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# NITROGEN-CONTAINING HETEROCYCLES BASED ON TETRACARBONYL COMPOUNDS AND THEIR ANALOGS. 2.* REACTIONS OF 2-(4,4-DIMETHYL-2,6-DIOXOCYCLOHEXYL)-4-OXO-4-PHENYLBUTANOIC ACID WITH N-NUCLEOPHILES

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*The adduct of dimedone and β-benzoylacrylic acid is shown to form quinoline derivatives in reactions with primary amines.*

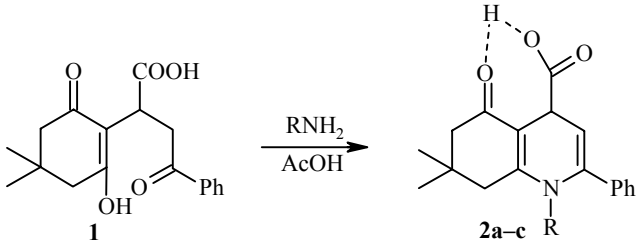
**Keywords:** β-benzoylacrylic acid, dimedone, 1,4,5,6,7,8-hexahydroquinolines, Michael reaction.

Earlier we have shown that the adduct of dimedone and *trans*-1,2-dibenzoylethylene forms pyrrole derivatives in reactions with ammonia and primary amines [1]. We also established that the adduct of dimedone and β-benzoylacrylic acid, when treated with ammonia, forms pyrrolo[4,3,2-*d,e*]quinoline structure that appears within the composition of some marine alkaloids [2].

With the objective of determining the prospects for synthesis of N-substituted pyrrolo[4,3,2-*d,e*]-quinolines, we thought it was advisable to study the characteristic features of the behavior of this triketo acid in reactions with various N-nucleophiles.

We carried out the reactions of 2-(4,4-dimethyl-2,6-dioxocyclohexyl)-4-oxo-4-phenylbutanoic acid with ammonium acetate, methylamine, benzylamine, and *p*-toluidine. We obtained only quinoline derivatives as a result.

As the model N-nucleophiles, we selected aliphatic, aliphatic-aromatic, and aromatic amines. Reactions with these amines in acetic acid lead to formation of compounds of type **2a-c**.




**1** **2a–c**

**2a** R = Me, **b** R = $PhCH_2$–, **c** R = 4-$MeC_6H_4$–

* For Communication 1, see [1].

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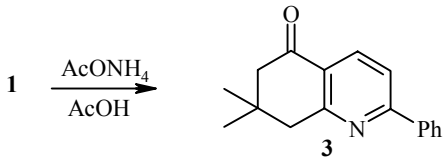
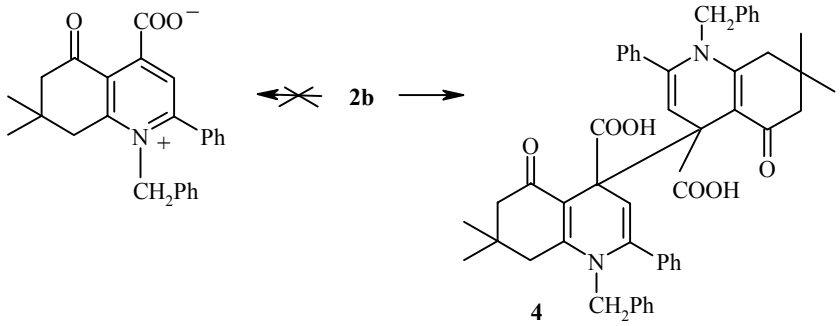
In the IR spectra of the indicated compounds, we observe an intense absorption band in the 1600 $cm^{-1}$ region (hydrogen-bonded carboxyl) and the 2350-2250 $cm^{-1}$ region ($C=O^{+}–H$), and also in the 1640 $cm^{-1}$ region (C=O). For the $^{1}H$ NMR spectra of these compounds, two doublet signals are typical in the 5-6 ppm and 8 ppm region (4-H and 3-H respectively). In the $^{1}H$ NMR spectrum of compound **2b**, the signals from protons of the $CH_2Ph$ group appear as two doublets with $J_{gem}$ = 15.5 Hz and $\Delta\delta$ = 1.42 ppm, which indicates a fixed conformation at the $N–CH_2–$ bond, where one of the protons of the $–CH_2–$ group falls within the deshielding cone of the phenyl substituent in the position 2.

