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CONDENSATION OF 1-SUBSTITUTED 1,2,3,9a-TETRAHYDRO-9H-IMIDAZO[1,2-*a*]-INDOL-2-ONE DERIVATIVES WITH AROMATIC ALDEHYDES

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Condensation of 1-alkyl-, 1-allyl-, and 1-benzyl-1,2,3,9a-tetrahydro-9H-imidazo[1,2-a]indol-2-ones with benzaldehydes in acetic acid and subsequent treatment of the reaction mixture with potassium hydroxide afforded 1-substituted 9a-(2-phenylethenyl)-1,2,3,9a-tetrahydro-9H-imidazo[1,2-a]indol-2-one derivatives. 1-Methyl- and 1-ethyl-9a-[2-(4-dimethylaminophenyl)ethenyl]-1,2,3,9a-tetrahydro-9H-imidazo[1,2-a]indol-2-ones were synthesized by alkylation of 9a-[2-(4-dimethylaminophenyl)ethenyl]-1,2,3,9a-tetrahydro-9H-imidazo[1,2-a]indol-2-one with methyl- and ethyl iodides in DMF in the presence of a strong base.

Keywords: 9a-(2-phenylethenyl)-1,2,3,9a-tetrahydro-9H-imidazo[1,2-*a*]indol-2-one, 1,2,3,9a-tetrahydro-9H-imidazo[1,2-*a*]indol-2-one, alkylation, condensation.

Derivatives of 2-styrylindoline possessing annelated heterocycles at the *a*-edge have important applications as organic dyes for synthetic fiber [1-5] and color formers in information registration processes [6-13].

We have previously investigated the synthesis of 9a-(2-phenylethenyl)-1,2,3,9a-tetrahydro-9H-imidazo- and 10a-(2-phenylethenyl)-1,2,3,4,10,10a-hexahydropyrimido[1,2-*a*]indol-2-one derivatives by condensation of 1-carba-moylmethyl-2,3,3-trimethyl-3H-indolium chlorides and, correspondingly, 10,10,10a-trimethyl-1,2,3,4,10,10a-hexahydropyrimido[1,2-*a*]indol-2-one deri-vatives with various benzaldehydes [14-18].

Continuing our work on the synthesis of new color formers for information processing, in the present paper we report the synthesis of 1-substituted 9a-(2-phenylethenyl)-1,2,3,9a-tetrahydro-9H-imidazo[1,2-*a*]indol-2-one derivatives.

The starting 1-substituted imidazo[1,2-*a*]indol-2-one derivatives **1a-f** were prepared by methods described in [19, 20]. Reactions of **1a-f** with substituted benzaldehydes were carried out in acetic acid. Treatment of the reaction mixtures containing condensation products **2a-l** with potassium hydroxide gave 1-alkyl-, 1-allyl-, and 1-benzyl-9a-(2-phenylethenyl)-1,2,3,9a-tetrahydro-9H-imidazo[1,2-*a*]indol-2-ones **3a-l** (Table 1).

The ^{1}H NMR spectra (Table 2) of compounds **3a-l** are characterized by the presence of singlets of two diastereotopic methyl groups in the area of 1.08-1.49 and a singlet or AB-quadruplet of NCH_2CO moiety protons in the area of 3.05-4.04 ppm. The protons of methylene group of the substituents at the nitrogen atom of **3b-l** are also diastereotopic due to the presence of the chiral center at C-9a in the molecule. Therefore, the

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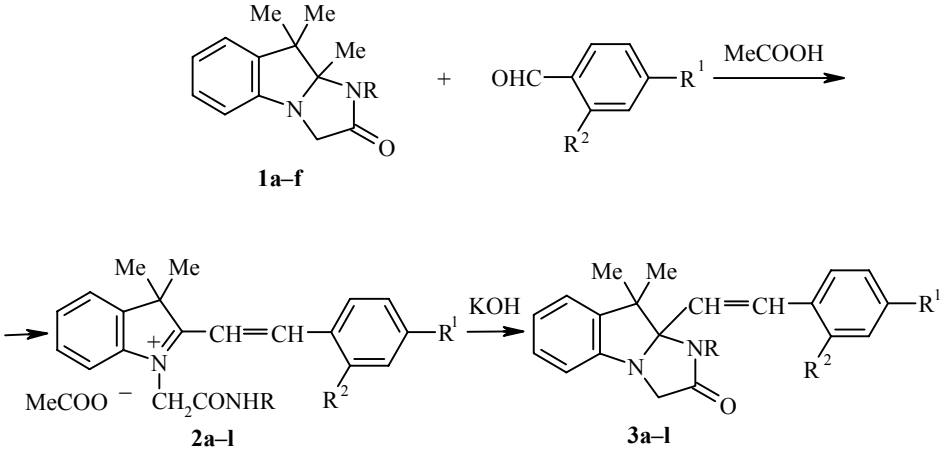
methylene protons of the benzyl group of compounds **3f-l** give an AB-quadruplet (J = 15.5-16.0 Hz) in the area of 4.25-4.87 ppm. The signal of one of the ethene protons is present as a doublet of AB-system in the area of 6.04-6.70 ppm. The spin-spin coupling constant of the vicinal ethene protons is 15.0-16.4 Hz and attests to their *trans*-orientation. The IR spectra of compounds **3a-l** have an absorption band of the lactam C=O group at 1695-1700 cm^{-1}.



