

Conformation-Related Reaction Efficiency of Glutarimides with Phenyllithium. Structures of 3,3,5,5-Tetramethylglutarimide and 2-Hydroxy-2-phenyl-3,3,5,5-tetramethyl-6-piperidone. X-ray and Theoretical Study

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Abstract

Crystal structures of 3,3,5,5-tetramethylglutarimide [3,3,5,5-tetramethylazacyclohexane-2,6-dione] (8) and the product of its reaction with phenyllithium, 2-hydroxy-2-phenyl-3,3,5,5-tetramethyl-6-piperidone (9), have been determined by X-ray structural methods [(8), monoclinic, $P2_1/c$, $a = 7.715$ (2), $b = 11.136$ (2), $c = 11.707$ (2) Å, $\beta = 105.63$ (3)°; (9), triclinic, $P\bar{1}$, $a = 6.1685$ (6), $b = 11.1475$ (10), $c = 11.526$ (2) Å, $\alpha = 117.100$ (10), $\beta = 103.390$ (10), $\gamma = 91.288$ (7)°]. Molecular structures of three different glutarimides are discussed. Their energy optimal structures were determined with the use of *ab initio* calculations. The results of crystallographic and theoretical studies show that the conformational changes in glutarimide introduced by substitution with methyl groups resulted in electron-charge distribution changes. These differences in charge distribution are the reason for the observed variation in yields of the reaction of glutarimides with phenyllithium.

1. Introduction

In the course of our synthetic evaluation of the reactivity of organolithium compounds towards substituted glutarimides we have found (Wróbel, Cybulski & Dąbrowski, 1977; Czarnocki & Wróbel, 1984) that phenyllithium reacts with polymethyl-substituted glutarimides to form products whose structures depend on the number of methyl groups attached to the imide ring. When glutarimide (2,6-piperidinedione) (1) itself was used as a substrate, a ketoamide (2) was found to be the only product. With traces of acids it dehydrated quantitatively forming an enamide (3). Treatment of 4,4-dimethylglutarimide (4) with phenyllithium caused the formation of two compounds (5) and (6) in a ~ 1:1 ratio, which are in a relatively fast tautomeric equilibrium. The addition of acids, even in trace amounts, accelerated the equilibration, also causing dehydration into the final enamide (7). The structures of both tautomeric compounds (5) and (6) were established on the basis

of their spectroscopic examination (¹H NMR) upon separation into the pure forms (Czarnocki & Wróbel, 1984).

When 3,3,5,5-tetramethylglutarimide (8) was reacted with phenyllithium a single compound (9) was formed in 95% isolated yield (Czarnocki & Wróbel, 1984). The yield of (9) is much better than (3), (5) and (6), proving a higher susceptibility of the imide carbonyls in (8) towards nucleophilic attack. The cyclic form of (9) was proposed by comparison of its ¹H NMR spectrum with the spectra of tautomers (5) and (6).

The increasing stability of the cyclic structures of the products derived from imides (1), (4) and (8) can be rationalized in terms of the gem-dialkyl groups'

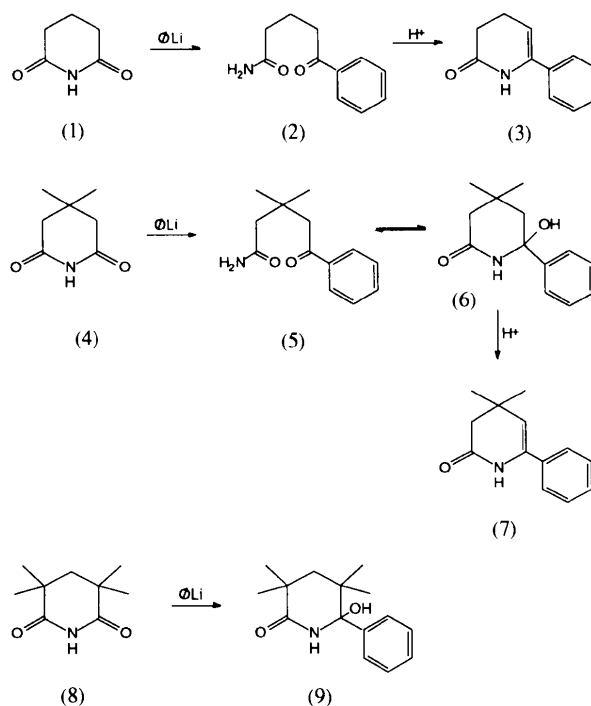


Fig. 1. Reactivity of various glutarimides with phenyllithium.

stabilization, which is known as the Thorpe–Ingold effect (Eliel, 1962).

X-ray structure determinations of 3,3,5,5-tetramethylglutarimide (8) and 2-hydroxy-2-phenyl-3,3,5,5-tetramethyl-6-piperidone (9) were performed in order to establish the ring structure of (9) as well as evaluate the reasons for the relatively high reactivity of imide (8) with organolithium reagent.

