Flavonoids. 43 [1,2]. Deprotonation-initiated Aryl Migration with Sulfur Dioxide Extrusion: A Route to 2,3-Dihydro-2,3-diaryl-3-hydroxy-4*H*-1-benzopyran-4-ones

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Treatment of *trans*-2,3-dihydro-2-aryl-3-nosyloxy-4*H*-1-benzopyran-4-ones with various bases afforded 2,3-dihydro-*r*-2-aryl-*t*-3-hydroxy-*c*-3-(4-nitrophenyl)-4*H*-1-benzopyran-4-ones in a deprotonation-initiated aryl migration followed by sulfur dioxide extrusion. In the presence of hydroxide and methoxide ions a secondary ring cleavage has also been observed. However, the reaction of *trans*-2,3-dihydro-2-aryl-3-nosyloxy-4*H*-1-benzopyran-4-ones with cyanide ions gave 2,3-dihydro-*r*-2-aryl-*t*-4-cyano-*c*-3,*c*-4-epoxy-4*H*-1-benzopyrans in a carbonyl attack of cyanide followed by an internal substitution reaction.

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In contrast with the widely investigated and well-documented [3] chemistry of α-haloaldehydes and ketones, only a limited number of papers have been published in the field of α-sulfonyloxyketones [4-9]. The development of two new methodologies utilizing arenesulfonylperoxides [6] or [hydroxy(tosyloxy/mesyloxy)iodo]benzene [7] for their preparation proved a great stimulus to our studies. Their solvolytic behavior has been summarized [8] in 1985 and a fully updated review [9] on their synthesis and chemistry has also been published more recently. The outstanding leaving group ability of the nosyloxy group, the finding that nosylates generally give much cleaner reactions than the other sulfonates and the possibility of some unique transformations [5,9] prompted us to study the chemistry of nosylates **2** as a continuation of our work on the reactivity of *trans*-2,3-dihydro-2-aryl-3-(alkane/arenesulfonyloxy)-4*H*-1-benzopyran-4-ones [10].

Starting material *trans*-2,3-dihydro-2-aryl-3-nosyloxy-4*H*-1-benzopyran-4-ones **2a-e** were prepared by condensing the appropriate α-ketols **1a-e** with nosyl chloride by the use of the known procedures [11-13] (Scheme 1). The sulfonylation required a longer reaction period because of the low basicity of the hydroxy function and the steric hindrance in the α-ketol **1**. However, the susceptibility of nosylates **2** toward bases resulted in moderated yields under these conditions. Better yields were generally achieved in case nosylate **2** precipitated.

Treatment of α-nosyloxyketones **2a-e** with various bases listed in Table 1 gave 2,3-dihydro-*r*-2-aryl-*t*-3-hydroxy-*c*-3-(4-nitrophenyl)-4*H*-1-benzopyran-4-ones **3a-e** beside 2-aryl-4*H*-1-benzopyran-4-ones (flavones) **4a-e** and 2-aryl-3-hydroxy-4*H*-1-benzopyran-4-ones **5a-e** (Scheme 1). Formation of any substitution product could not have been detected contrary to the analogous reaction of the other *trans*-2,3-dihydro-2-aryl-3-(alkane/arenesulfonyloxy)-4*H*-1-benzopyran-4-ones (mainly mesylates **10**) [10,14]. Product-ratio **3:4:5** depended on the used nucleophile (Table 1), best yields were achieved using cyanide ions. In accor-