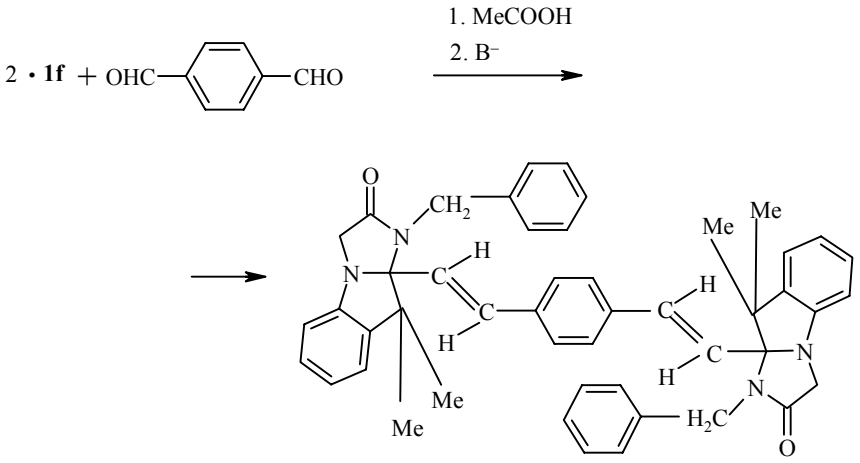
1-3 a R = Me; **b** R = Et; **c** R = *n*-Pr, **d** R = *n*-C_4H_9; **e** R = $CH_2CH{=}CH_2$; **1f**, **2 f-l** R = CH_2Ph; **2**, **3 a-f** R^1 = NMe_2, **g** R^1 = F, **h**, **j** R^1 = Cl, **i** R^1 = H, **k** R^1 = Br, **l** R^1 = OMe; **a-h**, **k**, **l** R^2 = H; **i**, **j** R^2 = Cl

TABLE 1. 1-R-9,9-Dimethyl-9a-(2-phenylethenyl)-1,2,3,9a-tetrahydro-9H-imidazo[1,2-*a*]indol-2-ones (**3a-l**)

Compound	Empirical formula	Found, % / Calculated, %			mp, °C*	Yield, %
		C	H	N		
3a	$C_{23}H_{27}N_3O$	77.02 / 76.76	7.71 / 7.78	11.69 / 11.62	58-59	65
3b	$C_{24}H_{29}N_3O$	—	—	11.47 / 11.19	72-74	44
3c	$C_{25}H_{31}N_3O$	—	—	10.76 / 10.79	67-69	52
3d	$C_{26}H_{33}N_3O$	—	—	10.13 / 10.41	60-61	43
3e	$C_{25}H_{29}N_3O$	—	—	10.98 / 10.84	99-100	61
3f	$C_{29}H_{31}N_3O$	—	—	9.50 / 9.60	101-102	47
3g	$C_{27}H_{25}FN_2O$	78.80 / 78.62	6.41 / 6.11	—	137-138	20
3h	$C_{27}H_{25}ClN_2O$	75.92 / 75.60	5.89 / 5.87	6.39 / 6.53	131-132	18
3i	$C_{27}H_{25}ClN_2O$	76.21 / 75.60	6.21 / 5.87	6.24 / 6.53	141-142	12
3j	$C_{27}H_{24}Cl_2N_2O$	69.89 / 69.98	4.82 / 5.22	5.72 / 6.04	174-175	15
3k	$C_{27}H_{25}BrN_2O$	68.38 / 68.91	5.62 / 5.32	5.97 / 5.92	132-133	38
3l	$C_{28}H_{28}N_2O_2$	79.59 / 79.22	6.25 / 6.65	6.59 / 6.60	103-104	42

* **3a-f** from cyclohexane–hexane, **3g-l** from acetone.

