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# Crystal structures of two polysubstituted derivatives of cyclohexanone

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The structure of 2,4-diacetyl-5-hydroxy-5-methyl-3-(4-nitrophenyl)-cyclohexanone (I) was determined by X-ray crystallography. The symmetry operation (-x + 2, - y + 1, -z) generates the whole molecule. The compound crystallizes in an orthorhombic system and was characterized thus: $P_{bca}$, a = 8.6405(10), b=18.682(2), c=20.187(4), α= β=γ=90 °, Z =.8, V = 3258.7 (8) Å$^3$ . The crystal structure was solved by direct methods and refined by full-matrix least-squares on $F^2$ to final values of R1 = 0.0687 and wR2 = 0.1225. The structure of 2,4-Diacetyl-3-(4-fluorophenyl)-5-hydroxy-5-methylcyclohexanone (II) was determine by X-ray crystallography. The symmetry operation (-x + 2, - y + 1, -z) generates the whole molecule. The compound crystallizes in a monoclinic system and was characterized thus: $P2_1/c$, a=5.7045 (5), b=18.120 (3), c=16.1678 (11), α= γ= 90 °, β= 96.192 (6) °, Z = 4, V = 1661.5 (3) Å$^3$. The crystal structure was solved by direct methods and refined by full-matrix least-squares on $F^2$ to final values of R1 = 0.0699 and wR2 = 0. 0.2100.

**Key words:** 2,4-Diacetyl-5-hydroxy-5-methyl-3-(4-nitrophenyl)-cyclohexanone, 2,4-Diacetyl-3-(4-fluorophenyl)-5-hydroxy-5-methylcyclohexanone, 1,3-dicarbonyl compounds, crystal structure, aldol condensation reaction

## INTRODUCTION

The investigations on the interaction between 1,3-dicarbonyl compounds (2,4-pentanedione or ethylacetoacetate) and aldehydes or ketones began at the end of the 19$^{th}$ century and are continuing till present [1-4]. The results are diverse. It has been accepted that different condensation products are synthesized at different molar ratios of the reactants, by varying temperature or type of catalyst.

In this research the interaction between some aromatic aldehydes and 2,4-pentanedione at a molar ratio of 1:1, 1:2 or 1:4 in the presence of piperidine as a catalyst and glacial acetic acid was studied. The interaction was performed at room temperature for 2 h (Fig. 1).

## EXPERIMENTAL

The crystal structure of the compounds was determined using the single crystal X-ray diffraction method. Data collection was carried out at –60 °C using graphite-monochromated Mo$K_\alpha$ radiation ($\lambda$ = 1.5418 Å) on an ENRAF NONIUS four circle diffractometer. The unit cell was determined and refined using the CAD4-EXPRESS program. A semiempirical absorption correction was performed using the PLATON/ABS PSI program [5]. The structure was solved with direct methods by SHELXS97 [6] and refined with SHELXL97 [7] by least-squares methods based on $F^2$. All non-hydrogen atoms were fully refined and all hydrogen atom positions were taken from the electron density map and refined isotropically. The plots of the molecular structure were made using the DIAMOND program (CRYSTAL IMPACT GbR, Bonn, Germany).

Complete data collection parameters and details of the structure solution and refinement are given in Table 1. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif

## RESULTS AND DISCUSSION

The structure of the synthesized compounds was proven by IR, $^1$H-NMR and mass-spectral analyses. Single crystals suitable for X-ray structure analysis could be obtained by crystallization from an ethanol solution, which afforded colorless crystals. The crystal and structure-refinement data are summarized in Tables 1 – 7.