2. Experimental

X-ray structural methods have been employed to determine the crystal and molecular structures of the title compounds. The spectroscopic methods were used for the characterization of substrates, intermediates and products of the reaction. *Ab initio* theoretical calculations have been used to obtain the optimized molecular structures of the discussed substrates, verify crystallographic results and to find the reasons for different yields of the reaction when using different methyl-substituted glutarimides as substrates.

2.1. Spectroscopic studies

IR spectra were obtained using a Nicolet Magna IR 500 spectrophotometer.

NMR spectra were recorded on a Varian Gemini spectrometer operating at 200 MHz for ^1H NMR and at 50.3 MHz for ^{13}C NMR. Tetramethylsilane (TMS) was used as an internal standard. Chemical shifts are reported in p.p.m.

2.2. Preparation of 2-hydroxy-2-phenyl-3,3,5,5-tetramethyl-6-piperidone (9)

A stirred suspension of 1.54 g (9.1 mmol) of 3,3,5,5-tetramethylglutarimide (8) (Hall, 1964) in 50 ml of diethyl ether was cooled to 195 K and treated dropwise with 11.1 ml of a 1.8 M solution of phenyllithium (20.02 mmol) in diethyl ether. The resulting suspension was stirred for 1 h at the same temperature and allowed to stand overnight without external cooling. A saturated solution of sodium chloride (10 ml) was then added and volatile solvents were evaporated. The resulting mass was then diluted with 30 ml of saturated sodium chloride solution and extracted three times with 20 ml portions of chloroform. Combined organic extracts were dried over anhydrous magnesium sulfate and evaporated leaving a crystalline solid, which was then recrystallized from methanol/diethyl ether giving (9) as a white powder in 95% yield; m.p. 474–476 K. IR (KBr, ν , cm^{-1}): 3380, 3230, 1650. ^1H NMR (CDCl_3 , δ): 0.87 and 0.93 (two s, 3H each, two CH_3 at C3); 1.23 and 1.34 (two s, 3H each, two CH_3 at C5); 1.46 and 2.31 (ABq, $J = 14.2$ Hz, 2H at C4); 3.15 (broad s, 1H, disappeared with D_2O , —OH); 6.20 (broad s, 1H, disappeared with D_2O ,

NH); 7.34–7.38 (m, 3 H_{arom}); 7.47–7.52 (m, 2 H_{arom}). ^{13}C NMR (CDCl_3 , δ): 24.60, 25.06, 29.24, 30.94, 37.43, 38.32, 46.26, 88.72, 127.36, 127.85, 128.43, 141.14, 179.82. Elemental analysis: calc. for $\text{C}_{15}\text{H}_{21}\text{NO}_2$: C 72.84, H 8.56, N 5.66; found: C 72.71, H 8.85, N 5.41%. Reactions involving organolithium reagent were carried out under an argon atmosphere using anhydrous diethyl ether as a solvent.

2.3. Crystallographic studies

Columnar colorless crystals $0.4 \times 0.3 \times 0.25$ (8) and $0.4 \times 0.2 \times 0.2$ (9) mm were mounted on a KUMA KM-4 single-crystal diffractometer. Unit-cell parameters were obtained by the least-squares treatment of 25 reflections with $40 < 2\theta < 50$ (8) and $36 < 2\theta < 58$ (9)°. Systematic absences [$0k0$, k odd; $h0l$, l odd for (8); none for (9)] indicated $P2_1/c$ for the 3,5-tetramethylglutarimide structure (8) and either $P1$ or $P\bar{1}$ for 2-hydroxy-2-phenyl-3,3,5,5-tetramethyl-6-piperidone (9). In both cases the intensity statistics suggested the centrosymmetric space group. Intensities have been collected at room temperature using graphite-monochromatized $\text{CuK}\alpha$ radiation. Structures have been solved using *SHELXS86* (Sheldrick, 1990) and then refined on F^2 using *SHELXL93* (Sheldrick, 1993). All non-H atoms were located from E maps. Detailed information on data collection and refinement can be found in Table 1.

After refining part of the 3,3,5,5-tetramethylglutarimide structure (8) the $\Delta\rho$ map revealed some relatively high peaks which could be ascribed to the statistical disorder of the structure where molecules are in their opposite conformations. In the last least-squares cycles of refinement for (8) the positions of all non-H atoms were refined together with their anisotropic displacement parameters. Most of the H atoms, but not the imide H atom, were included in their calculated positions during refinement with the isotropic displacement parameters being 1.5 times larger than the respective isotropic parameters of the C atoms they are bonded to. The positional parameters and isotropic thermal coefficients for imide hydrogen, as well as the isotropic extinction parameter was refined. During the refinement the bond lengths and displacement parameters of the respective disordered parts of the molecule were tied together.