When 1-benzylimidazo[1,2-*a*]indol-2-one **1f** reacted with terephthaldehyde, both *para*-situated formyl groups underwent condensation with the active methyl group. Therefore, treatment of the reaction mixture with a strong base afforded 1,4-di(1-benzylimidazo[1,2-*a*]indol-9a-yl)benzene **4.**



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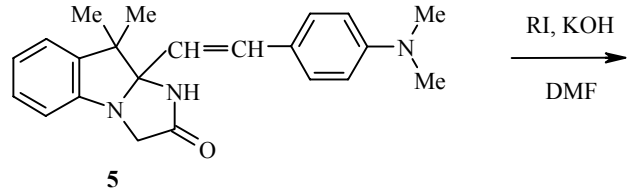
It is known that N-alkylation of the amide moiety can be easily achieved when the reaction with haloalkanes is performed in polar aprotic solvents in the presence of a strong base [21]. In order to obtain 1-substituted derivative compound **5** [22] was alkylated with methyl iodide in DMF containing powdered KOH. The reaction predominantly afforded 9a-[2-(4-dimethylaminophenyl)ethenyl]-1-methyl-1,2,3,9a-tetrahydro-9H-imidazo[1,2-*a*]indol-2-one **3a**, and only traces of O-alkylated product **6a** could be found in the reaction mixture.



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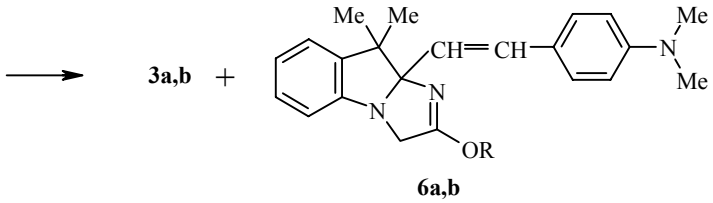

6a,b

6a R = Me, **b** R = Et

However, when compound **5** was treated with ethyl iodide under similar conditions, the regioselectivity of the reaction was lower and the ratio of formed N- and O-alkylated products **3b** and **6b** was 7:3. In the ^{1}H NMR spectrum of **6b** the signal of methylene protons of the OCH_2CH_3 group is shifted about 0.8 ppm towards lower fields in comparison with methylene protons of the ethyl group at the nitrogen atom of **3b**.

TABLE 2. ^{1}H NMR Spectra of 9,9-Dimethyl-9a-(2-phenylethenyl)-1,2,3,9a-tetrahydro-9H-imidazo[1,2-*a*]indol-2-ones (**3a-l**)

