NMR study of (6-X-7-Y-8-Z)-substituted 3-dimethylamino-2*H*-1-benzopyranones

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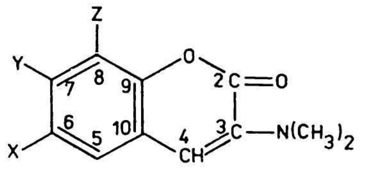
Previous suggestion, concerning the product formed in the reaction of salicylaldehyde, betaine, and acetic anhydride, was confirmed by an in-depth NMR analysis. The product is 3-dimethylamino-2*H*-1-benzopyranone. In reactions with substituted salicylaldehydes, substituted products are formed. Unambiguous assignment of their NMR resonances was made on the basis of the results of several advanced NMR experiments. Transfer of the substituent chemical shift (SCS) between the two rings of the studied molecules, as well as SCS of dimethylamino group are briefly discussed.

Первоначальное предположение о продукте, образуемом в реакции салицилальдегида, бетаина и уксусного ангидрида было подтверждено с помощью анализа методом ЯМР спектроскопии. Продуктом является 3-диметиламино-2*H*-1-бензопиранон. В реакциях с замещенными салициловыми альдегидами образуются замещенные продукты. Однозначное приписание их ЯМР сигналов было проведено на основе результатов нескольких современных ЯМР экспериментов. Коротко обсуждаются перенос химического сдвига заместителя (SCS) между двумя циклами изучаемых молекул, а также SCS диметиламино-группы.

Recently, we have suggested that in the reaction of salicylaldehyde or its substituted analogues with betaine and acetic anhydride, 3-dimethylamino-2*H*-1-benzopyran-2-one (*I*) or its derivatives are formed [1, 2].

Our proposal differs from that of Masaaki who had identified the same product as 2-dimethylamino-1,3-indandione [3]. It should be noted that he deduced the structure mainly on the basis of an evidence obtained from its IR spectrum, *i.e.* he had assigned a doublet observed in the region of the carbonyl group stretching vibrations, to the two carbonyls of the 1,3-indandione struc-



Ia–If

	X	Y	Z		X	Y	Z
a	H	H	H	*d*	H	Br	H
b	H	OCH_3	H	*e*	Cl	H	Cl
c	H	H	OCH_3	*f*	NO_2	H	H

ture. Strong solvent dependence of the doublet splitting, however, indicates that the two absorption lines belong to the symmetrical and antisymmetrical vibrations of one carbonyl group [4].

Here we present further evidence in favour of the proposed coumarin-type structure of *I*. Our evidence is based on a detailed NMR analysis exploiting the results of several advanced NMR experiments.

Experimental

All studied substances were prepared according to published procedures [2]. Prior to use they were purified by recrystallization. Melting points were in accord with Ref. [2].

For NMR measurements, saturated solutions in $CDCl_3$ were prepared. Because of different solubility, concentrations of the samples were different. Although we have observed the concentration effect on chemical shifts, this effect was small and did not influence the assignment of the resonances and the conclusion drawn from the study. All NMR spectra were taken on a Varian VXR-300 spectrometer operating at 75.43 MHz for carbons and 299.93 MHz for protons. All measurements were carried out at the temperature of 28 °C. Digital resolution in the transformed spectra was better than 0.3 Hz/ /point, but because of the above-mentioned concentration effect, results reported in the tables were rounded to 0.01 ppm for ^1H and to 0.1 ppm for ^{13}C chemical shifts.

Results and discussion

All substituted derivatives of *I* provide simple first-order ^1H NMR spectra. Their analysis was therefore straightforward and unambiguous: assignment was achieved by the examination of the characteristic splitting of the aromatic proton multiplets and by the evaluation of the SCS's observed on aromatic protons [5]. Four aromatic protons in nonsubstituted derivative *Ia* form a strongly coupled spin system. Their chemical shifts were estimated indirectly from homo- and heteronuclear correlated 2D NMR spectra [6, 7]. Correctness of the estimation was then checked by comparison with simulated spectra [8]. ^1H NMR chemical shifts for all derivatives are shown in Table 1.

Table 1

^1H NMR chemical shifts of the substituted 3-dimethylamino-2*H*-1-benzopyran-2-ones*

Compound	H-4	H-5	H-6	H-7	H-8
Ia	6.71	7.35	7.19	7.28	7.25
Ib	6.72	7.25	6.80	—	6.78
Ic	6.67	6.94**	7.12	6.85**	—
Id	6.51	7.01	7.31	—	7.44
Ie	6.44	7.19**	—	7.27**	—
If	6.63	8.26	—	8.11	7.34

* Chemical shifts in ppm relative to TMS.