In the last least-squares cycles for (9) the positions of all atoms, anisotropic for non-H and isotropic displacement parameters for H atoms, were refined. The isotropic extinction parameter was also varied. Crystal data are present in Table 1.

2.4. Theoretical calculations

Quantum mechanical *ab initio* calculations were used to determine the three-dimensional molecular structures

Table 1. *Experimental details*

	(8)	(9)
Crystal data		
Chemical formula	C ₉ H ₁₅ NO ₂	C ₁₅ H ₂₁ NO ₂
Chemical formula weight	169.22	247.33
Cell setting	Monoclinic	Triclinic
Space group	<i>P</i> 2 ₁ / <i>c</i>	<i>P</i> 1
<i>a</i> (Å)	7.715 (2)	6.1685 (6)
<i>b</i> (Å)	11.136 (2)	11.1475 (10)
<i>c</i> (Å)	11.707 (2)	11.526 (2)
α (°)		117.100 (10)
β (°)	105.63 (3)	103.390 (10)
γ (°)		91.288 (7)
<i>V</i> (Å ³)	968.6 (3)	678.84 (15)
<i>Z</i>	4	2
<i>D_s</i> (Mg m ⁻³)	1.160	1.210
Radiation type	Cu <i>K</i> α	Cu <i>K</i> α
Wavelength (Å)	1.54178	1.54178
No. of reflections for cell parameters	25	25
θ range (°)	20–25	18–29
μ (mm ⁻¹)	0.661	0.631
Temperature (K)	293 (2)	293 (2)
Crystal form	Columnar	Plate-like
Crystal size (mm)	0.4 × 0.3 × 0.25	0.4 × 0.2 × 0.2
Crystal color	Colorless, transparent	Colorless, transparent
Data collection		
Diffractometer	Kuma KM-4 single crystal	Kuma KM-4 κ axis
Data collection method	Profile data from ω -2 θ scans	Profile data from ω -2 θ scans
Absorption correction	None	None
No. of measured reflections	1967	2449
No. of independent reflections	1887	2226
No. of observed reflections	1195	1800
Criterion for observed reflections	$I > 2\sigma(I)$	$I > 2\sigma(I)$
<i>R</i> _{int}	0.0954	0.0463
θ_{\max} (°)	80.28	64.94
Range of <i>h</i> , <i>k</i> , <i>l</i>	-9 → <i>h</i> → 6 0 → <i>k</i> → 14 -14 → <i>l</i> → 0	-7 → <i>h</i> → 0 -13 → <i>k</i> → 13 -13 → <i>l</i> → 13
No. of standard reflections	3	3
Frequency of standard reflections	Every 200 reflections	Every 200 reflections
Refinement		
Refinement on	<i>F</i> ²	<i>F</i> ²
$R[F^2 > 2\sigma(F^2)]$	0.0549	0.0410
$wR(F^2)$	0.2158	0.1250
<i>S</i>	1.115	1.005
No. of reflections used in refinement	1884	2225
No. of parameters used	138	248
H-atom treatment	H-atom parameters not refined	All H-atom parameters refined
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.1434P)^2 + 0.0153P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0711P)^2 + 0.1785P]$, where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\max}$	0.000	0.000
$\Delta\rho_{\max}$ (e Å ⁻³)	0.222	0.239
$\Delta\rho_{\min}$ (e Å ⁻³)	-0.168	-0.202
Extinction method	<i>SHELXL93</i> (Sheldrick, 1993)	<i>SHELXL93</i> (Sheldrick, 1993)
Extinction coefficient	0.0457 (66)	0.0281 (25)
Source of atomic scattering factors	<i>International Tables for Crystallography</i> (1992, Vol. C)	<i>International Tables for Crystallography</i> (1992, Vol. C)
Computer programs		
Data collection	<i>KM-4</i> (Kuma, 1991)	<i>KM-4</i> (Kuma, 1991)
Cell refinement	<i>KM-4</i> (Kuma, 1991)	<i>KM-4</i> (Kuma, 1991)
Data reduction	<i>KM-4</i> (Kuma, 1991)	<i>KM-4</i> (Kuma, 1991)
Structure solution	<i>SHELXS86</i> (Sheldrick, 1990)	<i>SHELXS86</i> (Sheldrick, 1990)
Structure refinement	<i>SHELXL93</i> (Sheldrick, 1993)	<i>SHELXL93</i> (Sheldrick, 1993)
Preparation of material for publication	<i>SHELXL93</i> (Sheldrick, 1993)	<i>SHELXL93</i> (Sheldrick, 1993)

of 3,3,5,5-tetramethylglutarimide (8) as well as non-substituted glutarimide and 4,4-dimethylglutarimide. A search for the energy-optimal structures was performed in two steps. In the first step the optimal structures were obtained using the SCF/6-31G** method. Next the MP2

method involving two-electron correlations was used. The calculations were performed with the *Gaussian92* code (Frisch *et al.*, 1992) implemented on a CONVEX 3200 computer. For comparison the DFT formalism was also used with the application of *Gaussian94*.