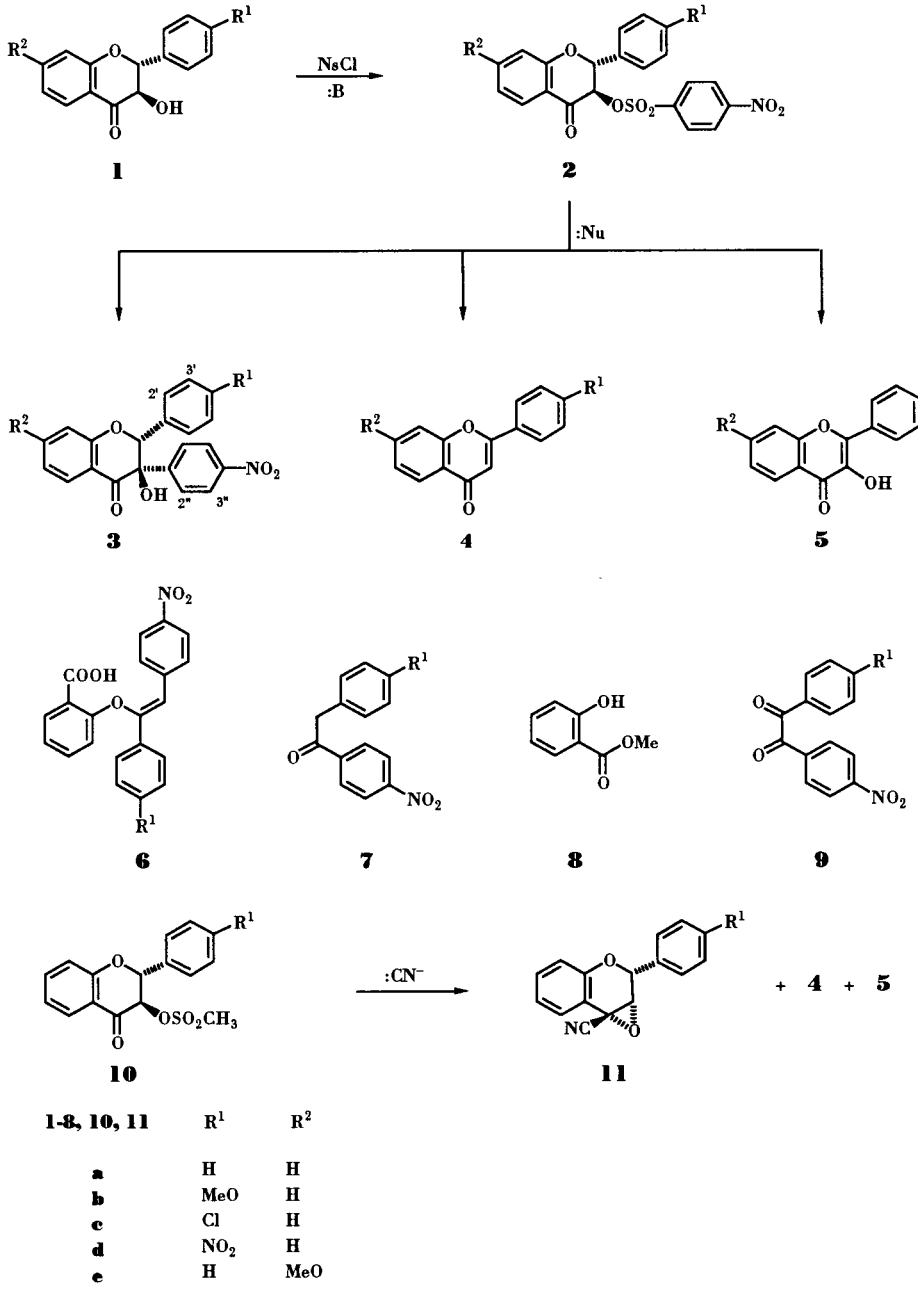
Table 1

Reaction of Nosylates **2** with Bases

Starting material	Base (equivalents)	Solvent	Time hours	Yield (%) **3**	**4**	**5**	Others
2a	*i*-$PrNH_2$ (3.0)	DMF	1.5	62	4.5	4.2	–
	piperidine (2.1)	DMSO	2.5	60	22	15	–
	DBU (3.0)	DMF	1.5	43	14	6.7	**6a**, 16
	KCN (2.0)	DMF	1.5	86	6.3	6.7	–
	KCN (2.0)	DMF-H_2O (5:1)	1.0	52	11	24	–
	NaOH (3.0)	DMF	1.5	32	4.5	4.2	**6a**, 32
	NaOMe (3.0)	DMF-MeOH (7:3)	1.0	tr	tr	48	**7a**, 50
2b	KCN (2.0)	DMF	1.0	87	2.3	4.3	**2b**, 1.7
	NaOMe (3.6)	DMF-MeOH (9:1)	1.0	tr	tr	54 [a]	**7b**, 12 [a]
2c	KCN (2.0)	DMF	1.5	58	18	9.5	–
2d	KCN (2.1)	DMF	0.6	21	40	37	–
2e	KCN (2.0)	DMF	2.0	69	2.8	4.7	–

[a] With benzene as eluent in column chromatography; tr: traces.

Scheme 1



1-8, 10, 11	R^1	R^2
a	H	H
b	MeO	H
c	Cl	H
d	NO_2	H
e	H	MeO

dance with our earlier results [14], the presence of electron-withdrawing group in the ring B, *e.g.* **2c**, **2d**, favored the formation of **4**.

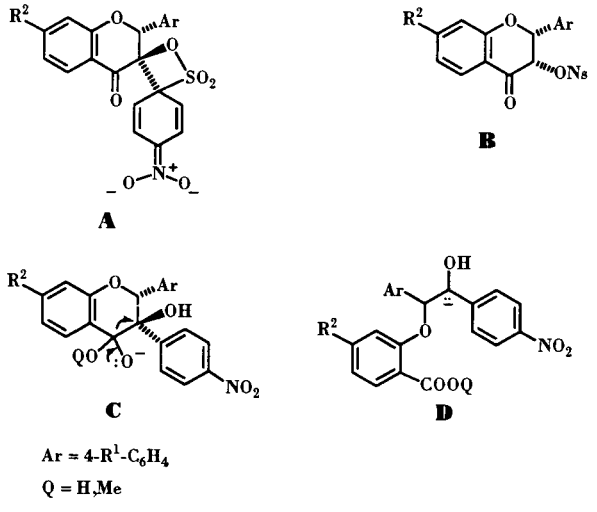
The only precedent of such a nitrophenyl group migration coupled with a loss of sulfur dioxide was reported by Hoffman *et al.* [5]. They observed this process in the reaction of 2-nosyloxytetralone and α-nosyloxydeoxybenzoin with DBU [5] or triethylamine [15] but treatment of nosylates with primary and secondary amines led to the formation of "regular" substitution products, *i.e.* α-aminoketones.

As shown by Table 1, the reaction of nosylates **2** with certain nucleophiles resulted in further products. Thus, 2-{[2-(4-nitrophenyl)-1-phenylethenyl]oxy}benzoic acid (**6a**) was isolated from the reaction mixture of **2a** and DBU or sodium hydroxide whereas 4-nitrodeoxybenzoins **7a,b** were obtained beside the products mentioned above treating nosylates **2a,b** with sodium methoxide. Both enol ether **6a** and deoxybenzoins **7a,b** originate from the primary products **3** corroborated by control experiments. In

the reaction of 2,3-dihydro-2-aryl-3-hydroxy-3-(4-nitrophenyl)-4*H*-1-benzopyran-4-ones **3a,b** with sodium hydroxide enol ethers **6a,b** were obtained. Treatment of **3a,b** with sodium methoxide afforded 4-nitrodeoxybenzoins **7a,b** and methyl salicylate (**8**) proving the total fission of the hetero ring of **3**. In this latter case small amount of 4-nitrobenzils **9a,b** and 4-nitrobenzoic acid were also isolated deriving presumably from a subsequent oxidation of **7a,b**.

