

# Novel Synthesis and Crystal Structures of Two $\alpha, \alpha'$ -bis-Substituted Benzylidene Cyclohexanones: 2,6-Bis-2-nitro(benzylidene)cyclohexanone and 2,6-Bis-4-methyl(benzylidene)cyclohexanone

Ali Amoozadeh · Salman Rahmani ·  
Grzegorz Dutkiewicz · Mehdi Salehi ·  
Firouze Nemati · Maciej Kubicki

Received: 6 December 2010/Accepted: 15 April 2011/Published online: 27 April 2011  
© The Author(s) 2011. This article is published with open access at Springerlink.com

**Abstract** Two  $\alpha, \alpha'$ -bis-substituted benzylidene cycloalkanones have been synthesized in presence of  $\text{SnCl}_4$  and their crystal structures have been determined by means of X-ray diffraction. The bis(*para*-methyl) derivative, 2,6-bis-4-methyl(benzylidene)cyclohexanone **1** crystallizes in the orthorhombic space group  $\text{Pbca}$  with  $a = 9.413(2)$  Å,  $b = 10.787(2)$  Å, and  $c = 33.702(5)$  Å, while bis(*ortho*-nitro) derivative, 2,6-bis-2-nitro(benzylidene)cyclohexanone in monoclinic  $\text{P}2_1/n$  space group with  $a = 8.482(2)$  Å,  $b = 13.435(2)$  Å,  $c = 15.377(3)$  Å, and  $\beta = 92.96(2)^\circ$ . In both compounds the olefinic bonds are in *E*-configuration, and the cyclohexyl rings adopt a sofa conformation. The phenyl rings are not coplanar with the planes of  $\text{C}=\text{C}(\text{C}=\text{O})-\text{C}=\text{C}$  fragments; the dihedral angles between these planes are 14.25(11) and 19.37(11)° in **1** and 60.50(6) and 63.26(6)° in **2**. This twist might be regarded as the effect of the repulsive interactions between the hydrogen atoms from phenyl and cyclohexyl rings, and much larger values in **2** are certainly connected with the presence of nitro group in *ortho*-positions of the phenyl ring. It seems that, because of the lack of specific interactions the close packing requirements and the van der Waals forces are main factors determining the crystal packing.

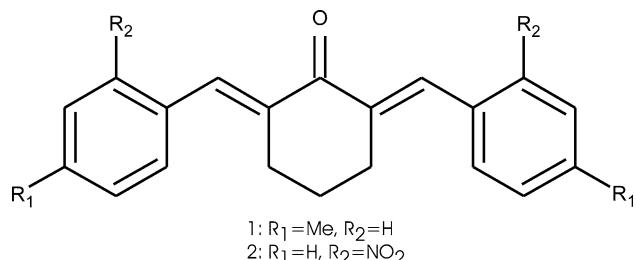
**Keywords** Cyclohexanone · Conformation · Crystal packing · Crystal structure

## Introduction

Bis(substituted-benzylidene) cycloalkanones are very important synthetic precursors for synthesis of biologically active pyrimidine derivatives [1, 2]. These compounds have gained lots of attention due to their uses as agrochemical, pharmaceutical, and perfume intermediates and as liquid crystal polymer units [3–5]. Many of these methods suffer, however, from side reactions giving the corresponding products in low yields [6]. Recently some new kinds of Lewis acids have been used but in some cases the yields are less than 38% [7]. We have recently described the use of poly(ethylene) glycol/ $\text{AlCl}_3$  as a green and reusable system for the synthesis of  $\alpha, \alpha'$ -bis(substituted-benzylidene) cycloalkanones [8]. In recent study, the versatility of  $\text{SnCl}_4$  and the environmentally benign nature of ethanol as a green, inexpensive, and accessible solvent encouraged us to couple them together and study their utility for aldol condensation. Comparing the other methods, our synthetic procedure for preparation of different  $\alpha, \alpha'$ -bis(substituted-benzylidene) cyclohexanones (Scheme 1) provides good yields for a vast variety of substituted aromatic aldehydes with both electron withdrawing and electron releasing groups furthermore. Also the simplicity of operation, lack of unexpected by-products and mild condition of temperature are the others advantages of this method [9]. In recent study for the first time we have used  $\text{SnCl}_4$  as a mild, inexpensive and efficient catalyst for the synthesis of different  $\alpha, \alpha'$ -bis(substituted-benzylidene) cycloalkanones (Scheme 1). Use of ethanol as a green solvent helped us to improve total yields and this new combination for the first time provided excellent conditions to obtain good single crystals for X-ray studies of some obtained  $\alpha, \alpha'$ -bis(substituted-benzylidene) cyclohexanones. Here we report the results of the X-ray

