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RECYCLIZATION OF 2-IMINO-2H-1-BENZOPYRANS USING NUCLEOPHILIC REAGENTS
3.* REACTION OF 2-IMINOCOUMARIN-3-CARBOXAMIDES WITH o-PHENYLENEDIAMINES AND o-AMINO(THIO)PHENOLS

S. N. Kovalenko, M. V. Vasil'ev, I. V. Sorokina, V. P. Chernykh, A. V. Turov, and S. A. Rudnev

Using o-phenylenediamines, o-aminophenol or o-aminothiophenol, 2-iminocoumarin-3-carboxamide can be recyclized to the corresponding 3-(1H-benzimidazol-2-yl), 3-(benzoxazol-2-yl), or 3-(benzothiazol-2-yl) coumarins. An alternative synthesis has been carried out and an analytical comparison of the synthetic routes made.

In previous publications we have described recyclization processes for 2-iminocoumarin-3-carboxamides which can give N-benzoylamidrazones of coumarin-3-carboxylic acids, 3-(1,3,4-oxadi-, thiadi-, and triazol-2-yl)coumarins [1], and 3-(1,1-dioxo-2H-benzo-1,2,4-thiadiazin-3-yl)coumarins [2]. Continuing this investigation we have studied the reaction of 2-iminocoumarin-3-carboxamides with o-phenylenediamines, o-aminophenol, and o-aminothiophenol.

It was found that refluxing 2-iminocoumarins with o-phenylenediamines, o-aminophenol, or o-aminothiophenol in butan-1-ol gives, respectively, 3-(1H-benzimidazol-2-yl), 3-(benzoxazol-2-yl), or 3-(benzothiazol-2-yl)coumarins IIIa-j (see Scheme 1).

We had previously shown that reaction of 2-iminocoumarins with primary amines gave high yields of 2-N-R-substituted iminocoumarins [3]. In the present case it might be expected that 2-(N-[o-amino(hydroxy, mercapto)phenyl]imino)coumarins A would be formed. However, as shown by spectroscopic investigation (Tables 1 and 2), this reaction does not stop at the stage of formation of the 2-N-R-iminocoumarins (A) but goes further via a recyclization step to give the 3-heterylcoumarins IIIa-j. In the PMR spectra of the products IIIa-j (Table 2) the signals of the non equivalent NH_2 protons of the carbamide group at 8.20-8.40 and 7.45-7.65 ppm have disappeared and, in the case of the benzimidazole derivatives IIIa-e, a singlet for the NH proton appears at 12.31-12.60 ppm appears. A singlet signal for the proton at position 4 of the coumarin is seen at 9.00-9.70 ppm. The IR spectra of these compounds (Table 1) show an intense lactone C=O stretching band at 1726-1674 cm^{-1}. Compounds IIIa-e show a broad NH band at 3354-3262 cm^{-1}. In addition, 3-(1H-benzimidazol-2-yl), 3-(benzoxazol-2-yl), and 3-(benozthiazol-2-yl) coumarins IIIa-j have UV spectra which are typical of 3-heterylcoumarins [1] and have marked fluorescence properties.

The reaction course indicated can be explained via formation in the first stage of the 2-N-R-iminocoumarin A (which is subsequently recyclized through attack of a second nucleophilic center (OH, NH_2, SH) at the carbon atom of the C=N bond) followed by opening of the "iminolactone" ring and then closing of the coumarin ring.

During the reaction of 2-iminocoumarin-3-carboxamide with o-phenylenediamine there is also formed in 5-10% yield 2-(2-hydroxyphenyl)benzimidazole which was isolated from the basic recyclization product via chromatography of the reaction medium and was identified by a mass spectrometric method. The formation of the same product was also noted when fusing the unsubstituted coumarin with o-phenylenediamine [4].

*For Communication 2 see [2].

Ukraine Pharmaceutical Academy, Khar'kov 310002. E-mail: kosn@ukrfa.kharkov.ua. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 12, pp. 1664-1667, December, 1998. Original article submitted December 7, 1997.