3. Results and discussion

The different glutarimides represent a class of attractive starting materials in the synthesis of 2- and/or 6-substituted piperidines by means of the reaction of imide carbonyl groups with Grignard or organolithium compounds. However, when the *N*-protecting group is omitted the first reaction to occur is the salt formation, in which the negative charge at the N atom diminishes the electrophilic character of the carbonyls. This accounts for the low to rarely fair yields of these reactions (Sekiya & Terao, 1971). Contrary to these results we found that (8) reacts with phenyllithium, giving product (9) in virtually quantitative yield. This difference may be attributed to the presence of neighboring gem-disubstituted C atoms in (8). Indeed, there are some literature indications of an unexpected increase in reactivity of the carbonyl group at C2 in 3,3-dialkylsuccinimides (Wijnberg, Speckamp & Schoemaker, 1974).

3.1. Structure of 3,3,5,5-tetramethylglutarimide (8)

The molecular structure together with the numbering scheme of (8) are shown in Fig. 2. The structure is partly disordered. Only one orientation for C4 and methyl groups connected to C3 and C5 are shown. The second orientation is roughly a mirror image of the molecule defined by the plane of atoms N, C2, C3, C5 and C6. The refined occupancy factors are 0.773 (3) and 0.227 (3), respectively. The fractional coordinates are given in Table 2, whereas the bond lengths and angles involving the non-H atoms are collected in Table 3.* The glutarimide ring forms a sofa conformation with N, C2, C3, C5 and C6 being almost in-plane and C4 displaced out-of-plane. Also, both carbonyl O atoms are shifted

* Lists of atomic coordinates, anisotropic displacement parameters and structure factors have been deposited with the IUCr (Reference: AB0372). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

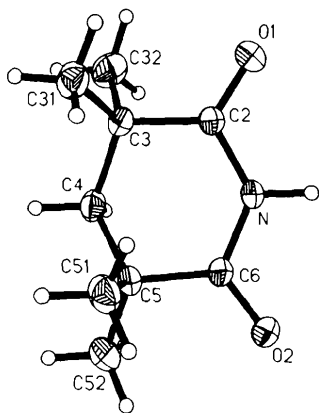


Fig. 2. Molecular geometry of the major component of disordered structure (8). Non-H atoms are shown as 20% probability ellipsoids.

Table 2. Fractional atomic coordinates and equivalent isotropic displacement parameters (\AA^2) for (8)

$$U_{eq} = (1/3)\sum_i \sum_j U^{ij} a_i^* a_j^* a_i a_j$$

	x	y	z	U_{eq}
N	0.1959 (2)	0.4104 (2)	-0.04127 (14)	0.0559 (5)
C2	0.3596 (3)	0.3526 (2)	-0.0197 (2)	0.0531 (5)
O1	0.4629 (2)	0.3594 (2)	0.07849 (13)	0.0775 (6)
C3	0.3996 (3)	0.2806 (2)	-0.1198 (2)	0.0568 (6)
C31	0.5646 (5)	0.3261 (4)	-0.1477 (4)	0.0794 (10)
C31'	0.6103 (18)	0.2874 (15)	-0.0996 (14)	0.0794 (10)
C32	0.4377 (6)	0.1493 (3)	-0.0712 (4)	0.0893 (11)
C32'	0.3239 (21)	0.1661 (10)	-0.1205 (14)	0.0893 (11)
C4	0.2312 (4)	0.2700 (3)	-0.2277 (2)	0.0617 (7)
C4'	0.3272 (13)	0.3626 (8)	-0.2351 (8)	0.0617 (7)
C5	0.1166 (3)	0.3861 (2)	-0.2588 (2)	0.0602 (6)
C51	0.2079 (5)	0.4876 (3)	-0.3030 (3)	0.0789 (10)
C51'	0.0986 (21)	0.5060 (12)	-0.3416 (11)	0.0789 (10)
C52	-0.0574 (6)	0.3502 (4)	-0.3529 (3)	0.0865 (11)
C52'	-0.0076 (20)	0.2986 (14)	-0.3186 (12)	0.0865 (11)
C6	0.0718 (3)	0.4302 (2)	-0.1487 (2)	0.0527 (5)
O2	-0.0657 (2)	0.4850 (2)	-0.15184 (14)	0.0736 (6)

Table 3. Selected geometric parameters (\AA , $^\circ$) for (8)