Formation of **3** can be rationalized assuming a deprotonation at position 3 of nosylate **2** followed by an *ipso*-attack, sulfur dioxide extrusion from the intermediate **A** and reprotonation. This mechanism may be supported both the unaltered stereochemistry at C-3 determined by nOe difference measurements and by the failure of the attempted acid-catalysed dehydration. The concurrent epimerisation *via* carbanion formed in the first step leads to the *cis*-isomer of **2** (**B**), which gives **4** in an E2-type elimination step [16]. To explain the appearance of the cleavage products **6,7** and **8**, a nucleophilic attack on the carbonyl center followed by a rare C-3-C-4 bond fission [17] in the intermediate **C** should be supposed. The fate of carbanion **D** may depend on the nucleophile used. When it allows a proton transfer from the carboxylic function to the carbanion, the subsequent dehydration leads to enol ether **6**. In default of such a transfer another bond fission between O-1 and C-2 is the only possibility for the stabilization. Some of the postulated intermediates are shown in Scheme 2.

Scheme 2



The most reasonable pathway for the formation of 2-aryl-3-hydroxy-4*H*-1-benzopyran-4-ones **5** involves a base-induced O-S bond cleavage [18] of the sulfonate **2** and a subsequent dehydrogenation [19] of the formed 2,3-dihydro-2-aryl-3-hydroxy-4*H*-1-benzopyran-4-ones **1** in the basic medium.

In accordance with the proposed mechanism the migration with loss of sulfur dioxide seems to be limited to the α-nosyloxyketones since the analogous reaction of *trans*-2,3-dihydro-3-(4-bromophenylsulfonyloxy)-2-phenyl-4*H*-1-benzopyran-4-one with potassium cyanide gave only benzopyranones **4a** and **5a**. The same products were obtained treating *trans*-2,3-dihydro-3-mesyloxy-2-phenyl-4*H*-1-benzopyran-4-one (**10a**) with potassium cyanide but a new product, 2,3-dihydro-*t*-4-cyano-*c*-3,*c*-4-epoxy-*r*-2-phenyl-4*H*-1-benzopyran (**11a**) was also isolated. The formation of **11a** may be rationalized by a cyanide attack at the carbonyl group, the center of greatest kinetic electrophilicity, followed by an internal nucleophilic substitution. This sequence is well-documented among the α-haloketones [3a,b,20,21] but only one example is reported [21b] for α-sulfonyloxyketones. According to data summarized in Table 2, the participation of this reaction depends on both the used solvent and the character of substituents.

Table 2

Reaction of Mesylates 10 with KCN

Starting material	Solvent	Time hours	Yield (%) 11	4	5
10a	DMF	310	8.8	67	3.1
	DMF-H_2O (5:1)	48	21	40	5.3
	DMSO-H_2O (5:1)	46	12	36	13
	Me_2CO-H_2O (5:1)	73	1.9	26	32
	EtOH/Δ	0.5	17	29	12
10b	DMF-H_2O (5:1)	48	14	27	2.9
10c	DMF-H_2O (5:1)	3	0	47	3.4

EXPERIMENTAL

Instrumentation and Materials.

The nmr were taken with a Bruker WP 200 SY, spectrometer at 200 MHz (^1H) or 50.3 MHz (proton decoupled ^{13}C), in DMSO-d_6 unless otherwise stated, δ scale (ppm) from internal standard TMS. The ir were obtained on either a Perkin Elmer 283 or a Perkin Elmer 16 PC FT-IR spectrometer as potassium bromide discs unless otherwise specified. The mass spectra were determined with a VG 7035 GC-MS-DS spectrometer in the EI mode at 70 eV. The melting points were determined on a Boetius hot stage and are uncorrected. Analysis (tlc) was on Kieselgel 60 F_{254} (Merck) with toluene or toluene:ethyl acetate (4:1, v/v) as the developing system with detection by uv light or in an iodine chamber. Column chromatography was accomplished on silica gel 60 (70-230 mesh) (Reanal), under gravity.

General.

Drying of extracts was made over magnesium sulfate. Evaporation refers to the removal of the solvent under reduced pressure. Yields are given for homogenous materials, purity was checked by tlc and ^1H nmr. Identification of known compounds was performed by mp, mixed mp, tlc, ir and/or ^1H nmr.

General Procedures for Preparation of *trans*-2,3-Dihydro-2-aryl-3-nosyloxy-4*H*-1-benzopyran-4-ones **2**.

Nosylates **2a-e** were synthetized using Tipson's method [11] (Procedure A) [22] or modified Kabalka's method [12] (Procedure B) or method described by Crossland and Servis [13] (Procedure C).

Procedure B.

To a cooled (0-5°) and stirred solution of *trans*-2,3-dihydro-2-aryl-3-hydroxy-4*H*-1-benzopyran-4-one (**1**) (5.0 mmoles) and absolute pyridine (0.8 ml, 9.93 mmoles) in dry chloroform (20 ml) was added nosyl chloride (1.66 g, 7.49 mmoles) in one portion. After completion of the reaction (tlc) the precipitate was filtered off, washed with water and a small amount of cold chloroform to give pure **2**. The filtrate was diluted with a mixture of diethyl ether (30 ml) and water (10 ml), separated and the organic layer was washed with 2*M* hydrochloric acid. After drying, evaporation and recrystallization a second crop of product was obtained.

Procedure C.

To a cooled (0-5°) and stirred solution of **1** (20.82 mmoles) and triethyl amine (4.2 ml, 30.0 mmoles) in dry dichloromethane (100 ml) was added nosyl chloride (5.08 g, 22.92 mmoles) and allowed to react for 2 days. The precipitate was filtered off and washed with water to afford pure **2**. The filtrate was poured into brine, separated, washed successively with 10% hydrochloric acid, saturated sodium bicarbonate and water. After drying, evaporation and recrystallization further amount of **2** was obtained.

trans-2,3-Dihydro-3-nosyloxy-2-phenyl-4*H*-1-benzopyran-4-one (**2a**).

