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Synthesis of Novel Polycyclic Carbamate Derivatives of 2-Hydroxy-2,2'-biindane-1,1',3,3'-tetrone

A. V. Velikorodov[a,*], A. S. Zukhairaeva[a], S. B. Nosachev[a], and N. S. Markov[a]

[a] *Astrakhan State University, ul. Tatishcheva 20a, Astrakhan, 414056 Russia*
**e-mail: avelikorodov@mail.ru*

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Abstract—Methyl 1,3,11'-trioxo-1,3,10a',11'-tetrahydro-4β'*H*-spiro[inden-2,10'-indeno[1,2-*b*]chromene]-7'(8')-ylcarbamates and methyl (ethyl) 4-(1,1',3,3'-tetraoxo-2,2',3,3'-tetrahydro-1*H*,1'*H*-2,2'-biinden-2-yl)-phenylcarbamates were synthesized by condensation of 2-hydroxy-2,2'-biindane-1,1',3,3'-tetrone with methyl *N*-(3(4)-hydroxyphenyl)carbamates and methyl (ethyl) *N*-phenylcarbamates. Condensation of methyl *N*-(2-hydroxyphenyl)-carbamate with the tetrone gave methyl 2-hydroxy-5-(1,1',3,3'-tetraoxo-2,2',3,3'-tetrahydro-1*H*,1'*H*-2,2'-biinden-2-yl)phenylcarbamate. Methyl 4-(3'-amino-1,1',3-trioxo-2,3-dihydro-1*H*,1'*H*-2,2'-biinden-2-yl)-phenylcarbamate was obtained by boiling methyl 4-(1,1',3,3'-tetraoxo-2,2',3,3'-tetrahydro-1*H*,1'*H*-2,2'-biinden-2-yl)-phenylcarbamate with urea in glacial acetic acid. Condensation of methyl 4-(1,1',3,3'-tetraoxo-2,2',3,3'-tetrahydro-1*H*,1'*H*-2,2'-biinden-2-yl)-phenylcarbamate with hydrazine hydrate at room temperature gave methyl *N*-{4-[(1,3-dioxo-2,3-dihydro-1*H*-inden-2-yl)(4-oxo-3,4-dihydro-1-phthalazinyl)methyl]phenyl}-carbamate.

Keywords: 2,2-dihydroxyindane-1,3-dione, 2-hydroxy-2,2'-biindane-1,1',3,3'-tetrone, methyl *N*-(3(4)-hydroxyphenyl)-carbamates, alkyl-*N*-phenylcarbamates, urea, hydrazine hydrate, condensation reactions, polycyclic compounds

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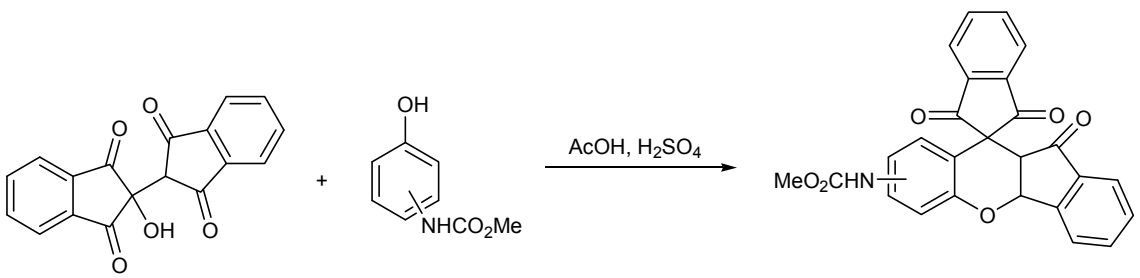
Ninhydrin and its derivatives are privileged structures in organic synthesis and are widely used to construct diverse linearly linked, fused, and spiro-fused heterocyclic compounds. 2-Hydroxy-2,2'-biindane-1,1',3,3'-tetrone (**1**) prepared by condensation of ninhydrin with indene-1,4-dione is among such structures [7, 8].

We studied the condensations of 2-hydroxy-2,2'-biindane-1,1',3,3'-tetrone (**1**) with methyl *N*-(3(4)-hydroxyphenyl)carbamates (**2** and **3**) in glacial acetic acid in the presence of concentrated sulfuric acid.

It was found that condensation proceeds at room temperature for 5–5.5 h and forms methyl 1,3,11'-trioxo-1,3,10a',11'-tetrahydro-4b'*H*-spiro[indene-2,10'-indeno[1,2-*b*]chromen]-7'(8')-ylcarbamates (**4** and **5**) in 74–76% yield (Scheme 1).

