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SYNTHESIS AND THE MOLECULAR AND CRYSTAL STRUCTURES OF METHYL 2-SUBSTITUTED 7,7-DIMETHYL-5-OXO-5,6,7,8-TETRAHYDROQUINOLINE-4-CARBOXYLATES

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Methyl 7,7-dimethyl-5-oxo-5,6,7,8-tetrahydroquinoline-4-carboxylates were obtained as a result of 3-amino-5,5-dimethylcyclohex-2-enone reaction with the methyl esters of acyl(aroyl)pyruvic acids. The structure of methyl 7,7-dimethyl-5-oxo-2-phenyl-5,6,7,8-tetrahydroquinoline-4-carboxylate was established by X-ray structural analysis.

Keywords: 3-amino-5,5-dimethylcyclohex-2-enone, methyl acyl(aroyl)pyruvates, 2-substituted methyl 7,7-dimethyl-5-oxo-5,6,7,8-tetrahydroquinoline-4-carboxylates.

It is known that the reaction of methyl aroylpyruvates with aniline begins with attack by the amine nitrogen atom at the C-2 carbon atom of the ester [1]. In view of this it could be supposed that the products of the reaction of 3-amino-5,5-dimethylcyclohex-2-enone (**1**) with methyl acyl(aroyl)pyruvates **2a-f** would be methyl 4-aryl-2-[(5,5-dimethyl-3-oxocyclohex-1-en-1-yl)amino]-4-oxo-2-butenoates **3a-f** or their dehydration products – quinolines **4a-f**. Moreover, for the enaminone **1** many of its reactions with electrophiles begin with an attack on the C-2 carbon atom [2]. Therefore, the isomeric 2-substituted methyl 7,7-dimethyl-5-oxo-5,6,7,8-tetrahydroquinoline-4-carboxylates **6a-f** can be formed in the investigated reaction. As a rule, intermediates of the **5a-f** type, the formation of which is postulated for the reactions of the enaminone **1** with β-dicarbonyl compounds, are not isolated from the reaction mixture [2].

We established that 2-substituted methyl 7,7-dimethyl-5-oxo-5,6,7,8-tetrahydroquinoline-4-carboxylates **6a-f** are formed as a result of the reaction of compounds **1** and **2a-f** (Table 1).

Since the data from IR and ^{1}H NMR spectroscopy do not allow to make an unequivocal choice between the isomeric structures **4** and **6**, X-ray structural investigations of a single crystal of compound **6b** were undertaken. The general view of the molecule is shown in Figure 1.

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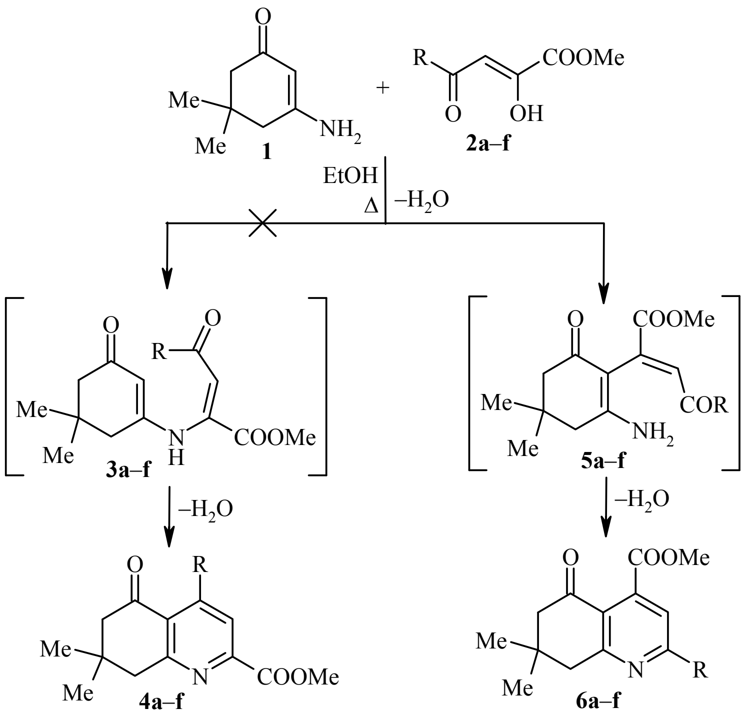

a R = *t*-Bu, **b** R = Ph, **c** R = 4-MeC_6H_4, **d** R = 4-$MeOC_6H_4$, **e** R = 4-BrC_6H_4, **f** R = 4-$O_2NC_6H_4$

According to the data from X-ray crystallographic analysis, compound **6b** crystallizes in a centrosymmetric space group of the monoclinic system. The conjugation system of the heterocycle is planar within 0.05 Å, and the C(3) atom deviates from the ring plane by 0.63 Å. The distribution of the bond lengths and the valence angles in the molecule is close to standard, and there are no significant shortened