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TABLE 1. Parameters for Coumarins IIIa-j and 2-Iminocoumarins VIa,b

Compound	Empirical formula	Found, % / Calculated, %		IR spectrum (KBr), cm^{-1}	UV spectrum (ethanol), λ_{max}, nm (ε, $mol \cdot cm^{-1} \cdot l^{-1}$)	Mp, °C	Yield, % (method)
		N	S				
IIIa	$C_{16}H_{10}N_2O_2$	10,66 10,68	—	3327 (NH) 1710 (C=O) 1608 (C=C	210 (47600) 240 (12300) 275 (18500) 284 (6300) 365 (20900)	338...339	75(A) 71(B)
IIIb	$C_{17}H_{12}N_2O_3$	9,55 9,58	—	3336 (NH) 1701 (C=O) 1574 (C=C)	219 (41900) 273 (7700) 287 (5700) 389 (2080)	203...204	81(A) 69(B)
IIIc	$C_{16}H_9BrN_2O_2$	8,19 8,21	—	3354 (NH) 1706 (C=O) 1598 (C=C)	217 (41900) 273 (8030) 373 (22500)	276...277	69
IIId	$C_{17}H_{11}ClN_2O_3$	8,36 8,37	—	3334 (NH) 1699 (C=O) 1570 (C=C)	210 (71700) 281 (12000) 390 (32000) 483*	273...274	50
IIIe	$C_{20}H_{11}ClN_2O_2$	8,10 8,08	—	3262 (NH) 1674 (C=O) 1570/1601 (C=C)	220 (58900) 408 (29100) 460*	280...281	35
IIIf	$C_{17}H_{11}NO_4$	4,80 4,78	—	1726 (NH) 1570/1535 (C=C)	209 (29300) 230 (25100) 332 (16600) 381 (13700) 481*	231...234	60
IIIg	$C_{20}H_{10}NO_3$	4,50 4,48	—	1718 (C=O) 1603/1562 (C=C)	215 (37900) 233 (40100) 260 (14300) 400 (23600) 485*	263...264	71
IIIh	$C_{16}H_9NO_2S$	5,03 5,01	11,45 11,48	1718 (C=O) 1603/1562 (C=C)	218 (39700) 250 (9510) 291 (6220) 363 (26700) 479*	210...211	63
IIIi	$C_{17}H_{11}NO_3S$	4,55 4,53	10,35 10,37	1715 (C=O) 1570 (C=C)	222 (39800) 295 (6150) 359 (18600) 393 (19500) 481*	215...217	70
IIIj	$C_{20}H_{11}NO_2S$	4,23 4,25	9,70 9,73	1724 (C=O) 1562/1513 (C=C)	222 (54700) 263 (37900) 412 (29000) 482*	274...276	61
VIa	$C_{16}H_{11}N_3O$	16,05 16,08	—	3168 (NH) 1648(C=N) 1591/1536 (C=C)	242 (41300) 242 (39800) 251 (36700) 272 (35300) 282 (27500) 363 (26500)	265...268	85
VIb	$C_{17}H_{13}N_3O_2$	14,40 14,42	—	3256 (NH) 1652(C=N) 1612/1532 (C=C)	233 (42700) 242 (41200) 272 (36600) 352 (28400) 393 (25400) 414 (24100)	225...227	78