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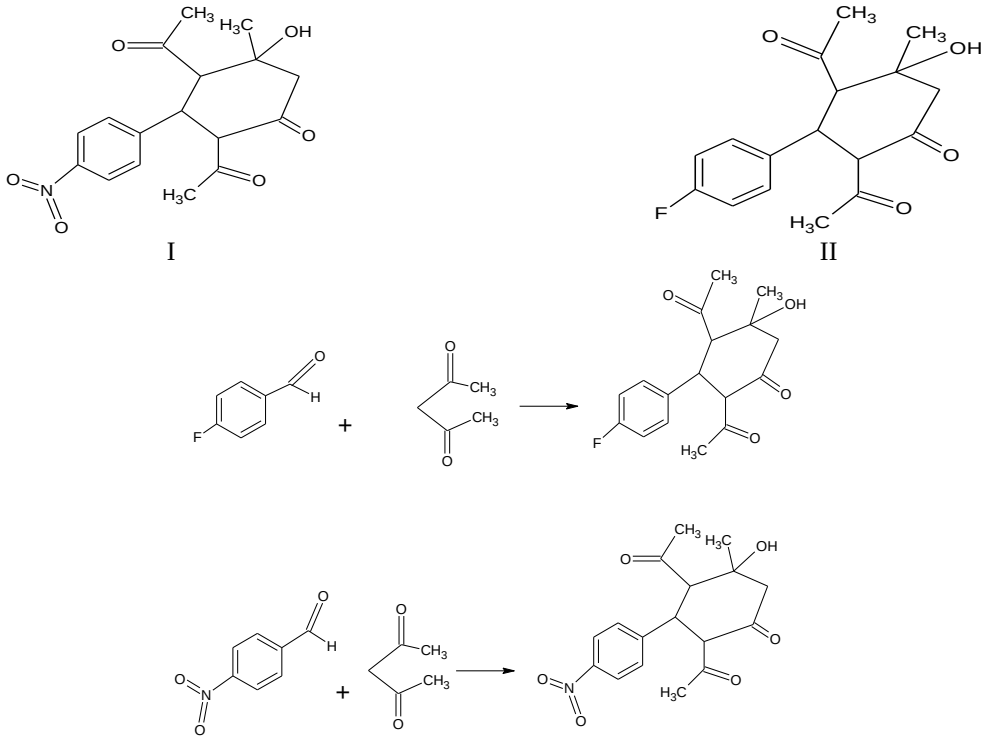

**Fig.1.** Chemical formula of the title compounds

**Table 1.** Crystal and experimental data for 2,4-Diacetyl-5-hydroxy-5-methyl-3-(4-nitrophenyl)-cyclohexanone (I) and 2,4-Diacetyl-3-(4-fluorophenyl)-5-hydroxy-5-methylcyclohexanone (II).

| | **I** | **II** |
|---|---|---|
| Chemical formula | $C_{17}H_{19}NO_6$ | $C_{17}H_{19}FO_4$ |
| Formula weight | 333.33 | 306.32 |
| Temperature | 213 (2) K | 223 (2) K |
| Crystal system: | Orthorhombic | Monoclinic |
| Space group: | Pbca | P $2_1$/n |
| | a = 8.6405(10)Å | a=5.7045(5)Å |
| | b = 18.682 (2)Å | b=18.120 (3)Å |
| | c = 20.187 (4)Å | c=20.1 |
| | α= β=γ=90 º | β=96.192 (6) º |
| | | α=γ=90 º |
| Volume | 3258.7 (8) Å$^3$ | 1661.5 (3) Å$^3$ |
| Z | 8 | 4 |
| Density (calculated) | 1.359 Mg/m$^3$ | 1.225 Mg/m$^3$ |
| Radiation : | MoKα (λ= 0.71073 Å) | MoKα (λ= 1.5418 Å) |
| F(000) | 1408 | 648 |
| Crystal size | 0.30 x 0.15 x 0.15 mm | .50 x 0.15 x 0.15 mm |
| No. of reflections collected | 2205 | 3998 |
| No. of independent reflections | 1673 | 2827 |
| θ range for data collection [°] | 5.83 to 20.81 | 5.50 to 64.96 |
| Data / restraints / parameters | 1673 / 0 / 273 | 2827 / 0 / 276 |
| Goodness-of-fit on F$^2$ | 1.078 | 1.067 |
| R indices [I>2σ (I)] | R1 = 0.0687, wR2 = 0.1225 | R1 = 0.0699,wR2 = 0.2100 |
| R indices (all data) | R1 = 0.2550, wR2 = 0.1590 | R1 = 0.0792,wR2 = 0.2210 |
| Refinement: | Full matrix | Full matrix |
| | $(\Delta/\sigma)_{max}$ = 0.001 | |
| | $(\Delta/\rho)_{max}$ = 0.38 eÅ$^{-3}$ | |
| | $(\Delta/\rho)_{min}$ = - 0.21 eÅ$^{-3}$ | |
| Measurement: | Enraf-Nonius CAD4 | Enraf-Nonius CAD4 |
| Program system: | Enraf-Nonius SDP | Enraf-Nonius SDP |
| Structure determination: | MULTAN | MULTAN |
| CCDC deposition number: | 706401 | 706402 |