Com-pound	Solvent	Chemical shifts, ppm
3a	Acetone-d_6	1.20 (3H, s, 9-CH_3); 1.44 (3H, s, 9-CH_3); 2.88 (6H, s, N,N-CH_3); 2.94 (3H, s, 1-CH_3); 3.78 (2H, s, NCH_2CO); 6.33-7.40 (10H, m, CH=CH, ArH)
3b	$CDCl_3$	1.23 (3H, t, *J* = 7.0 Hz, $CH_2\underline{CH_3}$); 1.29 (6H, s, 9,9-CH_3); 2.89 (6H, s, N,N–CH_3); 3.05-3.68 (2H, q, *J* = 7.0 Hz, $\underline{CH_2}CH_3$); 3.56-4.00 (2H, AB-q, *J* = 15.0 Hz, NCH_2CO); 6.04-7.43 (10H, m, CH=CH, ArH)
3c	Acetone-d_6	0.94 (3H, t, *J* = 7.0 Hz, $CH_2\underline{CH_3}$); 1.35 (3H, s, 9-CH_3); 1.38 (3H, s, 9-CH_3); 1.43-1.88 (4H, m, $\underline{CH_2}CH_3$); 2.93 (6H, s, N,N-CH_3); 3.05-3.55 (2H, m, $N\underline{CH_2}CH_2$); 3.82 (2H, s, NCH_2CO); 6.35-7.40 (10H, m, CH=CH, ArH)
3d	Acetone-d_6	0.89 (3H, t, *J* = 7.0 Hz, $CH_2\underline{CH_3}$); 1.35 (3H, s, 9-CH_3); 1.39 (3H, s, 9-CH_3); 1.40-1.95 (2H, m, $\underline{CH_2}CH_2CH_3$); 2.94 (6H, s, N,N-CH_3); 3.08-3.56 (2H, m, $N\underline{CH_2}CH_2$); 3.84 (2H, s, NCH_2CO); 6.38-7.48 (10H, m, CH=CH, ArH)
3e	Acetone-d_6	1.34 (3H, s, 9-CH_3); 1.43 (3H, s, 9-CH_3); 3.01 (6H, s, N,N-CH_3); 3.93 (2H, s, NCH_2CO); 4.00-6.23 (5H, m, $CH_2CH{=}CH_2$); 6.39-7.48 (10H, m, CH=CH, ArH)
3f	Acetone-d_6	1.34 (3H, s, 9-CH_3); 1.49 (3H, s, 9-CH_3); 2.98 (6H, s, N,N-CH_3); 4.04 (2H, s, NCH_2CO); 4.58-4.85 (2H, AB-q, *J* = 15.5 Hz, $\underline{CH_2}$Ar); 6.33-7.40 (10H, m, CH=CH, ArH)
3g	DMSO-d_6	1.22 (3H, s, 9-CH_3); 1.30 (3H, s, 9-CH_3); 3.87-4.01 (2H, AB-q, *J* = 16.0 Hz, NCH_2CO); 4.48-4.80 (2H, AB-q, *J* = 16.0 Hz, $N\underline{CH_2}$Ph); 6.50-7.37 (15H, CH=CH, ArH)
3h	DMSO-d_6	1.21 (3H, s, 9-CH_3); 1.30 (3H, s, 9-CH_3); 3.88-4.00 (2H, AB-q, *J* = 16.0 Hz, NCH_2CO); 4.50-4.87 (2H, AB-q, *J* = 16.0 Hz, $N\underline{CH_2}$Ph); 6.55-7.38 (15H, CH=CH, ArH)
3i	DMSO-d_6	1.22 (3H, s, 9-CH_3); 1.32 (3H, s, 9-CH_3); 3.87-4.04 (2H, AB-q, *J* = 16.0 Hz, NCH_2CO); 4.52-4.82 (2H, AB-q, *J* = 16.0 Hz, $N\underline{CH_2}$Ph); 6.58-7.42 (15H, CH=CH, ArH).
3j	DMSO-d_6	1.44 (3H, s, 9-CH_3); 1.49 (3H, s, 9-CH_3); 3.72-3.89 (2H, AB-q, *J* = 16.0 Hz, NCH_2CO); 4.30-4.44 (2H, m, $N\underline{CH_2}$Ph); 6.90-7.87 (14H, CH=CH, ArH)
3k	DMSO-d_6	1.22 (3H, s, 9-CH_3); 1.30 (3H, s, 9-CH_3); 3.87-4.00 (2H, AB-q, *J* = 16.0 Hz, NCH_2CO); 4.48-4.82 (2H, AB-q, *J* = 16.0 Hz, $N\underline{CH_2}$Ph); 6.57-7.48 (15H, CH=CH, ArH)
3l	$CDCl_3$	1.08 (6H, s, 9,9-CH_3); 3.55 (3H, s, OCH_3); 3.88 (2H, s, NCH_2CO); 4.25-4.84 (2H, AB-q, *J* = 16.0 Hz, $N\underline{CH_2}$Ph); 5.87-7.32 (15H, m, CH=CH, ArH)

EXPERIMENTAL

^{1}H NMR spectra were determined on a Tesla BS-487C (80 MHz), and a Bruker DPX (200 MHz) instruments, internal reference TMS. IR spectra were recorded on an IR-75 spectrometer (KBr pellets). The course of the reactions was observed using TLC on Silufol plates, eluent acetone–hexane, 1:2.

Yields of compounds **3a-l** are given in Table 1, ^{1}H NMR spectral data are presented in Table 2.

1-R-9a-[2-(4-Dimethylaminophenyl)ethenyl]-1,2,3,9a-tetrahydro-9H-imidazo[1,2-*a*]indol-2-ones (3a-f) (General Procedure). A solution of compound **1a-f** (5 mmol) and 4-dimethylaminobenzaldehyde (0.75 g, 5 mmol) in acetic acid (8 ml) was heated at 100°C for 2 h. The reaction mixture was poured into water

(100 ml), treated with 10% potassium hydroxide until alkaline reaction, and the substance separated was extracted with ether (2 × 20 ml). The extract was washed with water (2 × 20 ml), dried with sodium sulfate, and the solution passed through a column with aluminum oxide (100 × 30 mm). The solvent was then evaporated and the residue recrystallized from a mixture of hexane with cyclohexane and dried in vacuum.