N—C6	1.378 (2)	C3—C4'	1.601 (10)
N—C2	1.379 (3)	C4—C5	1.554 (4)
C2—O1	1.212 (3)	C4'—C5	1.594 (10)
C2—C3	1.518 (3)	C5—C52'	1.413 (13)
C3—C32'	1.402 (12)	C5—C51	1.496 (4)
C3—C31	1.486 (5)	C5—C6	1.503 (3)
C3—C4	1.554 (3)	C5—C52	1.542 (4)
C3—C32	1.568 (4)	C5—C51'	1.634 (12)
C3—C31'	1.581 (13)	C6—O2	1.216 (2)
C6—N—C2	128.2 (2)	C5—C4'—C3	110.4 (6)
O1—C2—N	118.7 (2)	C52'—C5—C6	111.6 (7)
O1—C2—C3	123.1 (2)	C51—C5—C6	106.8 (2)
N—C2—C3	118.2 (2)	C51—C5—C52	110.4 (3)
C32'—C3—C2	108.4 (7)	C6—C5—C52	109.9 (2)
C31—C3—C2	110.7 (2)	C51—C5—C4	114.7 (2)
C31—C3—C4	115.2 (2)	C6—C5—C4	108.6 (2)
C2—C3—C4	111.6 (2)	C52—C5—C4	106.4 (2)
C31—C3—C32	108.0 (3)	C52'—C5—C4'	119.8 (8)
C2—C3—C32	105.7 (2)	C6—C5—C4'	111.3 (4)
C4—C3—C32	104.9 (2)	C52'—C5—C51'	109.4 (8)
C32'—C3—C31'	117.0 (9)	C6—C5—C51'	103.8 (5)
C2—C3—C31'	105.9 (6)	C4'—C5—C51'	99.0 (7)
C32'—C3—C4'	117.6 (7)	O2—C6—N	119.6 (2)
C2—C3—C4'	104.6 (4)	O2—C6—C5	122.6 (2)
C31'—C3—C4'	102.1 (7)	N—C6—C5	117.8 (2)
C5—C4—C3	115.2 (2)		

out-of-plane and are *trans* to each other (see data in Table 7). The methyl C31 and C32 atoms, together with the connecting atom C3, form a plane which makes a dihedral angle of $76.5(2)^\circ$ with the previous plane. The respective dihedral angle formed by the C5, C51 and C52 plane is $82.8(1)^\circ$.

3.2. Structure of 2-hydroxy-2-phenyl-3,3,5,5-tetramethyl-6-piperidone (9)

The molecular structure together with the numbering scheme of (9) is shown in Fig. 3. The corresponding fractional coordinates and molecular geometry parameters are collected in Tables 4 and 5, respectively. The molecule of (9) is composed of four planar fragments: the imide ring fragment N, C2, C4, C5, C6; planes defined by methyl groups and adjacent ring C atoms

Table 4. Fractional atomic coordinates and equivalent isotropic displacement parameters (\AA^2) for (9)
$$U_{\text{eq}} = (1/3)\sum_i \sum_j U^{ij} a_i^* a_j^* \mathbf{a}_i \cdot \mathbf{a}_j.$$

	x	y	z	U_{eq}
O2	0.7400 (2)	0.71197 (12)	0.14133 (13)	0.0471 (4)
O1	0.0976 (2)	0.52412 (12)	-0.11829 (13)	0.0546 (4)
N	0.3560 (2)	0.62561 (14)	0.08216 (15)	0.0420 (4)
C2	0.5429 (3)	0.7290 (2)	0.1879 (2)	0.0388 (4)
C3	0.4847 (3)	0.8709 (2)	0.2079 (2)	0.0416 (4)
C4	0.4437 (3)	0.8666 (2)	0.0694 (2)	0.0477 (5)
C5	0.2691 (3)	0.7492 (2)	-0.0507 (2)	0.0468 (4)
C6	0.2349 (3)	0.6254 (2)	-0.0307 (2)	0.0414 (4)
C11	0.5779 (3)	0.7112 (2)	0.3139 (2)	0.0404 (4)
C12	0.3995 (3)	0.6634 (2)	0.3449 (2)	0.0479 (4)
C13	0.4361 (4)	0.6476 (2)	0.4599 (2)	0.0590 (5)
C14	0.6488 (4)	0.6786 (2)	0.5457 (2)	0.0629 (6)
C15	0.8264 (4)	0.7267 (2)	0.5167 (2)	0.0600 (5)
C16	0.7921 (3)	0.7428 (2)	0.4022 (2)	0.0504 (5)
C31	0.6830 (3)	0.9825 (2)	0.3077 (2)	0.0551 (5)
C32	0.2785 (3)	0.9040 (2)	0.2632 (2)	0.0521 (5)
C51	0.0371 (4)	0.7944 (3)	-0.0777 (3)	0.0737 (7)
C52	0.3520 (6)	0.6993 (3)	-0.1788 (3)	0.0760 (7)

Table 5. Selected geometric parameters (\AA , $^\circ$) for (9)