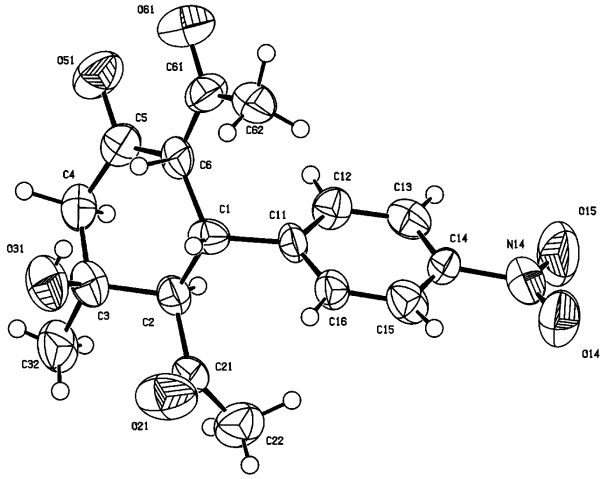


**Fig. 2.** ORTEP structurte of 2,4-diacetyl-5-hydroxy-5-methyl-3-(4-nitrophenyl)-cyclohexanone (I), showing 50% probability ellipsoids.

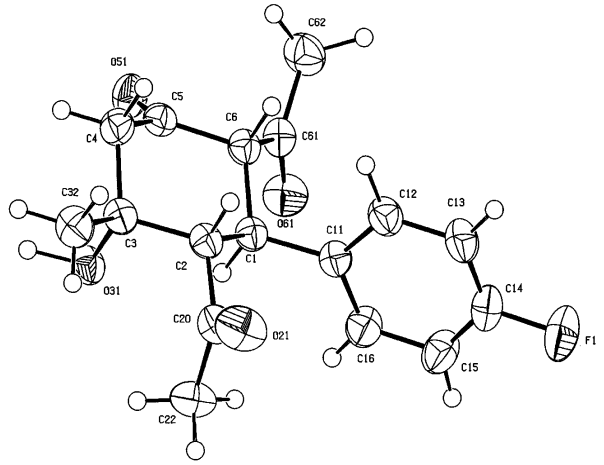


**Fig. 3.** ORTEP structure of 2,4-diacetyl-3-(4-fluorophenyl)-5-hydroxy-5-methylcyclohexanone (II), showing 50% probability ellipsoids.

The interaction of 4-bromobenzaldehyde, 4-hydroxybenzaldehyde and 4-methoxybenzaldehyde with 2,4-pentandione results in the formation of the respective 3-(4-substituted-benzylidene)pentane-2,4-dione [8].We established that the condensation process between aromatic aldehydes (containing a nitro group or a fluorine atom at para-position of the aromatic nucleus compared to aldehyde group) and 1,4-pentandione produced polysubstituted derivative of cyclohexanone (fig.: 2 and 3). These two substituents reveal –I-effect and strong -M-effect. X-ray crystal analysis proved a carbocyclic product, a result of the interaction between one mole aldehyde and two moles 2,4-pentandione, namely 2E-4-diacetyl-5-hydroxy-5-methyl-3-(4'-nitro-phenyl)-cyclohexanone or 2E-4-diacetyl-5-hydroxy-5-methyl-3-(4'-fluorophenyl)-cyclohexanone

**Table 2.** Atomic coordinates ( x $10^4$) and equivalent isotropic displacement parameters ($A^2x10^3$) for 2,4-diacetyl-5-hydroxy-5-methyl-3-(4-nitrophenyl)-cyclohexanone (I).