1-Benzyl-9a-(2-phenylethenyl)-1,2,3,9a-tetrahydro-9H-imidazo[1,2-*a*]indol-2-ones (3g-l) (General Procedure). A mixture of 1-benzylimidazo[1,2-*a*]indol-2-one **1f** (1.53 g, 5 mmol) and an aromatic aldehyde (5 mmol) in acetic acid (10 ml) was heated at 100°C for 4 h, after which the mixture was poured into water (150 ml), treated with 5% potassium hydroxide until alkaline reaction, and extracted with 20 ml of ether. After 18 h, the precipitated substance was removed by filtration, dried, and recrystallized from acetone.

1,4-Di[2-(1-benzyl-9,9-dimethyl-2-oxo-1,2,3,9a-tetrahydro-9H-imidazo[1,2-*a*]indol-9a-yl)ethenyl]-benzene (4). A mixture of chloride **1f** (3.06 g, 10 mmol) and terephthaldicarboxaldehyde (0.67 g, 5 mmol) in acetic acid (10 ml) was heated at 100°C for 3.5 h; then the mixture was poured into water (150 ml), treated with 5% potassium hydroxide until alkaline reaction, and extracted with 20 ml of ether. The mixture was made to stand at 5°C for 18 h, the precipitated substance was filtered off, dried, and recrystallized from ethanol to give 1.63 g (44%) of a product with mp 195-196°C. IR spectrum: 1700 cm^{-1} (C=O). ^{1}H NMR spectrum (DMSO-d_6): 1.24 (6H, s, 2 × CH_3); 1.30 (6H, s, 2 × CH_3); 3.95 (4H, s, 2 × NCH_2CO); 4.50-4.88 (4H, AB-q, J = 16.0 Hz, 2 × N$\underline{CH_2}$Ph); 6.51-7.35 (26H, 2 × CH=CH, ArH). Found, %: C 80.77; H 6.70; N 7.86. $C_{20}H_{24}N_2O$. Calculated, %: C 81.09; H 6.52; N 7.88.

Alkylation of 9a-[2-(4-Dimethylaminophenyl)ethenyl]-1,2,3,9a-tetrahydro-9H-imidazo[1,2-*a*]-indol-2-one (5) with Methyl Iodide. To a solution of compound **5** (1.74 g, 5 mmol) in DMF (20 ml) was added powdered potassium hydroxide (1.12 g, 20 mmol), and methyl iodide (2.13 g, 0.93 ml, 15 mmol) was added dropwise. The mixture was stirred for 2 h at 20°C, poured into water (150 ml), and extracted with ether (3 × 15 ml). The extract was washed with water (2 × 15 ml), dried with sodium sulfate, the solvent removed, and the residue crystallized from a mixture of hexane with cyclohexane. Yield of **3a** 1.30 g (72%). This sample gave identical IR and ^{1}H NMR data and mp to one prepared by condensation of compound **1a** with 4-dimethylaminobenzaldehyde, as described above.

Alkylation of 5 with Ethyl Iodide. To a solution of compound **5** (3.47 g, 10 mmol) in DMF (35 ml) was added powdered potassium hydroxide (2.24 g, 40 mmol), and ethyl iodide (4.64 g, 2.42 ml, 30 mmol) was added dropwise. The mixture was stirred for 2 h at 20°C, poured into 250 ml of water, and extracted with ether (3 × 20 ml). The extract was washed with water (2 × 20 ml) and dried with sodium sulfate.The solvent was removed and the residual material subjected to flash chromatography on a column (500 × 25 mm) with Al_2O_3 (eluent acetone–hexane, 3:5). From the first fraction, with R_f 0.79, after the solvent had been driven off, **9,9-dimethyl-2-ethoxy-9a-[2-(4-dimethylaminophenyl)ethenyl]-9,9a-dihydro-3H-imidazo[1,2-*a*]indole (6b)** was obtained. Yield 0.68 g (18%); mp 61-62°C (hexane–cyclohexane). IR spectrum: 1650 cm^{-1} (C=N). ^{1}H NMR spectrum ($CDCl_3$): 1.15 (3H, s, 9-CH_3); 1.21 (3H, t, J = 7.0 Hz, $CH_2\underline{CH_3}$); 1.47 (3H, s, 9-CH_3); 2.90 (6H, s, N,N-CH_3); 3.85 (2H, s, NCH_2CO); 4.15 (2H, q, J = 7.0 Hz, $\underline{CH_2}CH_3$); 6.05-7.38 ppm (10H, m, CH=CH, ArH). Found, %: N 11.40. $C_{24}H_{29}N_3O$. Calculated, %: N 11.19.

The second fraction, with R_f 0.45, after the solvent was evaporated, afforded 1.60 g (43 %) of compound **3b** with mp identical to the sample synthesized from **1b** and 4-dimethylaminobenzaldehyde as described above.

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