



The synthesis of 3,3,4,4-tetraphenyl-2-butanone from 1,1-diphenylacetone

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Abstract—The preparation of 3,3,4,4-tetraphenyl-2-butanone by treatment of 1,1-diphenylacetone (1,1-DPA) with potassium-*t*-butoxide or lithium diisopropyl amide in THF at 0°C followed by heating with a diphenylmethylhalide is described. A single crystal X-ray analysis of the new ketone shows that the molecule crystallizes in a conformation in which the carbonyl group is not eclipsed with the benzylic hydrogen, but has a torsional angle of +41° toward a *gauche* (120°) conformation. © 2002 Elsevier Science Ltd. All rights reserved.

In previous work the coupling reactions of benzylic organolithium reagents with benzylic halides were found to form highly phenylated alkanes predominantly by S_N2 displacement.^{1–3} In an extension of those earlier synthetic efforts 1,1-diphenylacetone (1,1-DPA) was treated with potassium *t*-butoxide in THF at temperatures from 0–25°C and alkylated with diphenylmethylbromide by heating to afford 3,3,4,4-tetraphenyl-2-butanone, **1** (see Scheme 1 and literature reviews).^{4–9}

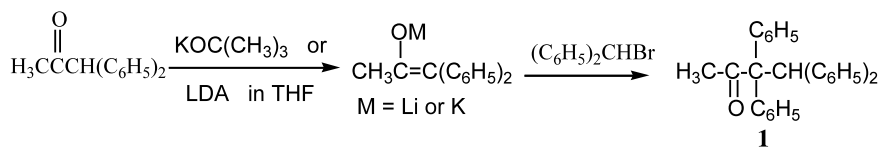
No alkylation products from the methyl group enolate or from oxygen alkylation of either enolate were isolated. The greater acidity of the benzylic hydrogen in 1,1-DPA (p*K*_a ~ 10.42) over the methyl hydrogens (p*K*_a ~ 18.27) can be estimated by comparison with diphenylacetaldehyde¹⁰ and benzylmethyl ketone¹¹ acidities.

When 1,1-DPA was treated with LDA at 0°C in THF (2.0 h) followed by dropwise addition of diphenylmethylchloride and 2.0 h of heating, only **1** was formed in 19–22% yields. 1,1-DPA was recovered (45%) together with *sym*-tetraphenylethane and diphenyl-

methanol. None of the isomeric 1,1,4,4-tetraphenyl-2-butanone expected from the methylene enolate could be found.¹²

A possible explanation for the failure to observe alkylation on the methyl carbon may be that it isomerizes rapidly in the presence of excess starting ketone into the diphenylmethylene enolate in a manner similar to Rathke's report on the isomerization of *E*- and *Z*-enolates of 3-pentanone by a reversible aldol condensation mechanism.¹³ Because LDA and 1,1-DPA in THF at 0°C did not undergo alkylation with diphenylmethylchloride, it might be possible that the methylene enolate forms first but isomerizes completely into diphenylmethylene enolate faster on heating than diphenylmethyl halides can alkylate it.

Although the new ketone, 3,3,4,4-tetraphenyl-2-butanone, **1**, mp 155–156°C, had a properly integrated proton NMR spectrum, ¹³C NMR peak at δ = 205.97 for C=O, a strong peak in the IR at 1700 cm⁻¹, analytical data that matched for C₂₈H₂₄O, and a MS with a molecular ion at *m/z* = 376, its melting point did not agree with the literature (117–118°C).^{14,15}



Scheme 1.

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The erroneous literature assignment was based on the assumption¹⁶ that oxidation of 2-methyl-1,1,3,3-tetraphenylpropene, **2**, with chromium trioxide in boiling acetic acid produced an epoxide, **3**, or a diol which subsequently experienced pinacol rearrangement to give **1**.

To verify the literature report a sample of **2** was prepared by the literature procedure and was oxidized with chromium trioxide in boiling acetic acid to give epoxide **3** as shown in Scheme 2. An IR spectrum showed that epoxide **3** had been mis-identified as ketone **1** as judged by the absence of the carbonyl signal and the presence of epoxide ring signals in the ¹³C NMR at $\delta=70.05$ and 71.64 ppm.

X-Ray analysis of the new ketone was undertaken not only to verify its structure but also to indicate whether **1** would be a suitable precursor in polyphenylethane syntheses. We thought that replacing a phenyl group of pentaphenylethane with an acetyl moiety might lead to a shorter central carbon–carbon bond. This goal was achieved in that the r_c value for pentaphenylethane¹⁷ is 1.606 \AA , while the new ketone has a C₃–C₄ bond distance of 1.587 \AA . See Figs. 1 and 2 for the atom numbering scheme and the torsion angles (ω).