| Atom | x | y | z | U (eq) |
|---|---|---|---|---|
| C 1 | 2663 (10) | 1890 (5) | 3991 (4) | 47 (2) |
| C 2 | 3546 (10) | 2560 (4) | 3769 (5) | 47 (2) |
| C 3 | 2533 (12) | 3219 (5) | 3687 (4) | 57 (2) |
| C 4 | 1370 (15) | 3065 (6) | 3149 (5) | 62 (3) |
| C 5 | 580 (12) | 2362 (5) | 3231 (4) | 54 (2) |
| C 6 | 1106 (10) | 1837 (5) | 3653 (4) | 47 (2) |
| C 11 | 3689 (9) | 1251 (4) | 3912 (4) | 43 (2) |
| C 12 | 3860 (12) | 927 (5) | 3308 (4) | 51 (3) |
| C 13 | 4914 (12) | 378 (5) | 3198 (5) | 56 (3) |
| C 14 | 5784 (9) | 176 (4) | 3732 (6) | 52 (2) |
| C 15 | 5664 (12) | 488 (5) | 4338 (5) | 59 (3) |
| C 16 | 4609 (11) | 1021 (5) | 4425 (4) | 48 (2) |
| C 21 | 4871 (12) | 2699 (4) | 4242 (5) | 52 (2) |
| C 22 | 6485 (14) | 2644 (7) | 3973 (7) | 75 (3) |
| C 32 | 3483 (17) | 3863 (6) | 3518 (7) | 77 (4) |
| C 61 | 123 (12) | 1223 (5) | 3760 (5) | 59 (2) |
| C 62 | 421 (10) | 709 (4) | 4314 (4) | 70 (3) |
| O 14 | 7672 (8) | - 617 (3) | 4112 (4) | 93 (2) |
| O 15 | 7166 (9) | - 637 (3) | 3075 (4) | 112 (3) |
| O 21 | 4639 (7) | 2839 (3) | 4825 (3) | 94 (2) |
| O 31 | 1678 (7) | 3386 (3) | 4293 (3) | 79 (2) |
| O 51 | - 722 (8) | 2282 (3) | 2893 (3) | 80 (2) |
| O 61 | - 1099 (7) | 1135 (3) | 3427 (3) | 84 (2) |
| N 14 | 6962 (11) | - 393 (4) | 3626 (5) | 77 (3) |

**Table 3.** Atomic coordinates ( x $10^4$) and equivalent isotropic displacement parameters ($A^2$ x $10^3$) for 2,4-diacetyl-3-(4-fluorophenyl)-5-hydroxy-5-methylcyclohexanone (II)

| Atom | x | y | z | U (eq) |
|---|---|---|---|---|
| C 1 | 455 (4) | 7077 (1) | 11011 (2) | 33 (1) |
| C 2 | 2355 (4) | 7048 (1) | 10391 (2) | 33 (1) |
| C 3 | 2335 (4) | 6307 (1) | 9931 (2) | 35 (1) |
| C 4 | 2871 (5) | 5686 (2) | 10577 (2) | 38 (1) |
| C 5 | 1031 (4) | 5701 (1) | 11171 (2) | 35 (1) |
| C6 | 816 (4) | 6427 (1) | 11629 (2) | 34 (1) |
| C 11 | 498 (5) | 7812 (1) | 11459 (2) | 34 (1) |
| C 12 | 2456 (5) | 8043 (2) | 11982 (2) | 42 (1) |
| C 13 | 2494 (6) | 8726 (2) | 12373 (2) | 47 (1) |
| C 14 | 550 (5) | 9167 (2) | 12231 (2) | 46 (1) |
| C 15 | - 1407 (6) | 8966 (2) | 11727 (2) | 50 (1) |
| C 16 | - 1433 (5) | 8281 (2) | 11339 (2) | 44 (1) |
| C 20 | 2182 (5) | 7707 (2) | 9803 (2) | 40 (1) |
| C 22 | - 66 (6) | 7860 (2) | 9261 (2) | 54 (1) |
| C 32 | 4110 (5) | 6290 (2) | 9288 (2) | 45 (1) |
| C 61 | - 1143 (5) | 6363 (1) | 12196 (2) | 38 (1) |
| C 62 | - 541 (7) | 5979 (2) | 13006 (2) | 52 (1) |
| O 21 | 3891 (4) | 8097 (1) | 9779 (2) | 63 (1) |
| O31 | - 3 (3) | 6195 (1) | 9531 (1) | 39 (1) |
| O51 | - 264 (4) | 5184 (1) | 11272 (1) | 45 (1) |
| O 61 | - 3095 (4) | 6606 (1) | 11985 (1) | 51 (1) |
| F 1 | 582 (4) | 9845 (1) | 12605 (1) | 66 (1) |

**Table 4.** Selected bond lengths (Å) for 2,4-diacetyl-5-hydroxy-5-methyl-3-(4-nitrophenyl)-cyclohexanone (I)

| Bond | Length | Bond | Length |
|---|---|---|---|
| C 1 – C 11 | 1.496 (10) | C 5 – C 6 | 1.377 (10) |
| C 1 – C 6 | 1.512 (10) | C 6 – C 61 | 1.444 (11) |
| C 1 – C 2 | 1.532 (10) | C 14 – N 14 | 1.487 (11) |
| C 2 – C 21 | 1.513 (10) | C 21 – O 21 | 1.223 (9) |
| C 2 – C 3 | 1.521 (10) | C 21 – C 22 | 1.500 (12) |
| C 3 – O 31 | 1.462 (8) | C 61 – O 61 | 1.261 (9) |
| C 3 – C 32 | 1.495 (12) | C 61 – C 62 | 1.496 (10) |
| C 3 – C 4 | 1.506 (11) | O 14 – N 14 | 1.231 (8) |
| C 4 – C 5 | 1.490 (12) | O 15 – N 14 | 1.214 (8) |
| C 5 – O 51 | 1.323 (9) | | |