A. Amoozadeh · S. Rahmani · M. Salehi · F. Nemati  
Department of Chemistry, Faculty of Science,  
Semnan University, Semnan, Iran

G. Dutkiewicz · M. Kubicki (✉)  
Department of Chemistry, Adam Mickiewicz University,  
Grunwaldzka 6, 60-780 Poznań, Poland  
e-mail: mkubicki@amu.edu.pl

**Scheme 1**

crystallographic studies for (*2E,6E*)-2,6-bis(4-methylbenzylidene)cyclohexanone (**1**, Scheme 1) and (*2E,6E*)-2,6-bis(2-nitrobenzylidene)cyclohexanone (**2**). Structures of some similar compounds have been reported earlier, for instance bis(3-nitro) [10] and bis(4-nitro) derivatives [11]. Interestingly, even for the very similar compounds there are no indications of isomorphism what can suggest that very weak interactions are responsible for crystal packing.

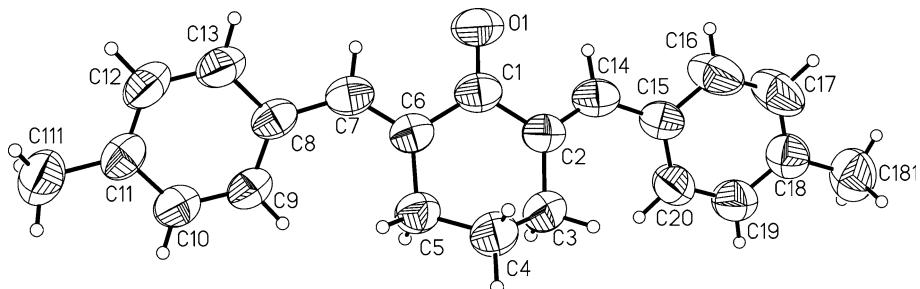
## Results and Discussion

Figures 1 and 2 show the perspective views of molecules **1** and **2**, respectively. Table 1 lists the relevant bond lengths, bond angles and torsion angles.

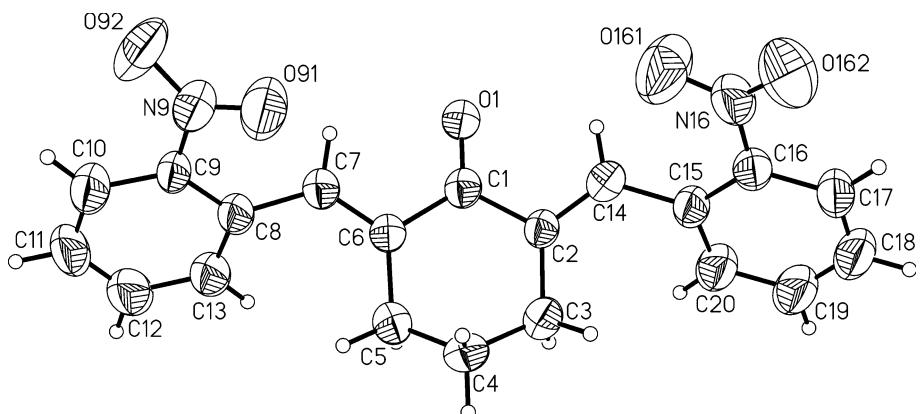
The overall conformation of the molecule might be described by the dihedral angles between the planar fragments: two phenyl rings, A ( $C_8 \cdots C_{13}$ ) and B ( $C_{15} \cdots C_{20}$ ),