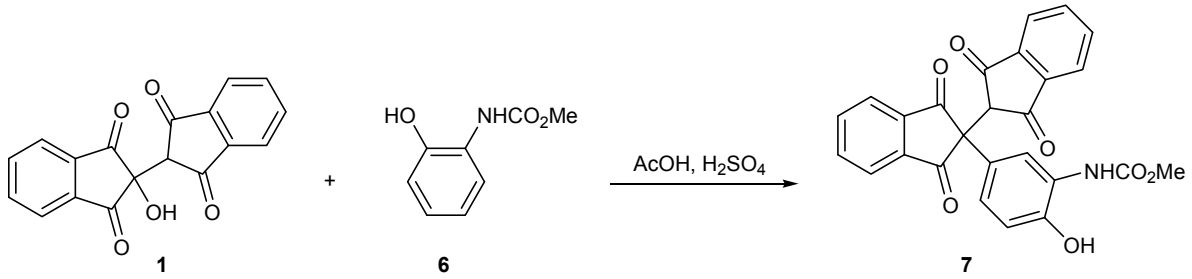
Scheme 1.



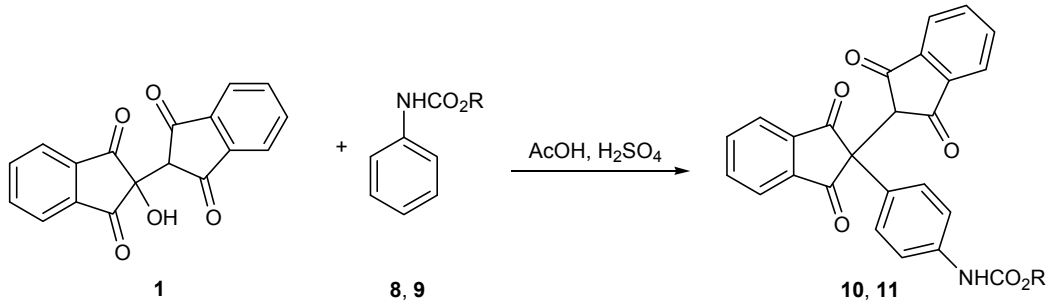
1 **2**, **3** **4**, **5**

3-$NHCO_2Me$ (**2**, **4**); 4-$NHCO_2Me$ (**3**, **5**)

Scheme 2.



Scheme 3.



R = Me (**8**, **10**); Et (**9**, **11**).

The structure of compounds **4** and **5** was confirmed by IR and ^{1}H and ^{13}C NMR spectroscopy.

The IR spectra of compounds **4** and **5** display an NH absorption band at 3330 cm^{-1} but show bands of the phenolic and alcoholic hydroxyls.

The ^{1}H NMR spectra of these products contain doublets of the protons on tertiary carbon atoms at 4.20 and 6.18 ppm (*J* 6.9 Hz).

The ^{13}C NMR spectrum of compound **4** shows a spiro carbon signal at 63.56 ppm, along with carbon signals of the benzene rings, carbonyl groups, and carbamate group.

At the same time, the reaction of compound **1** with methyl *N*-(2-hydroxyphenyl)carbamate (**6**) under the same conditions affords methyl 2-hydroxy-5-(1,1',3,3'-tetraoxo-2,2',3,3'-tetrahydro-1*H*,1'*H*-2,2'-biinden-2-yl)-phenylcarbamate (**7**) in 72% yield (Scheme 2).

The structure of compound **7** was confirmed by IR and ^{1}H NMR spectroscopy.

The IR spectrum of compound **7** shows, along with an NH stretching absorption band at 3340 cm^{-1}, a band at 3130 cm^{-1} assignable to stretching absorption of phenolic hydroxyl.

The ^{1}H NMR spectrum of compound **7** displays broadened singlets at 8.58 and 9.65 ppm, due to NH and OH protons, respectively.

Such reaction result is likely to be explained by the steric effect of the carbamate group located *ortho* to the phenolic hydroxyl, which prevents further heterocyclization of compound **7** to the corresponding chromene derivative.