O2—C2	1.422 (2)	C5—C6	1.518 (2)
O1—C6	1.238 (2)	C5—C52	1.538 (3)
N—C6	1.341 (2)	C5—C51	1.538 (3)
N—C2	1.468 (2)	C11—C16	1.391 (2)
C2—C11	1.521 (2)	C11—C12	1.398 (2)
C2—C3	1.555 (2)	C12—C13	1.382 (3)
C3—C31	1.531 (2)	C13—C14	1.373 (3)
C3—C32	1.531 (2)	C14—C15	1.380 (3)
C3—C4	1.534 (3)	C15—C16	1.381 (3)
C4—C5	1.545 (3)		
C6—N—C2	127.14 (14)	C52—C5—C51	109.0 (2)
O2—C2—N	109.28 (13)	C6—C5—C4	113.38 (15)
O2—C2—C11	111.08 (13)	C52—C5—C4	109.4 (2)
N—C2—C11	107.96 (12)	C51—C5—C4	111.7 (2)
O2—C2—C3	105.97 (12)	O1—C6—N	119.99 (15)
N—C2—C3	107.82 (13)	O1—C6—C5	120.4 (2)
C11—C2—C3	114.60 (13)	N—C6—C5	119.57 (15)
C31—C3—C32	108.3 (2)	C16—C11—C12	118.0 (2)
C31—C3—C4	108.56 (15)	C16—C11—C2	120.13 (15)
C32—C3—C4	111.6 (2)	C12—C11—C2	121.89 (15)
C31—C3—C2	110.41 (14)	C13—C12—C11	120.7 (2)
C32—C3—C2	111.11 (13)	C14—C13—C12	120.6 (2)
C4—C3—C2	106.86 (13)	C13—C14—C15	119.4 (2)
C3—C4—C5	117.01 (13)	C14—C15—C16	120.6 (2)
C6—C5—C52	105.8 (2)	C15—C16—C11	120.7 (2)
C6—C5—C51	107.3 (2)		

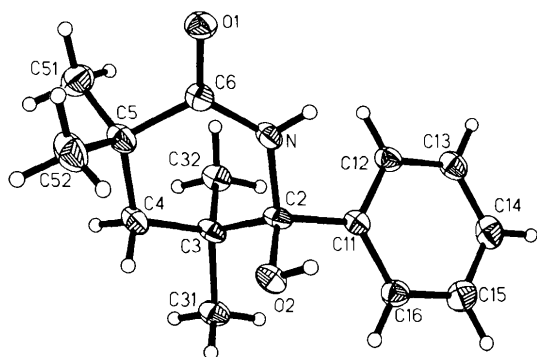


Fig. 3. Molecular geometry of (9). Non-H atoms are shown as 20% probability ellipsoids.

(C3, C31, C32 and C5, C51, C52, respectively); the phenyl ring. Both 'methyl' planes are approximately perpendicular to the planar fragment of the first ring [dihedral angles 89.6(1) and 88.1(1) $^\circ$, respectively]. The phenyl ring is rotated by 47.6(1) $^\circ$ around the C2—C11 direction with respect to the 'imide' plane.

3.3. Crystal packing of 3,3,5,5-tetramethylglutaramide (8) and 2-hydroxy-2-phenyl-3,3,5,5-tetramethyl-6-piperidone (9)

Figs. 4 (8) and 5 (9) show the crystal packing of both the title structures, respectively. Methyl group repulsion in (8) results in a relatively large dimension. This is in agreement with the low density of (8), giving much space for both conformers, which might explain the observed disorder. The structures are held together by a series of hydrogen bonds, shown as dashed lines. The geometries of the hydrogen bonds are collected in Table 6. The structure of 3,3,5,5-tetramethylglutaramide is composed of centrosymmetric hydrogen-bonded dimers. Only the carbonyl O2 atom is involved in hydrogen-bond formation.

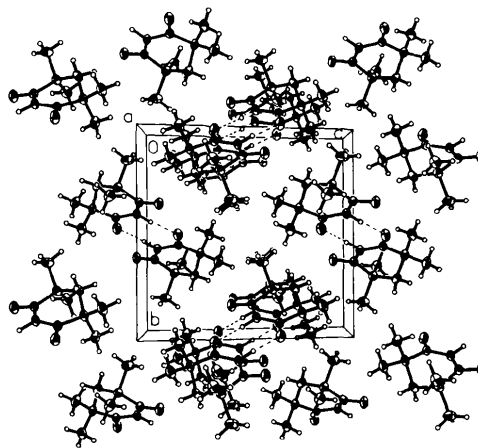


Fig. 4. Crystal packing of (8). The hydrogen bonds are shown as dashed lines.