This compound was prepared in 65% and 54% yield using Procedure A [22] and B (4 days), respectively and it was crystallized from ethanol, mp 199-200°, lit [22] mp 194-195°.

trans-2,3-Dihydro-2-(4-methoxyphenyl)-3-nosyloxy-4*H*-1-benzopyran-4-one (**2b**).

This compound was prepared in 11% yield using Procedure A (6 days), in 41% yield using Procedure B (6 days, room temperature) and in 68% yield using Procedure C (2 days). It was crystallized from ethyl acetate, mp 183-185°; ir: ν 3092 (CH), 2835 (OMe), 1708 (C=O), 1604, 1512, 1463 (aromatic CC), 1528, 1347 (NO_2), 1377, 1186 (SO_2), 1282, 1227, 1016 (flavanone skeleton + C-N), 1251 (C-O-C, OMe) cm^{-1}; ^1H nmr: δ 8.23 (d, 2H, H-3'', 5''), 7.84 (dd, 1H, H-5), 7.76 (d, 2H, H-2'', 6''), 7.64 (ddd, 1H, H-7), 7.29 (d, 2H, H-2', 6'), 7.20 (ddd, 1H, H-6), 7.10 (dd, 1H, H-8), 6.63 (d, 2H, H-3', 5'), 6.15 (d, 1H, H-3, J = 12.5 Hz), 5.63 (d, 1H, H-2, J = 12.5 Hz), 3.68 (s, 3H, OMe).

Anal. Calcd. for $C_{22}H_{17}NO_8S$ (455.45): C, 58.02; H, 3.76; N, 3.08; S, 7.04. Found: C, 58.21; H, 3.49; N, 3.01; S, 7.12.

trans-2,3-Dihydro-2-(4-chlorophenyl)-3-nosyloxy-4*H*-1-benzopyran-4-one (**2c**).

This compound was prepared in 72% yield using Procedure B (6 days) and crystallized from chloroform, mp 228-230°; ir: ν 3097 (CH), 1697 (C=O), 1603, 1489, 1470, 1462 (aromatic CC), 1525, 1347 (NO_2), 1382, 1183 (SO_2), 1283, 1228, 1210, 1019, 1009 (flavanone skeleton + C-N), 1082 (Ar-Cl), 828, 763 (aromatic CH) cm^{-1}; ^1H nmr: δ 8.26 (d, 2H, H-3'', 5''), ~7.80 (m, 3H, H-5 + H-2'', 6''), 7.69 (ddd, 1H, H-7), 7.41, 7.16 (m, 6H, H-6, 8 + H-2', 3', 5', 6'), 6.19 (d, 1H, H-3, J = 12.0 Hz), 5.75 (d, 1H, H-2, J = 12.0 Hz).

Anal. Calcd. for $C_{21}H_{14}ClNO_7S$ (459.87): C, 54.85; H, 3.07; N, 3.05; S, 6.97. Found: C, 54.59; H, 3.11; N, 3.02; S, 7.15.

trans-2,3-Dihydro-2-(4-nitrophenyl)-3-nosyloxy-4*H*-1-benzopyran-4-one (**2d**).

This compound was prepared in 34% and 40% yield using Procedure A (7 days) and C (2 days), respectively and was crystallized from a dimethyl formamide-ethyl acetate mixture, mp 237-240° dec; ir: ν 3100, 3040 (CH), 1699 (C=O), 1603, 1516, 1471, 1462 (aromatic CC), 1530, 1348 (NO_2), 1381, 1183 (SO_2), 1281, 1229, 1021, 979 (flavanone skeleton + C-N), 828, 734 (aromatic CH) cm^{-1}; ^1H nmr: δ 8.20 (d, 2H, H-3'', 5''), 7.99 (d, 2H, H-3', 5'), 7.85 (dd, 1H, H-5), 7.82 (d, 2H, H-2'', 6''), 7.77 (ddd, 1H, H-7), 7.68 (d, 2H, H-2', 6'), 7.24 (ddd, 1H, H-6), 7.16 (dd, 1H, H-8), 6.27 (d, 1H, H-3, J = 12.1 Hz), 5.96 (d, 1H, H-2, J = 12.1 Hz).

Anal. Calcd. for $C_{21}H_{14}N_2O_9S$ (470.42): C, 53.62; H, 3.00; N, 5.96; S, 6.82. Found: C, 53.46; H, 3.11; N, 5.95; S, 6.69.

trans-2,3-Dihydro-7-methoxy-3-nosyloxy-2-phenyl-4*H*-1-benzopyran-4-one (**2e**).

This compound was prepared in 68% yield using Procedure B (6 days) and was crystallized from ethyl acetate, mp 205-206°; ir: ν 3099, 3061, 3033 (CH), 2832 (OMe), 1700 (C=O), 1605, 1572, 1595 (aromatic CC), 1527, 1350 (NO_2), 1389, 1188 (SO_2), 1312w, 1024, 978 (flavanone skeleton + C-N), 1256, 1067 (C-O-C, OMe), 851, 789, 762, 740 (aromatic CH) cm^{-1}; ^1H nmr: δ 8.20 (d, 2H, H-3'', 5''), 7.79 (d, 2H, H-2'', 6''), 7.74 (d, 1H, H-5), 7.43 (m, 2H, H-2', 6'), 7.18 (m, 3H, H-3', 4', 5'), 6.76 (dd, 1H, H-6), 6.65 (d, 1H, H-8), 6.06 (d, 1H, H-3, J = 11.8 Hz), 5.63 (d, 1H, H-2, J = 11.8 Hz), 3.83 (s, 3H, OMe).