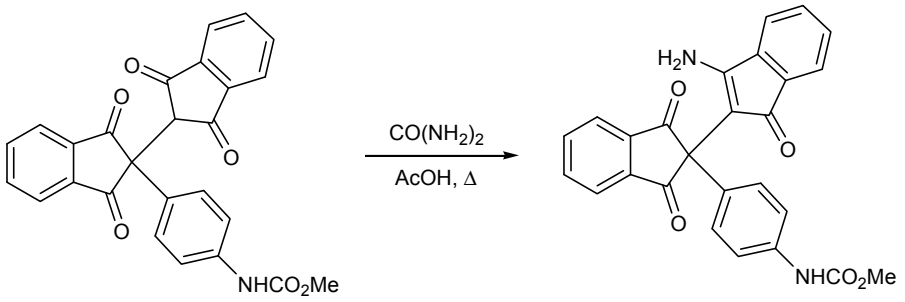
Aimed at preparing novel functionalized polycyclic compounds with a carbamate function, we explored the possibility of condensation of 2-hydroxy-2,2'-biindane-1,1',3,3'-tetrone (**1**) with methyl(ethyl) *N*-phenylcarbamates (**8** and **9**).

It was found that the reaction occurs regioselectively into the *para*-position to carbamate group to form methyl(ethyl) 4-(1,1',3,3'-tetraoxo-2,2',3,3'-tetrahydro-1*H*,1'*H*-2,2'-biinden-2-yl)phenylcarbamates (**10** and **11**) in 64–65% yield (Scheme 3).

Evidence for the fact that condensation involves the *para*-position of the benzene ring in aromatic carbamates **8** and **9** comes from the ^{1}H NMR spectrum, where this ring protons appear as two doublets at 7.48 and 7.53 ppm.

For further functionalization of methyl 4-(1,1',3,3'-tetraoxo-2,2',3,3'-tetrahydro-1*H*,1'*H*-2,2'-biinden-2-yl)-phenylcarbamate (**10**) we reacted it with urea in glacial acetic acid. It was found that the reaction is complete in 3 h and provides methyl 4-(3'-amino-1,1',3-trioxo-2,3-dihydro-1*H*,1'*H*-2,2'-biinden-2-yl)phenylcarbamate (**12**) in 60% yield (Scheme 4).

Scheme 4.

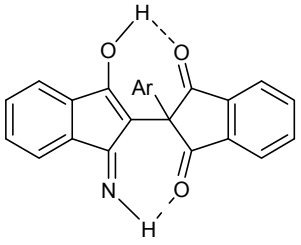


10 **12**

The structure of enamine **12** was confirmed by IR and ^{1}H and ^{13}C NMR spectroscopy.

In a DMSO solution, compound **12** is probably present in the iminoindenol form **12'** stabilized by two intramolecular hydrogen bonds [8] (Scheme 5).

Scheme 5.



12'

Ar = 4-$MeO_2CHNC_6H_4$

Actually, the ^{1}H NMR spectrum in DMSO-d_6 displays broadened signals of the OH and NH groups at 8.21 and 5.42 ppm, whereas the spectrum in $CDCl_3$ does not contain these signals and contains a broadened NH_2 proton signal at 5.10 ppm

The ^{13}C NMR spectrum of compound **12** shows, along with the carbon signals of the benzene ring, shows signals of the sp^3-carbon atoms of the methoxyl group (δ_C 52.7 ppm) and indane C^2 (δ_C 61.1 ppm), three carbonyl carbon signals (δ_C 154.6, 199.1, and 199.6 ppm), as well as a $C^{3'}$ signal (δ_C 159.4 ppm)

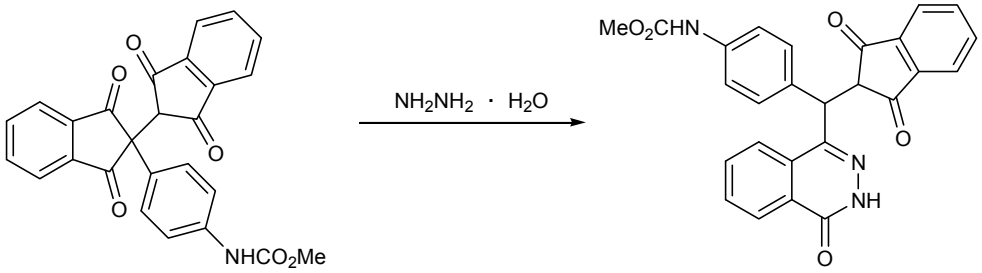
The reaction of methyl 4-(1,1',3,3'-tetraoxo-2,2',3,3'-tetrahydro-1*H*,1'*H*-2,2'-biinden-2-yl)phenylcarbamate **10** with 99% hydrazine hydrate at room temperature under stirring for 4 h gave phthalazine derivative **13** in 65% yield (Scheme 6).