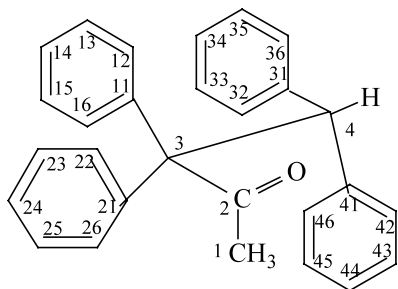


Figure 1. The numbering scheme for ketone **1**. C₃–C₄ = 1.587 \AA .

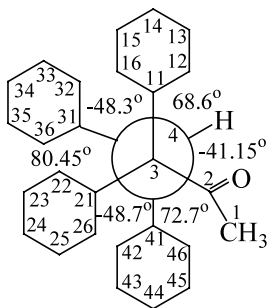
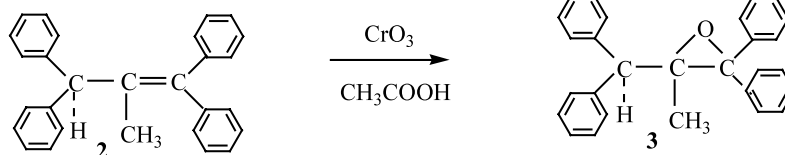


Figure 2. Projection of ketone **1** down the C₃–C₄ bond. Torsion angles are shown.



Scheme 2.

One of the more interesting aspects of the crystal structure is the fact that in the Newman projection of Fig. 2 where the bulky phenyl groups might have been expected to be all *anti* to each other, the acetyl group on C₃ is found to be *+syn* clinal ($30\text{--}90^\circ$)¹⁸ to the benzylic hydrogen. If we recall that the parent compound for ketone **1** is 2-butanone, which is known to have two conformations in which the C₄ methyl group or a C₃ methylene hydrogen are eclipsed with the carbonyl group (i.e. have an ω of 0°), then the observed dihedral angle of $+41.0^\circ$ displaced from $\omega=0^\circ$ for the benzylic hydrogen to carbonyl group plane in solid **1** is a measure of the degree to which the non-bonding steric interactions of the four substituent phenyl groups oppose the orbital interactions which stabilize eclipsed conformations in 2-butanone.^{19,20}

In the packing diagram there are eight molecules in the unit cell of space group $P\bar{1}$. Because of the inversion symmetry operation, one has four independent molecules (A, B, C, and D) and their mirror images. The values of the C₂–C₃–C₄–H torsion angles for A–D in the 295° data are: $-41.0, 48.0, -40.7, 44.7^\circ$.

In Fig. 3 of one of the four independent molecules, A, in the unit cell, it appears as if the *ortho* aromatic hydrogen atom on C-46 is pointing toward the π cloud of ring two (C₂₁–C₂₆) at a distance of 2.4 \AA from the π face. Such hydrogens are thought to provide an attractive edge-to- π -face interaction²¹ estimated to be ~ 0.5 kcal/mol.^{22,23} Unfortunately in molecules B, C and D the ring plane rotational angles vary widely so that the distance between the *ortho* hydrogen atom on C-46 and the face of ring two is increased to 3.82 \AA , 3.19 \AA and 3.27 \AA . Thus it does not appear that aromatic edge–hydrogen to aromatic π -face interactions play any significant role in the conformation in which ketone **1** crystallizes.^{21–23}

Experimental

Crystallographic data (excluding structure factors) for the title ketone have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 182217. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (0) 1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].

Crystals of **1** are triclinic, space group $P\bar{1}$, $a=9.721(2) \text{ \AA}$, $b=19.982(7) \text{ \AA}$, $c=21.856(6) \text{ \AA}$, $\alpha=89.67(3)^\circ$, $\beta=$