Anal. Calcd. for $C_{22}H_{17}NO_8S$ (455.45): C, 58.02; H, 3.76; N, 3.08; S, 7.04. Found: C, 57.92; H, 3.58; N, 2.97; S, 7.04.

General Procedure for the Synthesis of 2,3-Dihydro-*r*-2-aryl-*t*-3-hydroxy-*c*-3-(4-nitrophenyl)-4*H*-1-benzopyran-4-ones **3**.

To a stirred solution (12 ml) of nosylate **2** (1.5 mmoles) 3.0-4.5 mmoles of base (specified in Table 1) was added at room temperature. Having terminated the reaction (tlc check) the mixture was poured into brine, extracted with diethyl ether or ethyl acetate, dried and evaporated. (In the reaction of **2d** the solid precipitated after pouring into water was filtered off and only the filtrate was extracted.) Products were separated by column chromatography using toluene:ethyl acetate (8:1, v/v) or hexane:ethyl acetate (4:1, v/v) mixture as eluent.

Product ratio data and further details are given in Table 1. Compounds reported and characterized earlier are: **4a** [23], **4b** [24], **4c** [25], **4d** [26], **4e** [27], **5a** [28], **5b** [29], **5c** [30], **5d** [26], **5e** [31].

2,3-Dihydro-*t*-3-hydroxy-*c*-3-(4-nitrophenyl)-*r*-2-phenyl-4*H*-1-benzopyran-4-one (**3a**).

This compound was obtained as white crystals (ethanol-hexane), mp 189-190°; ir: ν 3408 (OH), 3066, 3038 (CH), 1695 sh, 1681 (C=O), 1613, 1470 (aromatic CC), 1527, 1353 (NO_2), 1318,

1310, 1236, 1043, 977 (flavanone skeleton + C-N), 1120, 1101 (C-OH), 859, 855, 767, 744, 698 (aromatic CH) cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.11 (d, 2H, H-3″, 5″), 7.94 (dd, 1H, H-5), 7.63 (ddd, 1H, H-5), 7.49 (d, 2H, H-2″, 6″), 7.08-7.33 (m, 7H, Ph + H-6, 8), 5.66 (s, 1H, H-2), 3.73 (s, 1H, OH, deuterium oxide-exchangeable); nOe: irradiation of H-2: H-2″, 6″ (13.5%), Ph (17.5%), OH (5.8%), irradiation of OH: H-5 (1.0%), H-2″, 6″ (9.8%): ^{13}C-nmr (DMSO-d_6-deuteriochloroform): δ 189.77 (C-4), 160.13 (C-8a), 146.10, 145.33 (C-1″ and C-4″), 135.15 (C-7), 133.07 (C-1′), 127.65, 127.50 (C-3′, 5′ and C-2″, 6″), 127.41, 126.96 (C-5 and C-4′), 126.38 (C-2′, 6′), 121.27 (C-3″, 5″), 120.76 (C-6), 118.58 (C-4a), 117.05 (C-8), 85.22 (C-2), 77.00 (C-3, overlapping with deuteriochloroform signal); ms: 361 ($M^{+\cdot}$, 1), 343 (0.5), 342 (0.5), 241 (17), 211 (67), 183 (5), 181 (3), 165 (5.5), 151 (49), 150 (11), 133 (66), 121 (100), 105 (6), 91 (10), 77 (2).

Anal. Calcd. for $C_{21}H_{15}NO_5$ (361.36): C, 69.80; H, 4.18; N 3.88. Found: C, 70.31; H, 4.43; N, 3.75.

2,3-Dihydro-*t*-3-hydroxy-*c*-3-(4-nitrophenyl)-*r*-2-(4-methoxyphenyl)-4*H*-1-benzopyran-4-one (**3b**).

This compound was obtained as white crystals (ethanol-hexane), mp 143-145°; ir: ν 3385 (OH), 3078 (CH), 2968, 2897, 2838 (OMe), 1678 (C=O), 1611, 1589, 1462 (aromatic CC), 1511 br, 1349 (NO_2), 1304, 1228, 1176, 981 (flavanone skeleton + C-N), 1251, 1031 (C-O-C, OMe), 1113, 1095 (C-OH), 849, 822, 740, 692 (aromatic CH), 782 (NO_2) cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.18 (d, 2H, H-3″, 5″), 8.00 (dd, 1H, H-5), 7.63 (ddd, 1H, H-7), 7.54 (d, 2H, H-2″, 6″), 7.10-7.15 (m, 2H, H-6, 8), 7.13 (d, 2H, H-2′, 6′), 6.79 (d, 2H, H-3′, 5′), 5.64 (s, 1H, H-2), 3.79 (br s, 4H, OH + OMe); ms: 391 ($M^{+\cdot}$, 9), 373 (1.5), 372 (5), 271 (18.5), 241 (100), 225 (4), 213 (26.5), 211 (4), 165 (8), 151 (60), 150 (10), 133 (89), 106 (15.5), 104 (16), 92 (20.5), 77 (31).

Anal. Calcd. for $C_{22}H_{17}NO_6$ (391.38): C, 67.52; H, 4.38; N, 3.58. Found: C, 67.39; H, 4.52; N, 3.70.

2,3-Dihydro-*r*-2-(4-chlorophenyl)-*t*-3-hydroxy-*c*-3-(4-nitrophenyl)-4*H*-1-benzopyran-4-one (**3c**).