The structure of methyl *N*-{4-[(1,3-dioxo-2,3-dihydro-1*H*-inden-2-yl)(4-oxo-3,4-dihydrophthalazin-1-yl)methyl]phenyl}carbamate (**13**) was confirmed by IR and ^{1}H NMR spectroscopy. The ^{1}H NMR spectrum of phthalazine **13** shows doublet signals at 4.34 and 5.02 ppm (*J* 3.8 Hz) due to the protons on the tertiary carbon atoms C^1 and C^2, respectively.

EXPERIMENTAL

The ^{1}H NMR spectra were obtained on a Bruker DRX 500 spectrometer (500.13 MHz) in $CDCl_3$ and DMSO-d_6, internal standard TMS. The ^{13}C NMR spectra were recorded on a Bruker DRX 500 spectrometer (126 MHz) in $CDCl_3$ in the complete proton decoupling mode. The IR spectra were

Scheme 6.



10 **13**

measured on an InfraLUM FT-02 FTIR spectrometer in the range 4000–400 cm^{-1} in KBr. The purity of the synthesized compounds was controlled by TLC on Silufol UV-254 plates, development in iodone vapor.

Methyl 1,3,11'-trioxo-1,3,10a',11'-tetrahydro-4b'*H*-spiro[indene-2,10'-indeno[1,2-*b*]chromen]-7'-ylcarbamate (4). A mixture of 0.43 g (1.4 mmol) of 2-hydroxy-2,2'-biindan-1,1'-3,3'-tetrone **1** and 8 mL of glacial acetic acid was heated until a transparent solution formed, after which 0.7 g (4.2 mmol) of methyl *N*-(3-hydroxyphenyl)carbamate **2** was added with stirring. After cooling, 0.5 mL of conc. H_2SO_4 was added dropwise, and the mixture was stirred for 5 h. The crystals that formed were filtered off, washed on the filter with 5 mL of glacial acetic acid and then with water (15 mL), dried in air, and recrystallized from ethyl acetate. Yield 0.46 g (74%), golden yellow crystals, mp 335–338°C. IR spectrum, ν, cm^{-1}: 3330 (NH), 1680, 1710 (C=O), 1610, 1575 (C–C_{arom}). ^1H NMR spectrum, δ, ppm: 3.71 s (3H, $NHCO_2\underline{Me}$), 4.20 d (1H_{tert}, *J* 6.9 Hz), 6.18 d (1H_{tert}, *J* 6.9 Hz), 7.02 d (1H_{arom}, *J* 7.8 Hz), 7.31 d (1H_{arom}, *J* 7.8 Hz), 7.65–7.74 m (3H_{arom}), 7.97–8.02 m (3H_{arom}), 8.11 t (1H_{arom}, *J* 7.5 Hz), 8.21 d (2H_{arom}, *J* 7.4 Hz), 8.58 br.s (1H, NH). ^{13}C NMR spectrum, δ, ppm: 48.72 (C_{tert}), 56.71 ($NHCO_2\underline{Me}$), 63.56 (spiro carbon), 77.38 (C_{tert}), 112.42, 114.01, 119.20, 123.30, 126.15, 127.84, 129.23, 130.54, 134.16, 134.90, 135.85, 136.22, 143.18, 144.15, 145.27 (C_{arom}), 155.18 ($NH\underline{C}O_2Me$), 196.73, 197.23, 198.23 (C=O). Found, %: C 70.93; H 3.71; N 3.47. $C_{26}H_{17}NO_6$. Calculated, %: C 71.07; H 3.87; N 3.19.