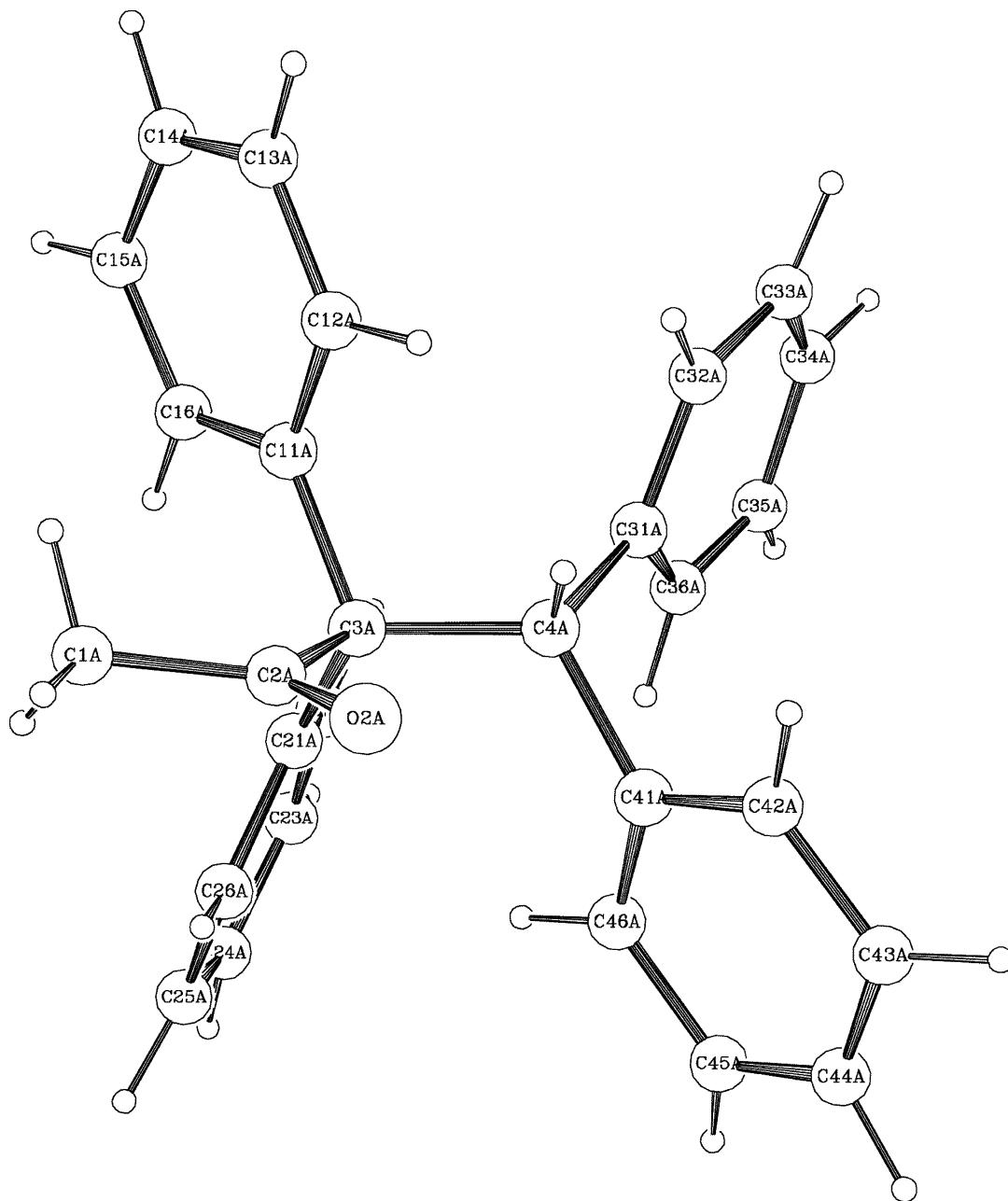


Figure 3. X-Ray structure of independent molecule A of **1** at 295 K.

81.87°, $\gamma = 81.49(2)^\circ$, $V = 4155.7(21) \text{ \AA}^3$, and $D_{\text{calc}} = 1.204 \text{ g/cm}^3$ for $Z = 8$ ($\text{C}_{28}\text{H}_{24}\text{O}$), = 376.503. The crystal used for data collection measured 0.16×0.20×0.40 mm. Intensity data were measured on an Enraf–Nonius CAD4 diffractometer with graphite monochromated Mo $K\alpha$ radiation, ω – 2θ scans having $\mu = 0.771 \text{ cm}^{-1}$. Data were not corrected for absorption. Of 5710 independent reflections for $\theta < 18^\circ$, 1850 were considered observed [$I > 3.0\sigma(I)$].

The structure was solved at Bruker-AXS using SHELXTL software by Dr. Charles Campana who collected data on a second crystal at 110 K. The application of low temperature parameters to room temperature data produced a refined structure by full-

matrix least-squares methods. The final discrepancy indices are $R = 0.0720$ and $R_w = 0.0722$ for the 1850 observed reflections. The final difference map has no peaks greater than $\pm 0.24 \text{ e \AA}^{-3}$. In the final refinement, the oxygen atoms were refined anisotropically and the carbon atoms were refined isotropically. The hydrogen atoms were included in the structure factor calculations, but their parameters were not refined.

Acknowledgements

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