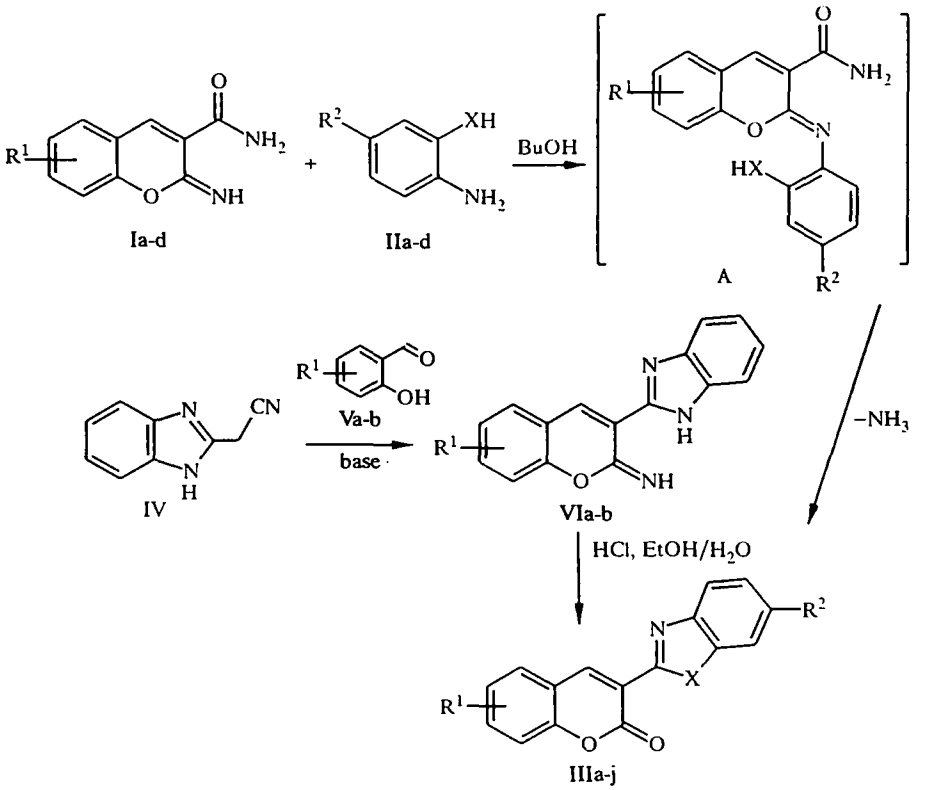
*Luminescence, λ_{max}, nm, in ethanol.

TABLE 2. Chemical Shifts in the PMR Spectra of Coumarins IIIa-j and 2-Iminocoumarins VIa,b, ppm in DMSO-D_6

Compound	1H, s, 4-H	1H, s, NH	H_{arom}, m	Other protons
IIIa	9,16	12,55	7,20...8,15 (8H)	—
IIIb	9,12	12,60	7,30...7,61 (7H)	3,85 (3H, s, CH_3)
IIIc	9,08	12,56	7,15...7,90 (7H)	—
IIId	9,10	12,56	7,25...7,70 (6H)	3,85 (3H, s, CH_3)
IIIe	9,70	12,31	7,15...8,65 (9H)	—
IIIf	9,00	—	7,30...7,90 (7H)	3,85 (3H, s, CH_3)
IIIg	9,49	—	7,45...8,70 (10H)	—
IIIh	9,23	—	8,00...8,30 (8H)	—
IIIi	9,20	—	7,25...8,21 (7H)	3,84 (3H, s, CH_3)
IIIj	9,01	—	7,35...8,00 (10H)	—
VIa	8,54	12,50	6,90...7,81 (8H)	—
VIb	8,54	12,75	7,00...7,80 (7H)	3,80 (3H, s, CH_3)

In order to confirm the structure of the reaction product we have carried out an alternative synthesis of 3-(1H-benzimidazol-2-yl)coumarins IIIa-b via Knoevenagel condensation of 2-(1H-benzimidazol-2-yl)acetonitrile IV with salicylaldehydes Va-b and subsequent acid hydrolysis of the 3-(1H-benzimidazol-2-yl)-2-iminocoumarins VIa-b formed.

Scheme 1



I a R^1 = H; b R^1 = 6-OCH_3; c R^1 = 6-Br; d R^1 = 5,6-benzo; II a R^2 = H, X = NH; b R^2 = 4-Cl, X = NH; c R^2 = H, X = O; d R^2 = H, X = S; III a R^1 = R^2 = H, X = NH; b R^1 = 6-OCH_3, R^2 = H, X = NH; c R^1 = 6-Br, R^2 = H, X = NH; d R^1 = 6-OCH_3, R^2 = 6-Cl, X = NH; e R^1 = 5,6-benzo, R^2 = 6-Cl, X = NH; f R^1 = 6-OCH_3, R^2 = H, X = O; g R^1 = 5,6-benzo, R^2 = H, X = O; h R^1 = R^2 = H, X = S; i R^1 = 6-OCH_3, R^2 = H, X = S; j R^1 = 5,6-benzo R^2 = H, X = S; V a R^1 = H; b R^1 = 5-OCH_3; VI a R^1 = H; b R^1 = 5-OCH_3

