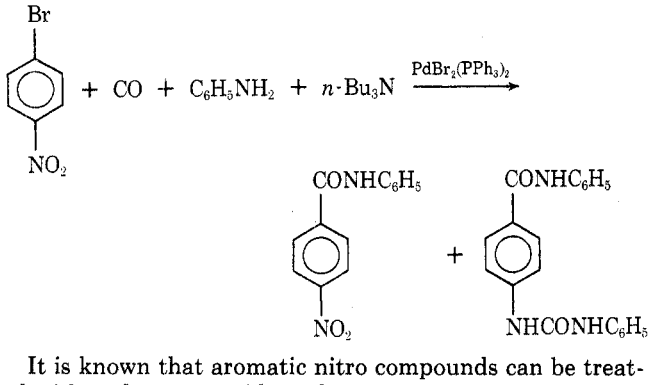
Aromatic primary amines, aromatic nitro compounds, and carbon monoxide react in the presence of catalytic amounts of palladium(II) salts, organic phosphines, a basic tertiary amine, and tetraethylammonium chloride at 90° under 1 atm pressure to form *N,N'*-diarylureas in moderate to good yields.

It was previously noted that the reaction of *p*-bromonitrobenzene, carbon monoxide, aniline, and a tertiary amine with $PdBr_2(PPh_3)_2$ as catalyst at 100° and 1 atm pressure led to the formation of considerable amounts of the *N*-phenylamide of 4-carboxydiphenylurea as well as the expected *N*-phenyl-*p*-nitrobenzamide.[1] We have now investigated the diarylurea formation in more detail.



It is known that aromatic nitro compounds can be treated with carbon monoxide under vigorous conditions to give urea derivatives. For example, nitrobenzene with water and 10,000 psi of carbon monoxide at 180° with a palladium–iron catalyst forms diphenylurea[2] and the same product is obtained in 54% yield when nitrobenzene is treated at 140° under 150 atm pressure with carbon monoxide and hydrogen using $[Ru(CO)_4]_3$ as catalyst.[3] We report in this paper a more versatile synthesis of diarylureas that occurs with only 1 atm pressure of carbon monoxide and at temperatures below 100°.

Results and Discussion

Preliminary experiments investigating the reaction of aniline and nitrobenzene with $Pd(OAc)_2$ plus 2 equiv of triphenylphosphine as catalyst under 1 atm of carbon monoxide revealed that both halide ion and a basic tertiary amine were necessary to cause the reaction to occur in reasonable yields. Without halide ion, the reaction stopped with less than 10% of the theoretical amount of CO being absorbed. It was also necessary to purge the apparatus frequently with fresh CO to remove accumulated CO_2 from the reaction vessel. The optimum reaction rate in xylene solution was achieved at about 90° using 15 mol % tetraethylammonium chloride, ~50 mol % tri-*n*-butylamine, 2 mol % palladium acetate, and 4 mol % triphenylphosphine based upon the aromatic amine used. The nitro compound was present in 10–100% excess of the molar amount of the aromatic amine. The reaction could be carried out in solvents other than xylene such as DMF, Me_2SO, and HMPA, but there appeared to be no rate or yield advantage in doing so. In xylene, the urea derivatives generally crystallized from the solution during the reaction while in DMF, Me_2SO, or HMPA they did not. The tetraethylammonium chloride salt was more effective than the bromide and it in turn was better than the iodide. The reaction rates were not very sensitive to the amount of the chloride added; however, the amount of tertiary amine which gave the greatest rate accelleration was about 1 g per 10 ml of xylene solvent. The reaction is presumed to occur according to the following equation.

$$ArNH_2 + ArNO_2 + 3CO \xrightarrow[n\text{-}Bu_3N]{Pd(PPh_3)_2X_2,\ Et_4N^+Cl^-} ArNHCONHAr + 2CO_2$$

The data obtained from these and related reactions appear in Table I. Reaction rates were estimated from the time required for half of the theoretical amount of CO required, according to the above equation, to be absorbed.

Various palladium complexes were tried as catalysts. Differences in the anions attached to the metal had only minor effects upon the reaction rates. Major effects were caused by changing the phosphine groups. Triphenylphosphine was the best ligand found. Tri-*o*-tolylphosphine and