Methyl 1,3,11'-trioxo-1,3,10a',11'-tetrahydro-4b'*H*-spiro[indene-2,10'-indeno[1,2-*b*]chromen]-8'-ylcarbamate (5) was prepared as described above from 0.43 g (1.4 mmol) of 2-hydroxy-2,2'-biindane-1,1',3,3'-tetrone **1** and 0.7 g (4.2 mmol) of methyl *N*-(4-hydroxyphenyl)carbamate **3**, reaction time 5.5 h. Yield 0.47 g (76%), yellow crystals, mp 203–205°C. IR spectrum, ν, cm^{-1}: 3330 (NH), 1680, 1710 (C=O), 1610, 1575 (C–C_{arom}). ^1H NMR spectrum, δ, ppm: 3.71 s (3H, $NHCO_2\underline{Me}$), 4.20 d (1H_{tert}, *J* 6.9 Hz), 6.18 d (1H_{tert}, *J* 6.9 Hz), 7.56 s (1H_{arom}), 7.66-7.72 m (3H_{arom}), 7.95-8.00 m (4H_{arom}), 8.08 d (1H_{arom}, *J* 7.5 Hz), 8.19 d (2H_{arom}, *J* 7.4 Hz), 8.59 br.s (1H, NH). Found, %: C 70.86; H 4.01; N 3.46. $C_{26}H_{17}NO_6$. Calculated, %: C 71.07; H 3.87; N 3.19.

2-Hydroxy-5-(1,1',3,3'-tetraoxo-2,2',3,3'-tetrahydro-1*H*,1'*H*-2,2'-biinden-2-yl)phenylcarbamate (7) was prepared as described above from 0.43 g (1.4 mmol) of 2-hydroxy-2,2'-biindane-1,1'-3,3'-tetrone **1** and 0.7 g (4.2 mmol) of methyl *N*-(2-hydroxyphenyl)carbamate **6**. Yield 0.46 g (72%), mp 143–144°C, light yellow crystals. IR spectrum, ν, cm^{-1}: 3340, 3130 (NH, OH), 1710, 1685 (C=O), 1612, 1590, 1575 (C–C_{arom}). ^1H NMR spectrum, δ, ppm: 3.71 s (3H, $NHCO_2\underline{Me}$), 4.57 s (1H_{tert}), 7.12 d (1H_{arom}, *J* 8.6 Hz), 7.34 d (1H_{arom}, *J* 8.6 Hz), 7.58 s (1H_{arom}), 7.67–7.71 m (4H_{arom}), 8.08–8.13 m (2H_{arom}, *J* 7.4 Hz), 8.34 d (2H_{arom}, *J* 7.4 Hz), 8.58 br.s (1H, NH), 9.65 br.s (1H, OH). Found, %: C 68.21; H 3.67; N 2.94. $C_{26}H_{17}NO_7$. Calculated, %: C 68.57; H 3.74; N 3.08.

Methyl 4-(1,1',3,3'-tetraoxo-2,2',3,3'-tetrahydro-1*H*,1'*H*-2,2'-biinden-2-yl)phenylcarbamate (10) was prepared as described above from 0.43 g (1.4 mmol) of 2-hydroxy-2,2'-biindane-1,1'-3,3'-tetrone **1** and 0.63 g (4.2 mmol) of methyl *N*-phenylcarbamate **8**. After 5 h stirring at room temperature, the mixture was poured onto ice, and the solid product that formed was filtered off, washed with water, dried in air, and recrystallized from chloroform–petroleum ether (1 : 3). Yield 0.40 g (65%), colorless crystals, mp 243–244°C. IR spectrum, ν, cm^{-1}: 3340 (NH), 1714, 1685 (C=O), 1615, 1585, 1574 (C–C_{arom}). ^1H NMR spectrum, δ, ppm: 3.71 s (3H, $NHCO_2\underline{Me}$), 4.58 s (1H_{tert}), 7.48 d (2H_{arom}, *J* 8.4 Hz), 7.53 d (2H_{arom}, *J* 8.4 Hz), 7.62–7.71 m (4H_{arom}), 8.09 t (2H_{arom}, *J* 7.4 Hz), 8.32 d (2H_{arom}, *J* 7.4 Hz), 8.56 br.s (1H, NH). Found, %: C 71.37; H 3.74; N 3.02. $C_{26}H_{17}NO_6$. Calculated, %: C 71.07; H 3.87; N 3.19.

Ethyl 4-(1,1',3,3'-tetraoxo-2,2',3,3'-tetrahydro-1*H*,1'*H*-2,2'-biinden-2-yl)phenylcarbamate (11) was prepared as described above in a yield of 0.41 g (64%), colorless crystals, mp 284–285°C. IR spectrum, ν, cm^{-1}: 3340 (NH), 1714, 1685 (C=O), 1613, 1585, 1573 (C–C_{arom}). ^1H NMR spectrum, δ, ppm: 1.23 t (3H, $NHCO_2CH_2C\underline{H}_3$, *J* 6.7 Hz), 4.12 q (2H, $NHCO_2C\underline{H}_2CH_3$, *J* 6.7 Hz), 4.59 s (1$H_{tert}$), 7.48 d (2$H_{arom}$, *J* 8.5 Hz), 7.53 d (2$H_{arom}$, *J* 8.5 Hz), 7.63–7.72 m (4H_{arom}), 8.09 t (2H_{arom}, *J* 7.2 Hz), 8.32 d (2H_{arom}, *J* 7.2 Hz), 8.58 br.s (1H, NH). Found, %: C 71.64; H 4.34; N 2.98. $C_{27}H_{19}NO_6$. Calculated, %: C 71.52; H 4.19; N 3.09.