and the planar fragment of the cyclohexanone ( $C_7=C_6-C_1(=\text{O})-\text{C}_2=\text{C}_{14}$ ; referred to as C). The appropriate values are listed in Table 1, and Fig. 3 shows the comparison of both the molecules. As it is evident from Fig. 3, compound **1** is significantly flatter than **2** as a consequence of the substituents in *ortho*-positions in **2**. In the Cambridge Structural Database ([12] version 5.31 of November 2009, updated August 2010) there are 24 compounds of similar, 3,5-diaryl-6-monosubstituted-cyclohex-2-enone, structure (with no additional substituents in the cyclohexanone ring and on bridging C-atoms). There are no clear trends in the overall conformation of the molecules. For instance, for the derivatives with the single substituents at *4,4'* positions the spread of dihedral angles is quite big, the twist between the terminal rings ranges from  $0.3^\circ$  in 4-methyl-4'-nitro derivative [13] to  $51.4^\circ$  in one of three symmetry-independent molecules of 4,4'-dibromo compound [14]. Even in unsubstituted 2,6-bis(benzylidene)cyclohexanone the angles between the planar fragments are quite large,  $38.3^\circ$  between the phenyl rings [15]. This lack of coplanarity which originates from the twist between the aryl rings and adjacent olefinic groups is regarded as the result of the repulsive interactions between the hydrogen atoms of the aryl rings and equatorial hydrogen atoms from cyclohexyl ring [e.g., 13]. This steric repulsion causes also the increase in the bond angles at the C-atoms joining the rings i.e.,  $C_6-C_7-C_8$  and  $C_2-C_{14}-C_{15}$  (cf. Table 1). The intra-annular angles in phenyl rings show the influence of the substituents (cf. for instance [16]), which is close to additivity in 1

**Fig. 1** Anisotropic ellipsoid representation of the molecule **1** together with atom labeling scheme [22]. The ellipsoids are drawn at 50% probability level, hydrogen atoms are depicted as spheres with arbitrary radii



**Fig. 2** Anisotropic ellipsoid representations of the molecule **2** together with atom labeling scheme [22]. The ellipsoids are drawn at 50% probability level, hydrogen atoms are depicted as spheres with arbitrary radii



**Table 1** Selected geometrical parameters ( $\text{\AA}$ ,  $^\circ$ ). A and B are phenyl rings (A: C8–C13, B: C15–C20), and C is the planar fragment of the cyclohexanone ( $\text{C}7=\text{C}6-\text{C}1(=\text{O}1)-\text{C}2=\text{C}14$ )

	<b>1</b>	<b>2</b>
C1–O1	1.2311(19)	1.227(2)
C2–C14	1.336(2)	1.329(2)
C6–C7	1.345(2)	1.336(2)
C2–C1–C6	118.60(16)	118.97(18)
C1–C6–C7	116.48(15)	116.21(17)
C6–C7–C8	130.90(16)	130.04(18)
C1–C2–C14	117.41(16)	116.11(17)
C2–C14–C15	131.69(16)	126.69(18)
C4–C3–C2–C14	154.71(17)	148.45(19)
C4–C5–C6–C7	−159.46(17)	−135.4(2)
C1–C2–C14–C15	−177.06(16)	−178.67(18)
C1–C6–C7–C8	176.45(16)	175.0(2)
C2–C14–C15–C20	27.1(3)	50.2(3)
C6–C7–C8–C9	−23.8(3)	−41.7(3)
A/B	5.24(10)	21.60(10)
A/C	14.25(11)	60.50(6)
B/C	19.37(11)	63.26(6)
A/ $\text{NO}_2$		26.4(3)
B/ $\text{NO}_2$		10.3(3)

(substituents in mutual *para* positions). As expected in case of **2** with *ortho*-substitution the additivity is hardly visible.

In both compounds the olefinic bonds are in *E*-configuration (torsion angles O1–C1–C6–C7 and O1–C1–C2–C14 are 11.5(2) and −9.0(2) $^\circ$  in **1**, and −20.3(3) and 12.8(3) $^\circ$  in **2**. It might be noted that in both cases the dihedral angles have opposite signs, as it is in majority—but not all, actually in 22 out of 31 fragments—structures from the CSD.