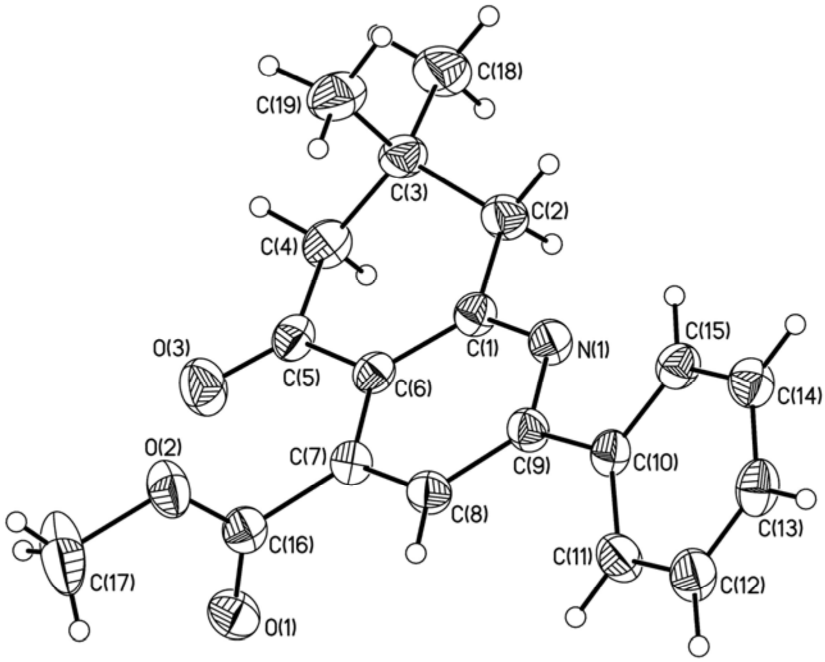

Fig. 1. The general appearance of the molecule of compound **6b** with the atoms represented by thermal vibration ellipsoids of 50% probability.

TABLE 1. The Spectral Characteristics of Compounds **6a-f**

Compound	IR spectrum, ν, cm^{-1}		^{1}H NMR spectrum, δ, ppm (*J*, Hz)					
	C=O	COOMe	7-C(CH$_3$)$_2$ (6H, s)	6-CH$_2$ (2H, s)	8-CH$_2$ (2H, s)	H-3 (1H, s)	OCH$_3$ (3H, s)	R
6a	1686	1735	1.09	2.56	3.06	7.33	3.84	1.36 (9H, s, C(CH$_3$)$_3$)
6b	1686	1732	1.12	2.60	3.15	7.86	3.89	7.50-7.54 (3H, m, H Ph); 8.21-8.24 (2H, m, H Ph)
6c	1689	1741	1.13	2.60	3.15	7.82	3.99	2.40 (3H, s, CH$_3$); 7.34 (2H, d, *J* = 9.0, H Ar); 8.14 (2H, d, *J* = 9.0, H Ar)
6d	1679	1736	1.13	2.60	3.13	7.78	3.88	3.87 (3H, s, OCH$_3$); 7.07 (2H, d, *J* = 9.0, H Ar); 8.22 (2H, d, *J* = 9.0, H Ar)
6e	1683	1736	1.13	2.61	3.16	7.89	3.88	7.71 (2H, d, *J* = 9.0, H Ar); 8.19 (2H, d, *J* = 9.0, H Ar)
6f	1695	1744	1.15	2.65	3.22	8.05	3.90	8.39 (2H, d, *J* = 9.0, H Ar); 8.52 (2H, d, *J* = 9.0, H Ar)

contacts in the molecular packing. The residual electron density is characterized by a significant maximum (0.726 e·Å^{-3}) at *x* 0.5737, *y* 0.8412, *z* 0.4340. The intensity of the peak is higher than the intensity corresponding to a hydrogen atom location, but significantly lower than the intensity corresponding to a location of atoms in the middle of the second period. This peak probably appears as a result of the generally poor quality of the crystal.

Thus, the X-ray investigations have shown that the products from the reaction of 3-amino-5,5-dimethylcyclohex-2-enone with methyl acyl(aroyl)pyruvates are 2-substituted methyl 7,7-dimethyl-5-oxo-5,6,7,8-tetrahydroquinoline-4-carboxylates.

EXPERIMENTAL

The IR spectra were recorded in vaseline oil on a Bruker IFS 66ps IR Fourier spectrometer. The ^{1}H NMR spectra were recorded in acetone-d$_6$ on a Varian Mercury 300 Plus instrument (300 MHz) with HMDS as internal standard (δ 0.059 ppm). Elemental analysis was performed on a LECO CHNS-932 instrument. The melting points were determined on a PTP instrument.

