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SYNTHESIS OF PHENYL-2,3-OXAZINE DERIVATIVES OF CHRYSENEQUINONECARBOXYLIC ACID

E. V. Tret′yakova,[1] O. B. Flekhter,[1] F. Z. Galin,[1] and G. A. Tolstikov[2]

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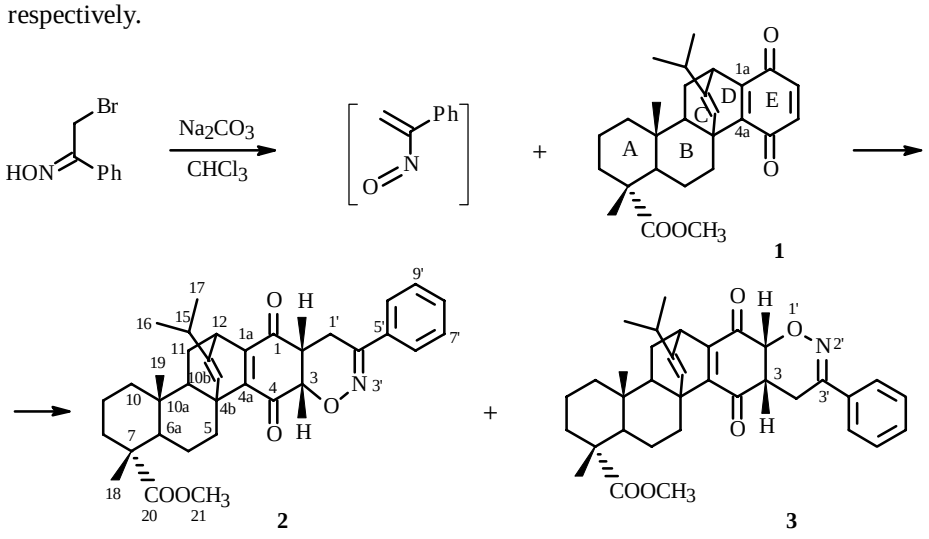
*A mixture of isomeric phenyloxazines (**2**, **3**) in a 5:4 ratio was synthesized via a [4 + 2] addition reaction of a heterocyclic diene-precursor prepared from bromoacetophenone oxime and the methyl ester of chrysenequinonecarboxylic acid (**1**). The structures of the synthesized compounds were confirmed using spectral methods.*

Key words: 1a,4a-dehydroquinopimaric acid, diene synthesis reaction, phenyl-2,3-oxazines.

It has been previously found that 1a,4a-dehydroquinopimaric (chrysenequinonecarboxylic) acid readily undergoes a Diels—Alder reaction with thebaine [1, 2], dehydrothebaine [3], methoxyoxazole [1], and substituted butadienes [4]. This same reaction of 1a,4a-dehydroquinopimaric acid with heterocyclic dienes has not been studied.

We investigated the diene-synthesis reaction of the methyl ester of 1a,4a-dehydroquinopimaric acid (**1**) and the heterocyclic diene-precursor prepared from bromoacetophenone oxime and a base and isolated a mixture (5:4 ratio) of isomeric phenyloxazines (**2**, **3**), like for oxazinetetrahydroquinolines [6]. This was confirmed by NMR spectra. The PMR spectrum of the mixture of **2** and **3** contains multiplets for aromatic protons at 7.22-7.44 (δ, ppm) and 7.70-7.92 for **2** and 7.48-7.60 and 7.95-8.10 for **3**. Signals for oxazine H-1′ (**2**) and H-4′ (**3**) appear at 4.85-5.00 (m) for both compounds; for H-2 and H-3, at 2.71-2.81 (m) and 5.32-5.40 (m) (**2**) and 2.82-2.98 (m) and 5.46-5.50 (m) (**3**), respectively. The ^{13}C NMR spectra of **2** and **3** have signals for aromatic C-5′-C-8′ at 128.2-130.6; heterocyclic C-1′ (**2**) and C-4′ (**3**), 34.1; C-2 and C-3, 49.2 and 108.5 (**2**) and 110.6 and 49.0 (**3**), respectively.