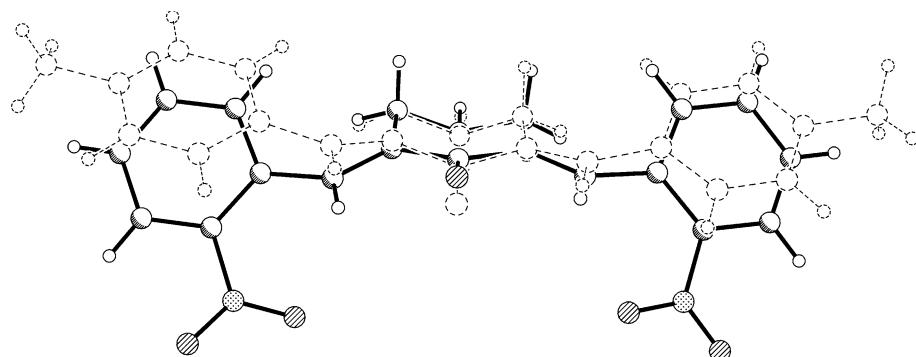
The cyclohexanone rings are in sofa conformations. The asymmetry parameters [17], which in principle show the deviation from the ideal symmetry of six-membered ring, in this case  $C_2$ , have the values of 3.2° in **1** and 8.6° in **2**, what suggests the much more distorted conformation in

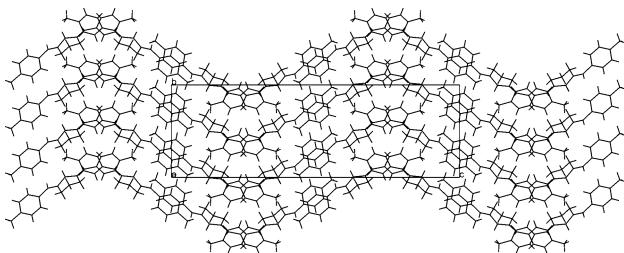
**Table 2** Short C–H···O contacts geometry ( $\text{\AA}$ ,  $^\circ$ )

D–H···A	D–H	H···A	D···A	D–H···A
<b>1</b>				
C111–H11C···O1 <sup>a</sup>	0.96	2.57	3.508(3)	165
<b>2</b>				
C3–H3A···O91 <sup>b</sup>	0.97	2.70	3.620(3)	159
C5–H5A···O1 <sup>c</sup>	0.97	2.66	3.417(3)	135
C7–H7···O162 <sup>d</sup>	0.93	2.60	3.321(3)	135
C11–H11···O161 <sup>e</sup>	0.93	2.59	3.429(3)	151
C12–H12···O91 <sup>e</sup>	0.93	2.56	3.287(3)	135
C17–H17···O1 <sup>f</sup>	0.93	2.75	3.668(3)	168
C18–H18···O92 <sup>g</sup>	0.93	2.56	3.476(3)	168
C20–H20···O162 <sup>h</sup>	0.93	2.66	3.476(3)	146
Symmetry codes				
<sup>a</sup> x + 1/2, y, 3/2 – z				
<sup>b</sup> −x, −y, 1 – z				
<sup>c</sup> 1 – x, −y, 1 – z				
<sup>d</sup> 1/2 + x, 1/2 – y, −1/2 + z				
<sup>e</sup> 1/2 – x, −1/2 + y, 1/2 – z				
<sup>f</sup> −1/2 + x, 1/2 – y, 1/2 + z				
<sup>g</sup> x, y, 1 + z				
<sup>h</sup> 1/2 – x, −1/2 + y, 3/2 – z				

this latter case. Also the calculations of the least-squares planes through five ring atoms (C1, C2, C3, C5, and C6) show that the ring in **2** is more deviated from the ideal sofa conformation (maximum deviation is 0.064(2)  $\text{\AA}$  in **1** and 0.095(2)  $\text{\AA}$  in **2**). The sixth atom, C5 is significantly out of the mean plane, by 0.729(3)  $\text{\AA}$  in **1** and 0.605(3)  $\text{\AA}$  in **2**.

In the crystal structures virtually no specific interactions are present. Some potential C–H···O contacts are listed in Table 2. What is quite puzzling, there are also no indications for either  $\pi\cdots\pi$  or C–H··· $\pi$  interactions which quite often play significant role in determination of crystal packing of similar compounds. Therefore, in both the structures probably the close packing requirements and the van der Waals contacts determine the packing (Fig. 4).