Methyl 4-(3'-amino-1,1',3-trioxo-2,3-dihydro-1*H*,1'*H*-2,2'-biinden-2-yl)phenylcarbamate (12). A mixture of 0.31 g (0.706 mmol) of methyl 4-(1,1',3,3'-tetraoxo-2,2',3,3'-tetrahydro-1*H*,1'*H*-2,2'-biinden-2-yl)-phenylcarbamate **10** and 1 g (8.4 mmol) of urea in 5 mL of glacial acetic acid was heated under reflux for

3 h, cooled, poured into 30 mL of ice water, the precipitate was filtered off, thoroughly washed with water on the filter, dried in air, and recrystallized from acetone. Yield 0.19 g (60%), orange crystals, mp 172–173°C. IR spectrum, ν, cm^{-1}: 3450, 3330, 3315, 3219, 1710, 1702, 1615, 1585, 1575. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.70 s (3H, $NHCO_2\underline{Me}$), 5.10 br.s (2H, NH_2), 7.32 d (2H_{arom}, *J* 8.4 Hz), 7.48 d (2H_{arom}, *J* 8.4 Hz), 7.58 t (1H_{arom}, *J* 7.6 Hz), 7.85 t (1H_{arom}, *J* 7.6 Hz), 8.00–8.05 m (3H_{arom}), 8.20 d (2H_{arom}, *J* 7.4 Hz), 8.26 d (1H_{arom}, *J* 7.6 Hz), 8.56 br.s (1H, NH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 52.7 ($NHCO_2\underline{Me}$), 61.1 (C_{indane}), 111.4, 117.2, 123.2, 119.5, 123.0, 123.5, 124.2, 128.1, 132.1, 134.4, 136.2, 142.3 (C_{arom}), 154.6 ($NH\underline{C}O_2Me$), 159.4 ($C^{3'}$), 199.1, 199.6 (C=O). Found, %: C 70.96; H 4.24; N 6.18. $C_{26}H_{18}N_2O_5$. Calculated, %: C 71.23; H 4.11; N 6.39.

Methyl *N*-{4-[(1,3-dioxo-2,3-dihydro-1*H*-inden-2-yl)(4-oxo-3,4-dihydrophthalazin-1-yl)methyl]-phenyl}carbamate 13. A mixture of 0.615 g of methyl 4-(1,1',3,3'-tetraoxo-2,2',3,3'-tetrahydro-1*H*,1'*H*-2,2'-biinden-2-yl)phenylcarbamate **10** and 10 mL of 99% hydrazine hydrate was stirred at room temperature for 4 h, acidified with 6 M HCl to pH 6, the solid product was filtered off, thoroughly washed with water, dried in air, and recrystallized from acetone. Yield 0.47 g (74%), colorless crystals, mp 193–194°C. IR spectrum, ν, cm^{-1}: 3320, 3059 (NH), 1710, 1700, 1658 (C=O), 1610, 1585, 1565 (C–C_{arom}). ^1H NMR spectrum, δ, ppm: 3.70 s (3H, $NHCO_2\underline{Me}$), 4.34 d (1H_{tert}, $CH(CO)_2$, *J* 3.8 Hz), 5.02 d (1H_{tert}, CH, *J* 3.8 Hz), 7.31 d (2H_{arom}, *J* 8.4 Hz), 7.39–7.48 m (4H_{arom}), 7.56 d (1H_{arom}, *J* 8.4 Hz), 7.66–7.71 m (4H_{arom}), 8.64 d (1H_{arom}, *J* 7.9 Hz), 8.56 br.s (1H, $N\underline{H}CO_2Me$), 9.70 s (1H, NH). Found, %: C 68.65; H 4.34; N 9.14. $C_{26}H_{19}N_3O_5$. Calculated, %: C 68.87; H 4.19; N 9.27.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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