In the reaction of triketo acid **1** with ammonium acetate, also carried out in acetic acid, the pyridine ring is closed; furthermore, decarboxylation occurs and the previously described compound **3** is formed [3].




Oxidation of dihydropyridine ring of compounds **2a-c** could lead to formation of betaines, which could act as lipophilic membrane stabilizers. But on oxidation of compound **2b** by chromic anhydride in pyridine, we obtained compound **4.**




In the $^{1}H$ NMR spectrum of the compound obtained, there are no signals from protons in the positions 4, 4'. The position of the other signals is similar to what is observed in the spectrum of the starting compound. The absorption bands in the IR spectrum are also similar to the starting data. The mass spectrum does not give molecular ion, showing only the molecular degradation products.

## EXPERIMENTAL

The IR spectra were recorded on a Perkin Elmer Spectrum BX in KBr. The mass spectra were determined on an HP 5972 MSD/HP chromatographic/mass spectrometric system with ionizing electron energy of 70 eV. The $^{1}H$ NMR spectra were obtained on a Bruker WM-250 spectrometer in $CDCl_3$ (internal standard TMS). The course of the reactions and the purity of the compounds obtained were monitored by TLC on Silufol UV-254 and Sorbfil plates, and also by gas chromatography.

**1,7,7-Trimethyl-5-oxo-2-phenyl-1,4,5,6,7,8-hexahydroquinoline-4-carboxylic Acid (2a).** Mixture of compound **1** (0.40 g, 1.3 mmol) and 25% aqueous methylamine (2 ml) in acetic acid (5 ml) was boiled for 30 min and then poured into ice water; the precipitating oil was triturated. A solid residue that was obtained was filtered, washed with water, and dried. Compound **2a** was obtained, yield 0.21 g (53%); mp 130-132°C (ethanol). IR spectrum (KBr), $\nu$, $cm^{-1}$: 2266, 1892, 1640, 1609, 1563. $^{1}H$ NMR spectrum ($CDCl_3$), $\delta$, ppm,

*J* (Hz): 15.44 (1H, s, OH); 8.13 (1H, d, *J* = 2.0, 3-H); 7.10-7.40 (5H, m, Ph); 5.10 (1H, d, *J* = 2.0, 4-H); 2.90 (3H, s, $CH_3$); 2.48 (2H, s, $CH_2$); 2.31 (2H, s, $CH_2$); 1.07 (6H, s, 2 $CH_3$). Mass spectrum: 311 $[M]^+$. Found, %: C 73.05; H 6.96; N 4.68. $C_{19}H_{21}NO_3$. Calculated, %: C 73.29; H 6.80; N 4.50.

**1-Benzyl-7,7-dimethyl-5-oxo-2-phenyl-1,4,5,6,7,8-hexahydroquinoline-4-carboxylic Acid (2b).** The acid was obtained according to similar procedure from compound **1** (0.40 g, 1.3 mmol) and benzylamine (1 ml, 9.2 mmol), yield 0.45 g (92%); mp 154-156°C (ethanol). IR spectrum (KBr), ν, $cm^{-1}$: 2337, 1889, 1638, 1601, 1566. $^1$H NMR spectrum ($CDCl_3$), δ, ppm, *J* (Hz): 15.37 (1H, s, OH); 8.12 (1H, d, *J* = 2.0, 3-H); 7.28-7.38 (5H, m, Ph); 7.05-7.14 (5H, m, Ph); 5.16 (1H, d, *J* = 15.5, $CH_2N$); 5.02 (1H, d, *J* = 2.0, 4-H); 3.74 (1H, d, *J* = 15.5, $CH_2$–N); 2.50 (2H, s, $CH_2$); 2.31 (2H, s, $CH_2$); 1.08 (6H, s, $2CH_3$). Mass spectrum: 387 $[M]^+$. Found, %: C 77.75; H 6.28; N 3.88. $C_{25}H_{25}NO_3$. Calculated, %: C 77.49; H 6.50; N 3.61.