This compound was obtained as white crystals (ethanol-hexane), mp 196-198°; ir: ν 3397 (OH), 3071 (CH), 1670 (C=O), 1599, 1478, 1459 (aromatic CC), 1514, 1345s (NO_2), 1304, 1223, 1012, 980 (flavanone skeleton + C-N), 1108 (C-OH), 1089 (Ar-Cl), 847, 812, 757, 740, 690 (aromatic CH), 773 (NO_2) cm^{-1}; ^1H nmr: δ 8.12 (d, 2H, H-3″, 5″), 7.94 (dd, 1H, H-5), 7.70 (ddd, 1H, H-7), 7.52 (d, 2H, H-2″, 6″), 7.35 (s, 1H, OH), 7.13-7.30 (m, 6H, H-6, 8 + H-2′, 3′, 5′, 6′), 6.03 (s, 1H, H-2).

Anal. Calcd. for $C_{21}H_{14}ClNO_5$ (395.80): C, 63.73; H, 3.57; Cl, 8.96; N, 3.54. Found: C, 63.63; H, 3.29; Cl, 9.11; N, 3.42.

2,3-Dihydro-*t*-3-hydroxy-*r*-2,*c*-3-bis(4-nitrophenyl)-4*H*-1-benzopyran-4-one (**3d**).

This compound was obtained as pale yellow crystals (ethanol-hexane), mp 183-185°; ir: ν 3405 (OH), 3115, 3080 (CH), 1690 (C=O), 1608, 1473, 1465 (aromatic CC), 1523, 1351 (NO_2), 1308, 1229, 1013 (flavanone skeleton + C-N), 1114, 1095 (C-OH), 850, 758, 742 (aromatics CH), 695 (aromatic CC) cm^{-1}; ^1H nmr: δ 8.13 (d, 2H, H-3″, 5″), 8.07 (d, 2H, H-3′, 5′), 7.95 (dd, 1H, H-5), 7.71 (ddd, 1H, H-7), 7.51 (d, 2H, H-2″, 6″), 7.48 (s, 1H, OH), 7.37 (d, 2H, H-2′, 6′), 7.23 (m, 2H, H-6, 8), 6.21 (s, 1H, H-2).

Anal. Calcd. for $C_{21}H_{14}N_2O_7$ (406.36): C, 62.07; H, 3.47; N, 6.89. Found: C, 62.21; H, 3.71; N, 6.79.

2,3-Dihydro-*t*-3-hydroxy-7-methoxy-*c*-3-(4-nitrophenyl)-*r*-2-phenyl-4*H*-1-benzopyran-4-one (**3e**).

This compound was obtained as white crystals (ethanol-ethyl acetate), mp 205-207°; ir: ν 3360 (OH), 3060, 3023 (CH), 2968, 2936, 2870, 2832 (OMe), 1648 (C=O), 1596, 1570, 1437 (aromatic CC), 1508, 1341 (NO_2), 1309, 1237, 1160, 1119 (flavanone skeleton + C-N), 1256, 1020 (C-O-C, OMe), 1108, 1092 (C-OH), 848, 836, 831 (aromatic CH), 690 (aromtic CC) cm^{-1}; ^1H nmr: δ 8.09 (d, 2H, H-3″, 5″), 7.83 (d, 1H, H-5), 7.49 (d, 2H, H-2″, 6″), 7.19 (m, 6H, Ph + OH), 6.78 (dd, 1H, H-6), 6.72 (d, 1H, H-8), 5.90 (s, 1H, H-2), 3.86 (s, 3H, OMe).

Anal. Calcd. for $C_{22}H_{17}NO_6$ (391.38): C, 67.52; H, 4.38; N, 3.58. Found: C, 67.44; H, 4.29; N, 3.53.

2-{[2-(4-Nitrophenyl)-1-phenylethenyl]oxy}benzoic Acid (**6a**).

This compound was obtained as yellow crystals (ethanol-ethyl acetate), mp 207-209°; ir: ν 3250 br (OH, COOH), 3075 (CH), 1687 (C=O), 1613 (C=C), 1596, 1480 (aromatic CC), 1509, 1344 (NO_2), 1447 (OH), 1296 (Ar-CO), 1272 (C-OH), 1196, 1074 (C-O-C), 853, 758 (CH), 689 (aromatic CC), cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.26 (d, 2H, H-3″, 5″), 8.19 (dd, 1H, H-6), 7.74 (d, 2H, H-2″, 6″), 7.58 (m, 3H, H-4 + H-2′, 6′), 7.34 (m, 3H, H-3′, 4′, 5′), 7.08 (m, 2H, H-3, 5), 6.99 (s, 1H, =CH-); (DMSO-d_6): δ 10.33 (br s, 1H, COOH), 8.28 (d, 2H, H-3″, 5″), 8.12 (dd, 1H, H-6), 7.96 (d, 2H, H-2″, 6″), 7.70 (m, 2H, H-2′, 6′), 7.63 (ddd, 1H, H-4), 7.46 (s, 1H, =CH-), 7.42-7.28 (m, 3H, H-3′, 4′, 5′), 7.09 (m, 2H, H-3, 5); ^{13}C-nmr (DMSO-d_6-polysol): δ 166.47 (COOH), 160.90 (C-2), 147.24 (=CPhO), 143.59 (C-4″), 141.43 (C-1″), 136.67 (C-4), 133.19 (C-1′), 130.62 (C-4′), 129.03, 128.70 (C-3′, 5′ and C-2″, 6″), 125.57 (C-2′, 6′), 123.95 (C-3″, 5″), 121.01, 119.92, 117.90 (=CH-, C-3 and C-5); ms: 361 ($M^{+\cdot}$, <0.5), 298 (0.6), 270 (<0.5), 241 (2), 194 (4), 165 (5), 150 (18), 121 (100), 120 (4), 104 (6), 93 (7), 91 (8), 76 (6).

Anal. Calcd. for $C_{21}H_{15}NO_5$ (361.36): C, 69.80; H, 4.18; N, 3.88. Found: C, 69.91; H, 4.12; N, 3.62.