**Fig. 3** Least-squares fit of molecules **1** and **2**; the cyclohexanone fragments of the molecules were fitted one onto another [22]



**Fig. 4** Fragment of the crystal packing of **1** as seen along *x*-direction [23]

## Experimental

### Preparation

A mixture of aldehyde (2 mmol) and ketone (1 mmol) and  $\text{SnCl}_4$  (0.3 mmol) in EtOH (2 mL) was stirred at 45 °C for an appropriate time. After completion of the reaction (Scheme 2) monitored by TLC, the reaction mixture was cooled in ice bath to precipitate the desired product. Colourless single crystals suitable for X-ray of compounds **1** and **2** were obtained by slow evaporation of an ethanol solution. **1**: Yellow needles; Yield: 89%; mp 171–172 °C; IR (KBr)  $\nu$ : 2938, 2914, 1660, 1600  $\text{cm}^{-1}$ ; **2**: Yellow needles; Yield: 75%; mp 157–159 °C; IR (KBr)  $\nu$ : 1638, 1617, 1519  $\text{cm}^{-1}$ .

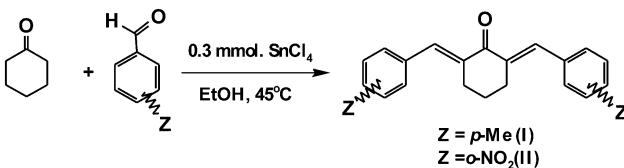
### Crystallography

Colourless transparent plate-like crystals (0.5, 0.4, 0.15 mm; 0.3, 0.3, 0.05 mm for **2**) were used for data collection. Diffraction data were collected at room temperature by the  $\omega$ -scan technique, on an Xcalibur Eos diffractometer [18] with graphite-monochromatized  $\text{MoK}_{\alpha}$  radiation ( $\lambda = 0.71073 \text{ \AA}$ ). The data were corrected for Lorentz-polarization and absorption effects [18]. Accurate unit-cell parameters were determined by a least-squares fit of 3533 (**1**) and 1991 (**2**) reflections of highest intensity, chosen from the whole experiment, and then the. Precision of the diffractometer was also taken into account in order to avoid unphysically small standard uncertainties [19]. The structures were solved by direct methods with SIR92 [20] and refined with the full-matrix least-squares procedure on  $F^2$  by SHELXL97 [21]. Scattering factors incorporated in

**Table 3** Crystal data, data collection, and structure refinement

Compound	<b>1</b>	<b>2</b>
Formula	$\text{C}_{22}\text{H}_{22}\text{O}$	$\text{C}_{20}\text{H}_{16}\text{N}_2\text{O}_5$
Formula weight	302.40	364.35
Crystal system	Orthorhombic	Monoclinic
Space group	Pbca	P2 <sub>1</sub> /n
<i>a</i> (Å)	9.413(2)	8.482(2)
<i>b</i> (Å)	10.787(2)	13.435(2)
<i>c</i> (Å)	33.702(5)	15.377(3)
$\beta$ (°)	90	92.96(2)
<i>V</i> (Å <sup>3</sup> )	3422.0(11)	1750.0(6)
<i>Z</i>	8	4
$D_x$ (g/cm <sup>3</sup> )	1.17	1.38
$F(000)$	1296	760
$\mu$ (mm <sup>-1</sup> )	0.07	0.10
$\theta$ range (°)	3.12–25.00	3.06–25.00
hkl range	$-11 \leq h \leq 7$ $-12 \leq k \leq 11$ $-39 \leq l \leq 40$	$-10 \leq h \leq 9$ $-15 \leq k \leq 9$ $-18 \leq l \leq 17$
Reflections		
Collected	7696	6293
Unique ( $R_{\text{int}}$ )	3002 (0.017)	3068 (0.030)
With $I > 2\sigma(I)$	1869	1433
No. of parameters	210	245
Weighting scheme		
<i>A</i>	0.067	0.0381
$R(F)$ [ $I > 2\sigma(I)$ ]	0.047	0.044
wR( $F^2$ ) [ $I > 2\sigma(I)$ ]	0.114	0.061
$R(F)$ [all data]	0.083	0.114
wR( $F^2$ ) [all data]	0.122	0.066
Goodness of fit	1.014	1.013
Max/min $\Delta\rho$ (e/Å <sup>3</sup> )	0.14/–0.17	0.21/–0.21