Hence, through reaction with o-phenylenediamine or o-amino(thio)phenols, 2-iminocoumarin-3-carboxamides are recyclized to 3-(1H-benzimidazol-2-yl), 3-(benzoxazol-2-yl), and 3-(benzothiazol-2-yl)coumarins and this can serve as an alternative to their preparation via the Knoevenagel method.

EXPERIMENTAL

IR spectra of the synthesized compounds were recorded on a Specord M-80 spectrophotometer for KBr tablets. UV spectra were measured on a Specord M-40 spectrophotometer using ethanol solvent. Luminescence spectra were recorded on a Hitachi F-4010 instrument using ethanol solvent. PMR spectra were taken on a Bruker WP-200 instrument with DMSO-D_6 solvent and TMS internal standard. Mass spectra were recorded on a Finnigan MAT-4615B instrument with ballistic sample heating and an ionization energy of 70 eV.

General Method for Preparing 2-Iminocoumarin-3-carboxamides Ia-d. Equimolar amounts (0.01 mole) of the corresponding salicylaldehyde and cyanoacetic acid amide were dissolved in the minimum quantity of ethanol and a few drops of piperidine added. The solution was stirred vigorously. The precipitate was filtered, dried, and crystallized from a suitable solvent.

General Method for Preparing 3-(1-H-benzimidazol-2-yl)coumarins, 3-(Benzoxazol-2-yl)coumarins, and 3-(Benzothiazol-2-yl)coumarins (IIIa-j). A. A mixture of the corresponding 2-iminocoumarin-3-carboxamide (Ia-d, 0.01 mole) and o-phenylenediamine (o-aminophenol, o-aminothiophenol) (IIa-d, 0.01 mole) was dissolved in the minimum amount of butan-1-ol and refluxed using a reflux condenser for 1-1.5 h. The reaction was accompanied by evolution of ammonia. The precipitate was filtered, dried, and crystallized from a suitable solvent.

General Method for Preparing 2-Imino-3-(1H-benzimdazol-2-yl)coumarins (VIa,b). 2-Benzimidazolylacetonitrile (0.01 mole) dissolved in the minimum amount of propan-2-ol was added to a solution of the corresponding salicylaldehyde (Va,b, 0.01 mole) in propan-2-ol (10 ml). The product was heated and piperidine catalyst (0.01 ml) was added. Heating was stopped and the precipitated iminocoumarin was filtered and recrystallized from a suitable solvent.

General Method for Preparing 3-(1H-benzimidazol-2-yl)coumarins (IIIa,b) by Hydrolysis of VIa,b. B. To the corresponding 2-imino-3-(1H-benzimidazol-2-yl)coumarin (0.01 mole) there were added ethanol (10 ml), water (10 ml), and concentrated HCl (5 ml) and the product was heated. The precipitate was recrystallized from a suitable solvent.

REFERENCES

1. S. N. Kovalenko, V. A. Zubkov, V. P. Chernykh, A. V. Turov, and S. M. Ivkov, Khim. Geterotsikl. Soedin., No. 2, 186 (1996).
2. S. N. Kovalenko, V. P. Chernykh, A. E. Shkarlat, I. V. Ukrainets, V. I. Gridasov, and S. A. Rudnev, Khim. Geterotsikl. Soedin., No. 7, 916 (1998).
3. V. A. Zubkov, S. N. Kovalenko, V. P. Chernykh, and S. M. Ivkov, Khim. Geterotsikl. Soedin., No. 6, 760 (1994).
4. I. I. Tkach and E. V. Luk'yanets, Khim. Geterotsikl. Soedin., No. 8, 1053 (1992).