**7,7-Dimethyl-1-(4-methylphenyl)-5-oxo-2-phenyl-1,4,5,6,7,8-hexahydroquinoline-4-carboxylic Acid (2c).** The acid was obtained similarly from compound **1** (0.40 g, 1.3 mmol) and *p*-toluidine (0.14 g, 1.3 mmol). Yield 0.20 g (41%); mp 156-158°C (ethanol). The material was purified by express chromatography on $Al_2O_3$ (eluent $CH_2Cl_2$). IR spectrum (KBr), ν, $cm^{-1}$: 2389, 2303, 1895, 1641, 1607, 1573. $^1$H NMR spectrum ($CDCl_3$), δ, ppm, *J* (Hz): 14.97 (1H, s, OH); 8.24 (1H, d, *J* = 2.5, 3-H); 7.07-7.28 (9H, m, $H_{arom}$); 5.75 (1H, d, *J* = 2.5, 4-H); 2.50 (2H, s, $CH_2$); 2.33 (2H, s, $CH_2$); 2.28 (3H, s, $CH_3$); 1.09 (6H, s, $2CH_3$). Mass spectrum: 387 $[M]^+$. Found, %: C 77.66; H 6.38; N 3.42. $C_{25}H_{25}NO_3$. Calculated, %: C 77.49; H 6.50; N 3.61.

**7,7-Dimethyl-2-phenyl-5,6,7,8-tetrahydroquinolin-5-one (3).** Mixture of compound **1** (0.40 g, 1.3 mmol) and ammonium acetate (1.00 g, 13 mmol) in acetic acid (5 ml) was boiled for 2 h, poured into ice water, the precipitated crystals were filtered off, washed with water, and dried. Yield 0.05 g (16%); mp 70-72°C (ethanol–water). Lit. mp 71.5-73°C [3]. The IR and $^1$H NMR data correspond to the literature values. Mass spectrum: 251 $[M]^+$. Found, %: C 81.47; H 6.96; N 5.28. $C_{17}H_{17}NO$. Calculated, %: C 81.24; H 6.82; N 5.57.

**Bis(1-benzyl-7,7-dimethyl-5-oxo-2-phenyl-1,4,5,6,7,8-hexahydro-4-quinolyl)-4,4'-dicarboxylic Acid (4).** Solution of compound **2b** (0.20 g, 0.52 mmol) was added to solution of chromic anhydride (0.02 g, 0.2 mmol) in pyridine (5 ml); this was held for 1 h at room temperature. The mixture was poured into water and extracted with methylene chloride. The extract was dried, the solvent was evaporated down, and the residue was triturated with acetone. Yield 0.10 g (50%); mp 177-179°C (acetone). IR spectrum (KBr), ν, $cm^{-1}$: 2249, 1899, 1610, 1568. $^1$H NMR spectrum ($CDCl_3$), δ, ppm, *J* (Hz): 15.14 (1H, s, OH); 7.95 (1H, s, 3-H); 7.27-7.38 (5H, m, Ph); 7.18 -7.25 (5H, m, Ph); 4.62 (1H, d, *J* = 15, $CH_2N$); 4.15 (1H, d, *J* = 15, $CH_2N$); 2.44 (2H, s, $CH_2$); 2.20 (2H, s, $CH_2$); 1.01 (6H, s, $2CH_3$). Mass spectrum: 281 $[M/2 - Ph - CO]^+$; 105 $[Ph - CO]^+$. Found, %: C 77.92; H 6.15; N 3.48. $C_{50}H_{48}N_2O_6$. Calculated, %: C 77.70; H 6.26; N 3.62.

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