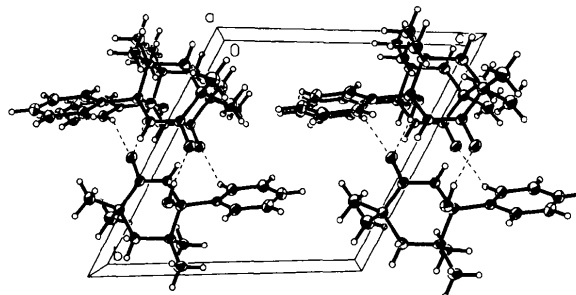


Fig. 5. Crystal packing of (9). The hydrogen bonds are shown as dashed lines.

Table 6. Hydrogen-bonding geometry (\AA , $^\circ$)

$D-H \cdots A$	$D \cdots H$	$H-A$	$D \cdots A$	$D-H \cdots A$
Structure (8)				
$N-H1 \cdots O2^i$	0.97 (3)	1.99 (3)	2.949 (2)	169 (2)
Structure (9)				
$O2-H2 \cdots O1^{ii}$	0.94 (2)	1.83 (2)	2.758 (2)	170 (2)
$C12-H12 \cdots O1^{iii}$	0.96 (2)	2.53 (2)	3.409 (2)	152 (2)

Symmetry codes: (i) $-x, 1-y, -z$; (ii) $1-x, 1-y, -z$; (iii) $-x, 1-y, -z$.

The structure of (9) presents a somewhat more complex situation. The carbonyl O atom acts here as an acceptor of both hydroxyl and phenyl ring H atoms. No close intermolecular contacts of the imide H atom are observed.

3.4. Comparison of structures of glutarimides

Since the different methyl-substituted glutarimides produce products with substantially different efficiencies, we looked more closely to their geometries searching for the reason for this effect. A first look at the bond lengths of structures of glutarimide (Petersen, 1971) (1), 4,4-dimethylglutarimide (Bocelli & Grenier-Loustalot, 1981) (4) and the present structure of 3,3,5,5-tetramethylglutarimide (8) (Table 7) gave no answer.

The presented bond lengths as well as the bond angles (not shown here) differ only slightly. However, a more careful analysis reveals some discrepancies. As far as the fragment N, C2, C3, C5 and C6 (in the notation used in this paper) is planar in structures of glutarimide and its 4,4-disubstituted derivative (r.m.s. deviations 0.008 and 0.015 \AA), it is significantly less planar in the present structure (r.m.s. deviation 0.069 \AA). The differences in carbonyl O-atom positions with respect to those planes could also be seen. In nonsubstituted glutarimide they are almost in the plane, whereas in disubstituted derivatives they deviate more and in tetrasubstituted glutarimides are distinctly out-of-plane. These findings motivate us to study this problem further, especially because of the observed disorder in the structure of 3,3,5,5-tetramethylglutarimide which might suppress the results slightly. We used the crystallographic results as starting points to the geometry optimization in terms of *ab initio* quantum chemical calculations.

3.5. Results of calculations

The molecular structures of glutarimide (1), 4,4-dimethylglutarimide (4) and 3,3,5,5-tetramethylglutarimide (8) were optimized using three different methods: the RHF SCF method with the standard basis 6-31G**, the MP2 method with the basis 6-31G**, which involves two electron correlations, and also the DFT formalism with the B3PW91 functional. All methods gave similar results, confirming the X-ray structural results and showing that 3,3,5,5-tetramethylglutarimide is the least planar molecule of the three glutarimides studied (Table 8).

Table 7. Comparison of selected geometrical parameters (\AA) for X-ray data of glutarimides

	Glutarimide	4,4-Dimethylglutarimide	(8)
N—H1	0.876	—	0.970 (28)
N—C2	1.380	1.385	1.379 (3)
C2—O1	1.219	1.219	1.212 (3)
C2—C3	1.487	1.492	1.518 (3)
C3—C4	1.504	1.539	1.554 (3)
C4—C5	1.480	1.526	1.554 (4)
C5—C6	1.493	1.491	1.503 (3)
C6—O2	1.210	1.225	1.216 (2)
C6—N	1.384	1.376	1.378 (2)
C3—C31	—	—	1.486 (5)
C3—C32	—	—	1.568 (4)
C5—C51	—	—	1.496 (4)
C5—C52	—	—	1.542 (4)
C4—C41	—	1.527	—
C4—C42	—	1.532	—
Deviation from plane	0.0082	0.1551	0.070
O1	0.0595	0.0777	0.310 (3)
O2	0.0017	0.0106	-0.153 (3)

The calculations also prove that in the tetra-substituted derivative both carbonyl oxygens are displaced from the plane defined by N, C2, C3, C5 and C6 atoms. The MP2 method gives the best restoration of the conformation for all three X-ray structures (Table 8). The conformational changes in 3,3,5,5-tetramethylglutarimide with respect to the geometry observed in nonsubstituted and dimethylsubstituted glutarimides could be understood in terms of changes in the hybridization of carbonyl C atoms. Such changes should be accompanied with bond-length elongations, however, which have not been observed. There is also no evidence of nonplanar carbonyl C surroundings. A convincing description of the situation is the slight rotation of both carbonyl fragments around C3—N and C5—N bonds, respectively. This leads to a less favorable condition for the interaction of the π -electron clouds of the carbonyl fragments and 2p free electron pair of the imide nitrogen, which should result in variations in the atomic net charges.