Methyl 2-(*tert*-Butyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydroquinoline-4-carboxylate (6a). A mixture of the ester **2a** (4.14 g, 22 mmol) and enaminone **1** (3.10 g, 22 mmol) was refluxed in EtOH (50 ml) for 5 h. The reaction mixture was cooled to 0°C, and the precipitate was filtered off. Yield 1.09 g (17%). White crystals, mp 135-136°C (MeOH). Found, %: C 70.50; H 7.90; N 4.70. $C_{17}H_{23}NO_3$. Calculated, %: C 70.56; H 8.01; N 4.84.

Methyl 7,7-Dimethyl-5-oxo-2-phenyl-5,6,7,8-tetrahydroquinoline-4-carboxylate (6b). This product was obtained similarly to the ester **6a** from the ester **2b** (7.88 g, 38 mmol) and enaminone **1** (5.32 g, 38 mmol). Yield 7.57 g (64%). Yellow crystals, mp 132-134°C (EtOH). Found, %: C 73.61; H 5.97; N 4.46. $C_{19}H_{19}NO_3$. Calculated, %: C 73.77; H 6.19; N 4.53.

Methyl 7,7-Dimethyl-2-(4-methylphenyl)-5-oxo-5,6,7,8-tetrahydroquinoline-4-carboxylate (6c). This product was obtained similarly to the ester **6a** from the ester **2c** (4.75 g, 22 mmol) and the enaminone **1** (3.10 g, 22 mmol). Yield 2.61 g (37%). Yellow crystals, mp 139-140°C (EtOH). Found, %: C 74.34; H 6.37; N 4.34. $C_{20}H_{21}NO_3$. Calculated, %: C 74.28; H 6.55; N 4.33.

Methyl 2-(4-Methoxyphenyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydroquinoline-4-carboxylate (6d). This product was obtained similarly to the ester **6a** from the ester **2d** (4.45 g, 19 mmol) and enaminone **1** (2.64 g, 19 mmol). Yield 2.54 g (39%). Pale-yellow crystals, mp 137-139°C (MeOH). Found, %: C 70.64; H 6.00; N 4.23. $C_{20}H_{21}NO_4$. Calculated, %: C 70.78; H 6.24; N 4.13.

Methyl 2-(4-Bromophenyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydroquinoline-4-carboxylate (6e). This product was obtained similarly to the ester **6a** from the ester **2e** (4.50 g, 16 mmol) and enaminone **1** (2.20 g, 16 mmol). Yield 1.96 g (32%). Colorless crystals, mp 114-115°C (2-PrOH). Found, %: C 59.00; H 4.50; N 3.55. $C_{19}H_{18}BrNO_3$. Calculated, %: C 58.78; H 4.67; N 3.61.

Methyl 7,7-Dimethyl-2-(*p*-nitrophenyl)-5-oxo-5,6,7,8-tetrahydroquinoline-4-carboxylate (6f). This product was obtained similarly to the ester **6a** from the ester **2f** (3.00 g, 14 mmol) and enaminone **1** (1.90 g, 14 mmol). Yield 1.50 g (31%). Yellow-brown crystals, mp 131-133°C (EtOH). Found, %: C 64.30; H 5.00; N 7.82. $C_{19}H_{18}N_2O_5$. Calculated, %: C 64.40; H 5.12; N 7.91.

X-Ray Structural Investigation of Compound 6b ($C_{19}H_{19}NO_3$, *M* 309.37). The investigation was carried out on an Xcalibur 3 single-crystal diffractometer with a CCD detector and SHELXTL97 software [3] using the standard procedure (MoKα radiation, *T* 130(2) K, ω scanning with 1° step). Crystals 0.51×0.46×0.39 mm, colorless, grown in 2-PrOH, monoclinic, space group $P2_1/c$, unit cell parameters: *a* 12.9499(14), *b* 7.6102(12), *c* 17.196(2) Å; β 100.424(10)°; *Z* 4. Experiment completeness at angles $\theta \leq 26.0°$ is 97.9%. The number of reflections collected was 4956, independent 3335 (R_{int} 0.0236), 1768 with $I > 2\sigma(I)$. The structure was interpreted by the direct method in isotropic approximation and refined in anisotropic approximation for the non-hydrogen atoms. The hydrogen atoms were placed at the geometrically calculated positions and were included in the refinement in isotropic approximation using the "rider" model. A correction for absorption was not made, μ 0.083 mm^{-1}. The final probability parameters were R_1 0.0427, wR_2 0.0917 (for reflections with $I > 2\sigma(I)$) with quality factor *S* 1.006. The maximum and minimum peaks of residual electron density were 0.726 and -0.262 e·Å^{-3}. The results of the X-ray structural investigation were deposited at the Cambridge Crystallographic Data Center (deposit CCDC 843787).

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