** Assignment may be interchanged.

^{13}C NMR chemical shifts were assigned by combination of procedures. The basic assessment was made by evaluation of SCS's [9] and by comparison of spectral line intensities (discrimination between protonated and quaternary carbons). In controversial cases, the results of the ^1H—^{13}C heteronuclear correlated experiments were utilized. Experiments based on the transfer of the proton coherence through one bond ^1H—^{13}C coupling helped to assign unambiguously all protonated carbons [6]. Assignment of quaternary carbons was confirmed by the semiselective 1D INEPT [10] or by the semiselective 2D-J heteronuclear [11, 12] experiments. The latter methods utilize characteristic properties of the long-range ^1H—^{13}C couplings [13]. Among them, vicinal couplings in planar configurations have usually the largest values. Couplings through more than three bonds are observed only in the planar W-type configurations. Geminal couplings have less characteristic behaviour. Taking these properties into consideration, one would expect, for example, that effects originating from long-range couplings of the H-4 proton could be observed on the C-2 and C-10 carbons. Less pronounced effects would be expected to be observed on the C-5 and C-8 carbons. Protons at *β*-position of the substituent can be used to mark the *ipso*-carbons. For example, by the coherence transfer from OCH_3 protons it was possible to discriminate between the two very close

Table 2

^{13}C NMR chemical shifts of the substituted 3-dimethylamino-2*H*-1-benzopyran-2-ones*

Compound	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	CH_3	OCH_3
Ia	158.0	137.3	116.5	125.4	123.7	126.6	114.9	149.2	120.3	41.0	
Ib	159.1	136.1	119.0	126.7	112.3	159.7	100.3	151.4	114.1	41.8	55.7
Ic	157.6	137.6	116.7	117.2	123.7	109.1	146.1	138.8	121.1	41.0	55.6
Id	157.9	138.3	114.4	127.7	129.4	122.7	117.2	148.4	116.8	41.5	
Ie	157.0	138.7	113.3	123.2	129.3	126.6	121.4	143.8	123.3	41.6	
If	157.2	138.7	113.5	121.1	144.4	121.6	116.6	152.9	121.6	41.6	
Coumarin [14]	159.8	115.8	142.8	127.4	123.8	131.1	115.8	153.3	118.2		

* Chemical shifts in ppm relative to TMS.

C-2 and C-7 resonances in the spectrum of *Ib*. In this way all carbon resonances were unambiguously assigned (Table 2).

The most striking discrepancy with the indandione-type structure of the product are the values of the chemical shifts of H-4 and C-4. In the indandione--type structure C-4 would be in the *sp*^{3} hybridized electronic state and the chemical shifts of H-4 and C-4 would be expected in fairly higher fields. Careful inspection of Tables 1 and 2 reveals further evidence in favour of a coumarin--type product. Relatively large unsymmetry of ^{1}H chemical shifts in the nonsubstituted derivative is in contradiction with the very symmetrical indandione-type structure. Similarly, the large NMR chemical shift differences for the carbons, which would have very similar chemical environment in indandione-type structure, could not be rationalized as a result of any disruption of the indandione ring symmetry; chemically different environment must be considered instead. For example, *ca.* 30 ppm difference between the C-9 and C-10 chemical shifts can be only rationalized as a result of the substituent effect of the oxygen directly bonded to the aromatic ring. Its *ipso*-effect significantly increases the C-9 chemical shift. *Ortho*-effect of this oxygen causes large difference between the C-5 and C-8 chemical shifts.

More evidence for the coumarin-type structure comes from the analysis of the SCS's and the study of the SCS transfer. Clearly, the two highest frequency resonances (*i.e.* C-2 and C-9, Table 2) would be in the indandione-type structure assigned to two carbonyls. It would be then reasonable to expect that they both would exhibit small, but similar SCS. Instead of this, fully different SCS consistent with coumarin-type products is observed.

Comparison of ^{13}C NMR chemical shift in *Ia* with the relevant shifts in coumarin [14] shows significant effect of the —N(CH$_3$)$_2$ group. The largest effect is observed in the *ortho* and *para* positions with respect to the C-3=C-4 double bond. This indicates that the polar effect from the pyranone ring is transferred to the aromatic ring *via* π-electrons through the C-3=C-4 bond being in conjugation with the aromatic ring. Transfer of the SCS between the two rings in opposite direction is also observed. The largest effect show substituents located on the aromatic ring in the *para* position to the C-3=C-4 bond. For example, the SCS of the —OCH$_3$ group in *Ib* can be readily observed on the resonances of C-2, C-3, and C-4. The effect has alternating character, typical for the effect transferred *via* π-electrons. Negligible effect observed in *Id* is due to the nature of the substituent (bromine). Transfer of the polar effect is not observed in *meta*-substituted (*i.e.* in the position 6 or 8) derivatives.

The effect of —N(CH$_3$)$_2$ group on the carbon resonances in the pyranone ring (Table 3) is in accord with the proposed structure. The observed effect is typical for the substituent on a double bond [9]. It is similar to the effect of —OH group but is different in a characteristic way from the effect of —Br or the —CH$_3$

Table 3

^{13}C NMR chemical shifts in 3-substituted 2*H*-1-benzopyran-2-ones*

Substituent	Ref.	C-2	C-3	C-4
H	[14]	159.8	115.8	142.8
$N(CH_3)_2$	This paper	158.0	137.3	116.5
OH	[15]	158.5	141.7	115.0
CH_3	[16]	161.6	125.5	138.2
Br	[14]	156.3	111.0	144.0

* Chemical shifts in ppm relative to TMS.

group. Small variations in the resonances of the C-2 carbon confirm the relative isolation of the carbonyl group from the paths used for transfer of the substituent effect in the studied molecules.

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