1-(4-Nitrophenyl)-2-phenylethanone (**7a**).

This compound was prepared as pale yellowish crystals (acetone-hexane), mp 159-161°, lit [32] mp 159-160.5°; ir: ν 3104 (CH), 2895 (CH_2), 1690 (C=O), 1600 (aromatic CC), 1518, 1338 (NO_2), 1318 (Ar-CO), 1210 (C-N), 1197 (CH), 848, 744 (aromatic CH), 702, 681 (aromatic CC) cm^{-1}; ^1H nmr: δ 8.36, 8.27 (A_2B_2, 4H, H-2′, 3′, 5′, 6′), 7.37-7.23 (m, 5H, Ph), 4.63 (s, 2H, CH_2); ms: 241 ($M^{+\cdot}$, 37), 195 (5), 165 (5), 150 (100), 134 (4), 120 (18), 104 (57), 91 (100), 78 (19), 76 (44), 65 (36).

Anal. Calcd. for $C_{14}H_{11}NO_3$ (241.25): C, 69.70; H, 4.60; N, 5.81. Found: C, 69.41; H, 4.35; N, 5.90.

2-(4-Methoxyphenyl)-1-(4-nitrophenyl)ethanone (**7b**).

This compound was prepared as pale yellowish crystals (ethanol-hexane), mp 116-118°; ir: ν 3102, 3076 (CH), 2968, 2928, 2882 (OMe + CH_2), 2838 (OMe), 1698 (C=O), 1608, 1601 (aromatic CC), 1513, 1342, 1331 (NO_2), 1315 (Ar-CO), 1242, 1028 (C-O-C, OMe), 1210 (C-N), 1194 (CH), 845, 745 (aromatic CH) cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.30 (dd, 2H, H-3′, 5′), 8.14 (dd, 2H, H-2′, 6′), 7.18 (dd, 2H, H-2, 6), 6.88 (dd, 2H, H-3, 5), 4.28 (s, 2H, CH_2), 3.80 (s, 3H, OMe).

Anal. Calcd. for $C_{15}H_{13}NO_4$ (271.28): C, 66.41; H, 4.83; N, 5.16. Found: C, 66.79; H, 4.85; N, 5.02.

Reaction of Benzopyranones **3a,b** with Sodium Hydroxide.

2,3-Dihydro-*t*-3-hydroxy-*c*-3-(4-nitrophenyl)-*r*-2-phenyl-4*H*-1-benzopyran-4-one (**3a**) (500 mg, 1.38 mmoles) and sodium hydroxide (60 mg, 1.50 mmoles) was stirred in absolute DMF (20 ml) at room temperature for 2 hours. The mixture was poured into brine, the precipitate was filtered off and recrystallized from an acetone-hexane mixture to give 140 mg (28%) of **6a**.

When the reaction was repeated starting from **3b** (250 mg, 0.64 mmoles) (reaction period, 26 hours), the fractionation of the crude product by column chromatography (hexane:ethyl acetate (4:1, v/v)) afforded 73 mg (29%) of **6b**.

2-{[1-(4-Methoxyphenyl)-2-(4-nitrophenyl)ethenyl]oxy}benzoic Acid (**6b**).

This compound was obtained as yellow crystals (ethanol-hexane), mp 154-156°; ir: ν 3220 (OH, COOH), 2968, 2930, 2837 (OMe), 1693 (C=O), 1613 (C=C), 1605, 1590, 1482 (aromatic CC), 1510, 1339 br (NO_2), 1440 (OH), 1300 (Ar-CO), 1279 (C-OH), 1250, 1029 (C-O-C, OMe), 1196, 1075 (C-O-C), 851, 847, 756 (aromatic CH), 690 (aromatic CC) cm^{-1}; ^1H nmr (deuteriochloroform): δ 10.23 (s, 1H, COOH), 8.24 (m, 3H, H-6 + H-3'', 5''), 7.69 (d, 2H, H-2'', 6''), 7.60 (m, 1H, H-4), 7.53 (d, 2H, H-2, 6), 7.08 (m, 2H, H-3, 5), 9.94 (s, 1H, =CH-), 6.87 (d, 2H, H-3', 5'), 3.80 (s, 3H, OMe).

Anal. Calcd. for $C_{22}H_{17}NO_6$ (391.38): C, 67.52; H, 4.38; N, 3.58. Found: C, 67.91; H, 4.11; N, 3.50.

Reaction of Benzopyranones **3a,b** with Sodium Methoxide.

Sodium methoxide (349 mg, 6.46 mmoles) in absolute methanol (4.4 ml) was added to a stirred solution of 2,3-dihydro-*t*-3-hydroxy-*c*-3-(4-nitrophenyl)-*r*-2-phenyl-4*H*-1-benzopyran-4-one (**3a**) (782 mg, 2.16 mmoles) in absolute DMF (30 ml) and allowed to react for 2 hours at room temperature. The mixture was poured into brine and extracted with ethyl acetate. Acidification of the aqueous layer with dilute hydrochloric acid followed by extraction (ethyl acetate) and evaporation afforded 81 mg (22%) of 4-nitrobenzoic acid.

The dried and evaporated extract was separated by two-fold column chromatography (first eluent: toluene, rechromatography:hexane:acetone (2:1, v/v)) to give 164 mg (50%) of methyl salicylate (**8**), 124 mg (23%) of 4-nitrobenzil (**9a**) and 171 mg (33%) of 4-nitrodeoxybenzoin (**7a**).

4-Nitrobenzil (**9a**).