1) Institute of Organic Chemistry, Ufa Scientific Center, Russian Academy of Sciences, 450054, Ufa, prospekt Oktyabrya, 71, fax (3472) 35 60 66, e-mail: obf@anrb.ru; 2) N. N. Vorozhtsov Novosibirsk Institute of Organic Chemistry, Siberian Division, Russian Academy of Sciences, Novosibirsk. Translated from Khimiya Prirodnykh Soedinenii, No. 4, pp. 319-320, July-August, 2004. Original article submitted April 21, 2004.

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Dreiding models were examined to refine the configuration of H-2 and H-3 in **2** and **3**. It has been found that ring E in the methyl ester of **1** is planar. This limits approach of the reagent to one side. Therefore, as expected, the new oxazine ring has a *cis*-fused ring E.

EXPERIMENTAL

IR spectra were recorded on Specord M80 and UR-20 spectrometers in mineral-oil mulls. ^{13}C NMR and PMR spectra were recorded on a Bruker AM-300 (75.5 and 300 MHz, respectively) spectrometer in $CDCl_3$ with $SiMe_4$ internal standard. Melting points were measured on a Boetius microstage.

TLC was performed on Silufol (Chemapol, Czech Rep.) plates using $CHCl_3$:CH_3OH (20:1). Compounds were detected with phosphotungstic acid in ethanol (10%) with subsequent heating at 100-120°C for 2-3 min. Elemental analyses of the compounds corresponded with those calculated. The methyl ester of **1** was prepared using the literature method [5].

Synthesis of 2. A solution of **1** (0.42 g, 1 mmol) in dry $CHCl_3$ (30 mL) was stirred, treated with bromoacetophenone oxime (0.46 g, 2 mmol) and anhydrous Na_2CO_3 (0.42 g, 5 mmol), stirred at room temperature for 24 h, treated with water (30 mL), and extracted with $CHCl_3$ (3 × 20 mL). The extract was washed with water (2 × 20 mL), dried over $MgSO_4$, and evaporated in vacuum. The solid was chromatographed over Al_2O_3 with elution by benzene to afford a mixture of isomers (5:4 ratio). Yield 64% (0.36 g), R_f 0.90. PMR spectrum ($CDCl_3$, δ, ppm): 2.71-2.81 (0.56 H, H-2), 2.82-2.98 (0.44 H, H-2), 5.32-5.40 (0.56 H, H-3), 5.46-5.50 (0.44 H, H-3). IR spectrum (ν, cm^{-1}): 1730 ($COOCH_3$), 1690 (C=O), 1600, 1470, 1380, 1325, 1300, 1255, 1230, 1200, 1115, 1085, 1045, 1015, 935, 840, 780, 730, 705.

Methyl (10a*R*,7*R*)-13-isopropyl-7,10a-dimethyl-1,4-dioxo-2′-phenyl-4′-oxa-3′-azahexacyclo[10.10.2.0^{4b,10b}.0^{4a,1a}.0^{3,2}.0^{10a,6a}]-tetracosa-4a(1a),3′,14-trien-7-carboxylate (2). PMR spectrum ($CDCl_3$, δ, ppm, J/Hz): 0.66 (s, 3H, H-18), 0.68-0.73 (m, 3H, H-10$_{a,e}$, H-10b), 0.90 and 0.94 (both d, 3H each, J = 6.9, H-16/H-17), 1.15 (s, 3H, H-19), 1.20-1.35 (m, 5H, H-6$_{a,e}$, H-9$_{a,e}$, H-11$_a$), 1.50-1.68 (m, 6H, H-8$_{a,e}$, H-5$_{a,e}$, H-6a, H-11$_e$), 2.08 (sept., 1H, J = 6.9, H-15), 2.74 (dt, 1H, J = 8.0, J = 2.5, J = 2.6, H-12), 2.71-2.81 (m, 1H, H-2), 3.65 (s, 3H, H-21), 4.85-5.00 (m, 2H, H-1′), 5.20 (br.s, 1H, H-14), 5.32-5.40 (m, 1H, H-3), 7.22-7.44 (m, 3H, arom. H-6′, H-8′, H-10′), 7.70-7.92 (m, 2H, arom. H-7′, H-9′).