The calculated atomic net charges for the interesting fragment of the molecules are given in Table 9. It shows clearly that in 3,3,5,5-tetramethylglutarimide the carbonyl O atoms have the most negative and the carbonyl C atoms the most positive charges in the series.

The higher positive charge concentration at carbonyl C atoms in imide (8) thus make it more susceptible to nucleophilic attack.

4. Conclusions

Comparison of both crystallographic results and the quantum chemical calculations for glutarimides led to the conclusion that in 3,3,5,5-tetramethylglutarimide the carbonyl groups are rotated slightly around respective N—C bonds, making their positions less favorable to participate in conjunction with the two 2p electrons of the N atom. This explains the larger negative charges located on the O and N atoms with increased positive

Table 8. *Optimized geometry of glutarimides*

	Glutarimide			4,4-Dimethylglutarimide			3,3,5,5-Tetramethylglutarimide		
	RHF 6-31G**	MP2 6-31G**	DFT	RHF 6-31G**	MP2 6-31G**	DFT	RHF 6-31-G**	MP2 6-31G**	DFT
N—H1	0.999	1.014	1.014	0.998	1.014	1.015	0.999	1.014	1.015
N—C2	1.381	1.397	1.393	1.386	1.395	1.391	1.378	1.393	1.389
C2—O1	1.192	1.223	1.214	1.192	1.224	1.215	1.194	1.227	1.217
C2—C3	1.511	1.512	1.514	1.511	1.511	1.513	1.525	1.522	1.527
C3—C4	1.527	1.525	1.527	1.537	1.532	1.538	1.543	1.536	1.542
C4—C5	1.526	1.524	1.527	1.537	1.532	1.537	1.541	1.535	1.541
C5—C6	1.511	1.512	1.514	1.511	1.511	1.513	1.520	1.517	1.525
C6—O2	1.192	1.224	1.213	1.193	1.224	1.215	1.194	1.226	1.215
C6—N	1.381	1.396	1.393	1.379	1.395	1.390	1.380	1.396	1.392
C3—C31	—	—	—	—	—	—	1.541	1.535	1.541
C3—C32	—	—	—	—	—	—	1.540	1.537	1.540
C5—C51	—	—	—	—	—	—	1.544	1.537	1.544
C5—C52	—	—	—	—	—	—	1.535	1.528	1.535
C4—C41	—	—	—	1.532	1.527	1.532	—	—	—
C4—C42	—	—	—	1.538	1.531	1.536	—	—	—
Deviation from plane	0.0018	0.0055	0.0008	0.0116	0.0204	0.0103	0.0463	0.0763	0.0427
O1	0.0082	-0.0083	0.0155	0.0269	0.0688	0.0221	0.1854	0.3182	0.1825
O2	0.0092	-0.0090	0.0139	0.0264	0.0687	0.0234	-0.1291	-0.2111	-0.1208

Table 9. *Atomic net charges for the selected atoms in optimized structures of glutarimides*

	Glutarimide			4,4-Dimethylglutarimide			3,3,5,5-Tetramethylglutarimide		
	RHF 6-31G**	MP2 6-31G**	DFT	RHF 6-31G**	MP2 6-31G**	DFT	RHF 6-31-G**	MP2 6-31G**	DFT
N	-0.780	-0.785	-0.590	-0.775	-0.777	-0.584	-0.808	-0.811	-0.620
H1(imide)	0.339	0.346	0.306	0.338	0.344	0.305	0.336	0.343	0.303
C2	0.758	0.768	0.595	0.754	0.761	0.584	0.816	0.823	0.636
O1	-0.565	-0.584	-0.476	-0.566	-0.585	-0.478	-0.577	-0.596	-0.488
C6	0.758	0.768	0.595	0.754	0.761	0.583	0.818	0.826	0.640
O2	-0.565	-0.584	-0.476	-0.566	-0.585	-0.478	-0.582	-0.603	-0.491

charges on both carbonyl carbons. Such a separation of partial charges in the carbonyl group should result in higher reactivity of this compound towards substitution.

Yet another problem to be solved in this study was the correctness of the assignment of structure (9) for the product of phenyllithium treatment on imide (8). We have already proposed the structure on the basis of spectroscopic investigations, but the final proof was still lacking. The results obtained by the X-ray structure determination are fully in accordance with earlier predictions.

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