This compound was prepared as yellow crystals (acetone-hexane), mp 140-142°, lit [33] mp 142°; ir: ν 3106, 3080 (CH), 1674, 1662 (C=O), 1604, 1594, 1450 (aromatic CC), 1528, 1346 (NO_2), 1324 (Ar-CO), 1204 (C-N), 842 (aromatic CH), 798 (NO_2), 718, 702 (aromatic CC) cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.37 (d, 2H, H-3, 5), 8.17 (d, 2H, H-2, 6), 7.99 (dd, 2H, H-2', 6'), 7.71 (dd, 1H, H-4'), 7.56 (ddd, 2H, H-3', 5'); ms: (30 eV, ammonium chloride addition) 256 (M + 1, 4), 255 ($M^{+\cdot}$, 0.3), 254 (0.4), 239 (2), 225 (2), 150 (21), 134 (4), 120 (2), 105 (100), 104 (12.5), 92 (6.5), 77 (89), 76 (20), 51 (47).

Anal. Calcd. for $C_{14}H_9NO_4$ (255.23): C, 65.88; H, 3.55; N, 5.49. Found: C, 65.90; H, 3.72; N, 5.64.

Analogous treatment of **3b** (461 mg, 1.18 mmoles) with sodium methoxide (190 mg, 3.52 mmoles) afforded 17 mg (8.6%) 4-nitrobenzoic acid, 111 mg (62%) of methyl salicylate (**8**), 45 mg (13%) of 4-methoxy-4'-nitrobenzil (**9b**) and 47 mg (15%) of 4'-methoxy-4-nitrodeoxybenzoin (**7b**).

4-Methoxy-4'-nitrobenzil (**9b**).

This compound was prepared as yellow crystals (acetone-hexane), mp 156-158°; ir: ν 3108, 3080 (CH), 1676, 1652 (C=O), 1598 (aromatic CC), 1528, 1348 (NO_2), 1322 (Ar-CO), 1266, 1028 br (C-O-C), 1212 (C-N), 846 (aromatic CH) cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.35 (d, 2H, H-3', 5'), 8.16 (d, 2H, H-2', 6'), 7.96 (d, 2H, H-3, 5), 7.00 (d, 2H, H-2, 6), 3.91 (s, 3H, OMe).

Anal. Calcd. for $C_{15}H_{11}NO_5$ (285.26): C, 63.16; H, 3.89; N, 4.91. Found: C, 63.11; H, 3.72; N, 4.77.

Reaction of *trans*-2,3-Dihydro-2-aryl-3-mesyloxy-4*H*-1-benzopyran-4-ones **10a-c** with Potassium Cyanide.

A mixture of **10** mesylate (3.00 mmoles), potassium cyanide (400 mg, 6.14 mmoles) and the appropriate solvent (see Table 2) was allowed to react at room temperature until the reaction was complete (tlc), poured into brine and extracted with diethyl ether. The dried extract was evaporated and separated by colum chromatography (hexane:ethyl acetate (4:1, v/v)). Details are given in Table 2.

2,3-Dihydro-*t*-4-cyano-*c*-3,*c*-4-epoxy-*r*-2-phenyl-4*H*-1-benzopyran (**11a**).

This compound was obtained as white crystals (hexane), mp 74-75°; ir: ν 3080, 3060, 3025 (CH), 2255w (CN), 1608, 1587, 1496, 1489 (aromatic CC), 1275, 931, 839 (epoxide ring), 1218, 1023 (flavan skeleton), 758, 750 (aromatic CH) cm^{-1}; ^1H nmr (deuteriochloroform): δ 7.72 (dd, 1H, H-5), 7.20-7.40 (m, 6H, Ph + H-7), 7.09 (ddd, 1H, H-6), 6.86 (dd, 1H, H-8), 5.63 (d, 1H, H-2, J = 1.2 Hz), 4.32 (d, 1H, H-3, J = 1.2 Hz); ^{13}C-nmr (deuteriochloroform): 151.23 (C-4a), 135.33 (C-1'), 132.55 (C-5), 129.37 (C-7), 129.19 (C-3', 5'), 128.59 (C-2', 6'), 122.09 (C-6), 118.42 (C-8), 115.27, 115.22 (C-8a and CN), 73.17 (C-2), 64.29 (C-3), 45.67 (C-4).

Anal. Calcd. for $C_{16}H_{11}NO_2$ (249.27): C, 77.10; H, 4.45; N, 5.62. Found: C, 76.95; H, 4.51; N, 5.72.

2,3-Dihydro-*t*-4-cyano-*c*-3,*c*-4-epoxy-*r*-2-(4-methoxyphenyl)-4*H*-1-benzopyran (**11b**).

This compound was obtained as an oil after column chromatography; ir (neat): ν 2948, 2942, 2830 (OMe), 2238w (CN), 1608, 1582, 1510, 1486, 1458 (aromatic CC), 1270, 921 (epoxide ring), 1214, 1022 (flavan skeleton), 829, 750 (aromatics CH) cm^{-1}; ^1H nmr (deuteriochloroform): δ 7.69 (dd, 1H, H-5), 7.30 (ddd, 1H, H-7), 7.15 (dd, 2H, H-2', 6'), 7.03 (ddd, 1H, H-6), 6.84 (dd, 2H, H-3', 5'), 6.79 (d, 1H, H-2, J = 1.5 Hz), 4.28 (d, 1H, H-3, J = 1.5 Hz), 3.74 (s, 3H, MeO); ms: 279 ($M^{+\cdot}$, 96), 263 (71), 262 (77), 250 (82), 248 (31), 235 (21), 220 (29), 219 (28), 207 (11), 190 (19), 159 (100), 156 (17), 150 (15), 144 (11), 135 (21), 121 (54), 120 (50), 108 (26).

Anal. Calcd. for $C_{17}H_{13}NO_3$ (279.30): C, 73.11; H, 4.69; N, 5.02. Found: C, 72.99; H, 4.66; N, 4.89.

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