^{13}C NMR spectrum ($CDCl_3$, δ, ppm): 199.3 (C-1), 143.8 (C-1a), 49.2 (C-2), 110.6 (C-3), 199.5 (C-4), 134.4 (C-4a), 51.5 (C-4b), 38.0 (C-5), 20.7 (C-6), 53.1 (C-6a), 51.8 (C-7), 40.5 (C-8), 16.9 (C-9), 41.9 (C-10), 41.7 (C-10a), 55.3 (C-10b), 23.3 (C-11), 47.1 (C-12), 147.5 (C-13), 121.3 (C-14), 36.5 (C-15), 18.8 (C-16), 18.0 (C-17), 16.6 (C-18), 15.9 (C-19), 179.0 (C-20), 59.4 (C-21), 34.1 (C-1′), 150.6 (C-2′), 130.6 (C-5′), 130.2 (C-6′), 128.5 (C-7′), 128.2 (C-8′), 128.6 (C-9′), 129.9 (C-10′).

Methyl (10a*R*,7*R*)-13-isopropyl-7,10a-dimethyl-1,4-dioxo-3′-phenyl-1′-oxa-2′-azahexacyclo[10.10.2.0^{4b,10b}.0^{4a,1a}.0^{3,2}.0^{10a,6a}]-tetracosa-4a(1a),2′,14-trien-7-carboxylate (3). PMR spectrum ($CDCl_3$, δ, ppm, J/Hz): 0.64 (s, 3H, H-18), 0.68-0.73 (m, 3H, H-10$_{a,e}$, H-10b), 0.90 and 0.94 (both d, 3H each, J = 6.9, H-16/H-17), 1.15 (s, 3H, H-19), 1.19-1.33 (m, 5H, H-6$_{a,e}$, H-9$_{a,e}$, H-11$_a$), 1.48-1.65 (m, 6H, H-8$_{a,e}$, H-5$_{a,e}$, H-6a, H-11$_e$), 2.08 (sept., 1H, J = 6.9, H-15), 2.74 (dt, 1H, J = 8.0, J = 2.5, J = 2.6, H-12), 2.82-2.98 (m, 1H, H-2), 3.65 (s, 3H, H-21), 4.85-5.00 (m, 2H, H-4′), 5.20 (br.s, 1H, H-14), 5.46-5.50 (m, 1H, H-3), 7.48-7.60 (m, 3H, arom. H-6′, H-8′, H-10′), 7.95-8.10 (m, 2H, arom. H-7′, H-9′).

^{13}C NMR spectrum ($CDCl_3$, δ, ppm): 199.1 (C-1), 143.8 (C-1a), 108.5 (C-2), 49.0 (C-3), 199.4 (C-4), 134.3 (C-4a), 51.3 (C-4b), 38.2 (C-5), 20.5 (C-6), 53.0 (C-6a), 51.7 (C-7), 40.2 (C-8), 16.7 (C-9), 41.9 (C-10), 41.4 (C-10a), 55.0 (C-10b), 23.3 (C-11), 47.3 (C-12), 147.2 (C-13), 121.0 (C-14), 36.1 (C-15), 18.5 (C-16), 18.0 (C-17), 16.6 (C-18), 15.9 (C-19), 179.3 (C-20), 59.0 (C-21), 150.2 (C-3′), 34.1 (C-4′), 130.4 (C-5′), 130.0 (C-6′), 128.5 (C-7′), 128.2 (C-8′), 128.6 (C-9′), 129.5 (C-10′).

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