**Table 5.** Selected bond angles (°) for 2,4-diacetyl-5-hydroxy-5-methyl-3-(4-nitrophenyl)-cyclohexanone (I)

| Bond | Angle | Bond | Angle |
|---|---|---|---|
| C 11 – C 1 – C 6 | 115.2 (7) | C 5 – C 6 – C 61 | 117.7 (9) |
| C 11 – C 1 – C 2 | 109.0 (7) | C 5 – C 6 – C 1 | 121.8 (9) |
| C 6 – C 1 – C 2 | 111.4 (8) | C 61 – C 6 – C 1 | 120.5 (9) |
| C 21 – C 2 – C 3 | 111.4 (7) | C 16 – C 11 – C 1 | 120.7 (8) |
| C 21 – C 2 – C 1 | 109.4 (7) | C 12 – C 11 – C 1 | 120.8 (8) |
| C 3 – C 2 – C 1 | 114.0 (8) | C 15 – C 14 – N 14 | 119.3 (10) |
| O 31 – C 3 – C 32 | 107.3 (8) | C 13 – C 14 – N 14 | 117.4 (10) |
| O 31 – C 3 – C 4 | 107.9 (8) | O 21 – C 21 – C 22 | 121.0 (9) |
| C 32 – C 3 – C 4 | 110.8 (9) | O 21 – C 21 – C 2 | 121.3 (9) |
| O 31 – C 3 – C 2 | 111.8 (7) | C 22 – C 21 – C 2 | 117.6 (9) |
| C 32 – C 3 – C 2 | 111.1 (10) | O 61 – C 61 – C 6 | 121.0 (9) |
| C 4 – C 3 – C 2 | 107.9 (8) | O 61 – C 61 – C 62 | 117.3 (9) |
| C 5 – C 4 – C 3 | 113.3 (9) | C 6 – C 61 – C 62 | 121.4 (9) |
| O 51 – C 5 – C 6 | 121.3 (9) | O 15 – N 14 – O 14 | 122.0 (9) |
| O 51 – C 5 – C 4 | 115.6 (9) | O 15 – N 14 – C 14 | 120.0 (10) |
| C 6 – C 5 – C 4 | 123.0 (10) | O 14 – N 14 – C 14 | 118.0 (9) |

**Table 6.** Selected bond lengths (Å) for 2,4-diacetyl-3-(4-fluorophenyl)-5-hydroxy-5-methylcyclohexanone (II)

| Bond | Length | Bond | Length |
|---|---|---|---|
| C 1 – C 11 | 1.515 (3) | C 5 – O 51 | 1.214 (3) |
| C 1 – C 6 | 1.543 (3) | C 5 – C 6 | 1.520 (3) |
| C 1 – C 2 | 1.555 (3) | C 6 – C 61 | 1.525 (4) |
| C 2 – C 20 | 1.522 (4) | C 14 – F 1 | 1.367 (3) |
| C 2 – C 3 | 1.535 (3) | C 20 – O 21 | 1.208 (4) |
| C 3 – O 31 | 1.432 (3) | C 20 – C 22 | 1.499 (4) |
| C 3 – C 32 | 1.528 (4) | C 61 – O 61 | 1.211 (3) |
| C 3 – C 4 | 1.544 (4) | C 61 – C 62 | 1.490 (4) |
| C 4 – C 5 | 1.498 (4) | | |