SHELXL97 were used. The function  $\Sigma w(|F_o|^2 - |F_c|^2)^2$  was minimized, with  $w^{-1} = [\sigma^2(F_o)^2 + (\text{AP})^2]$  (where P = [Max ( $F_o^2$ , 0) + 2 $F_c^2$ ]/3). All non-hydrogen atoms were refined anisotropically, hydrogen atoms were put in the calculated positions difference Fourier map, and refined as a “riding” model with the isotropic displacement parameters set at 1.2 (1.5 for methyl groups) times the  $U_{\text{eq}}$  value for appropriate non-hydrogen atom. Relevant crystal data are listed in Table 3, together with refinement details.



**Scheme 2**

### Supplementary Material

CCDC-800799 (**1**) and CCDC-800800 (**2**) contain supplementary crystallographic data for this paper. These data can be obtained free of charge via [www.ccdc.cam.ac.uk/data\\_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif), by e-mailing [data\\_request@ccdc.cam.ac.uk](mailto:data_request@ccdc.cam.ac.uk).

ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK.

**Acknowledgment** We thank Semnan University for supporting this study.

**Open Access** This article is distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author(s) and source are credited.

## References

1. Guilford WJ, Shaw KJ, Dallas JL, Koovakkat S, Lee W, Liang A, Light DR, McCarrick MA, Whitlow M, Ye B, Morrissey MM (1999) *J Med Chem* 42:5415
2. Deli J, Lóránd T, Szabó D, Földesi A (1984) *Pharmazie* 39:539
3. Dimmock JRA, Padmanilayam MP, Zello GA, Nienaber KH, Allen TM, Santos CL, Clercq E, De Balzarini J, Manavathu EK, Stables JP (2003) *Eur J Med Chem* 38:169
4. Gangadhara KK (1995) *Polymer* 36:1903
5. Artico M, Di Santo R, Costi R, Novellino E, Greco G, Massa S, Tramontano E, Marongiu ME, De Montis A, La Colla P (1998) *J Med Chem* 41:3948
6. Nakano T, Irihara S, Umano S, Inada A, Ishii Y, Ogawa M (1987) *J Org Chem* 52:2239
7. Watanabe K (1980) *Bull Chem Soc Jpn* 53:1366
8. Amoozadeh A, Nemati F (2009) *S Afr J Chem* 62:44
9. Motiur Rahman AFM, Jeong B-S, Kim DH, Park JK, Lee ES, Jahng Y (2007) *Tetrahedron* 63:2426
10. Li Z-H, Li J-J, Wang P (2007) *Z Kristallogr New Cryst Struct* 222:73
11. Quail JW, Das U, Dimmock JR (2005) *Acta Cryst* E61:o1150
12. Allen FH (2002) *Acta Cryst* B58:380
13. Quail JW, Doroudi A, Pati HN, Das U, Dimmock JR (2005) *Acta Cryst* E61:o1795
14. Zhou LY (2007) *Acta Cryst* E63:o3113
15. Jia Z, Quail JW, Arora VK, Dimmock JR (1989) *Acta Cryst* C45:285
16. Domenicano A, Murray-Rust P (1979) *Tetrahedron Lett* 24:2283
17. Duax WL, Norton DA (1975) *Atlas of steroid structures*. Plenum, New York, pp 16–22
18. Oxford Diffraction (2009) *CrysAlis PRO* (version 1.171.33.36d). Oxford Diffraction Ltd, Oxfordshire
19. Herbstein FH (2000) *Acta Cryst* B56:547
20. Altomare A, Cascarano G, Giacovazzo C, Gualandi A (1993) *J Appl Cryst* 26:343
21. Sheldrick GM (2008) *Acta Cryst* A64:112
22. Siemens (1989) *Stereochemical workstation operation manual*, Release 3.4. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin
23. Macrae CF, Bruno IJ, Chisholm JA, Edgington PR, McCabe P, Pidcock E, Rodriguez-Monge L, Taylor R, van de Streek J, Wood PA (2008) *J Appl Cryst* 41:466