**Table 7.** Selected bond angles (°) for 2,4-diacetyl-5-hydroxy-5-methyl-3-(4-fluorophenyl)-cyclohexanone (II)

| Bond | Angle | Bond | Angle |
|---|---|---|---|
| C 11 – C 1 – C 6 | 111.61 (19) | C 4 – C 5 – C 6 | 115.2 (2) |
| C 11 – C 1 – C 2 | 111.2 (2) | C 5 – C 6 – C 61 | 109.2 (2) |
| C 6 – C 1 – C 2 | 109.7 (2) | C 5 – C 6 – C 1 | 111.0 (2) |
| C 20 – C 2 – C 3 | 112.8 (2) | C 61 – C 6 – C 1 | 113.1 (2) |
| C 20 – C 2 – C 1 | 111.9 (2) | C 16 – C 11 – C 1 | 120.0 (2) |
| C 3 – C 2 – C 1 | 111.9 (2) | C 12 – C 11 – C 1 | 121.7 (2) |
| O 31 – C 3 – C 32 | 110.1 (2) | C 15 – C 14 – F 1 | 118.5 (3) |
| O 31 – C 3 – C 2 | 107.49 (19) | C 13 – C 14 – F 1 | 118.7 (3) |
| C 32 – C 3 – C 2 | 112.1 (2) | O 21 – C 20 – C 22 | 121.1 (3) |
| O 31 – C 3 – C 4 | 108.0 (2) | O 21 – C 20 – C 2 | 118.7 (3) |
| C 32 – C 3 – C 4 | 110.4 (2) | C 22 – C 20 – C 2 | 120.2 (2) |
| C 2 – C 3 – C 4 | 108.7 (2) | O 61 – C 61 – C 62 | 122.3 (3) |
| C 5 – C 4 – C 3 | 108.6 (2) | O 61 – C 61 – C 6 | 121.0 (2) |
| O 51 – C 5 – C 4 | 123.4 (2) | C 62 – C 61 – C 6 | 116.7 (2) |
| O 51 – C 5 – C 6 | 121.4 (2) | | |

Florencio at al.[9] established that during the reaction between nickel acetylacetonate dihydrate and p-nitrobenzyl chloride with dimethyl sulfoxide as a solvent only the monoalkylation product was obtained instead of the expected mixture of dialkylation and monoalkylation products. In this reaction a compound with empirical formula $C_{17}H_{19}NO_6$ was obtained, which was analyzed by X-ray diffraction methods in order to obtain conformational data. The product was 2E-4-diacetyl-5Z-methyl-3-(p-nitrophenyl)-cyclohex-1-en-1,5E-diol. The unit cell dimensions reported by Florencio were: a= 20.176(2), b=8.623(3), c=18.746(9) Å [9]. Our data do not correspond to their data: a = 8.6405 (10), b=18.682(2) and c=20.187(4)Å. analogous results were obtained using 4-fluorobenzaldehyde. The bond lengths were longer than the respective ones of the compound containing a nitro group. It seems that the electronegativity and the mesomeric effect of the nitro group is due to the difference in the bond length.The two cyclohexan rings were in a distorted half-chair conformation. The acetyl group was attached to C2 in a trans-equatorial position and the hydroxyl group attached to C3 was situated in an axial position for both compounds. Ponomarev et al.[10] described the synthesis of a cyclic product with the same molecular formula based only on the data of a spectral analysis as well as data of elemental analysis for carbon, hydrogen and fluorine. However, the results of the elemental analysis do not correspond to the formula suggested by them. The synthesized by us substance corresponds to the suggested formula. The results are based on the spectral, elemental and X-ray crystal structure analysis.

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# КРИСТАЛНИ СТРУКТУРИ НА ДВЕ ПОЛИСУБСТИТУИРАНИ ПРОИЗВОДНИ НА ЦИКЛОХЕКСАНОНА


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(Резюме)


Структурата на 2,4-диацетил-5-метил-5-хидрокси-3-(4-нитрофенил)циклохексанон (I) е определена чрез монокристален рентгеноструктурен анализ. Съединението кристализира в орторомбична кристална система и пространствена група $P_{cn}$, с параметри на елементарната клетка a=8.6405(10), b=18.682(2), c=20.187(4), $\alpha=\beta=\gamma=90^{o}$, Z =.8, V = 3258.7 (8) $Å^3$ . Кристалната структура е доказана с директни методи и точно определена с помощта на метода на най-малките квадрати за $F^2$ до стойност R1 = 0.0687. Структурата на 2,4-диацетил-3-(4-флуорофенил)-5-хидрокси-5-метилциклохексанон (II) е определена чрез монокристален рентгеноструктурен анализ. Съединението кристализира в моноклинна кристална система и пространствена група $P2_1/c$, с параметри на елементарната клетка , a=5.7045 (5), b=18.120 (3), c=16.1678 (11), $\alpha=\gamma=90^{o}$, $\beta=96.192\ (6)^{o}$, Z = 4, V = 1661.5 (3) $Å^3$. Кристалната структура е доказана с директни методи и точно определена с помощта на метода на най-малките квадрати за $F^2$ до стойност R1 = 0.0699.