A Convenient Synthesis of 3-Chloro-3,4-dihydro-4-hydroxy-3-nitro-2-phenyl-2*H*-1-benzopyrans

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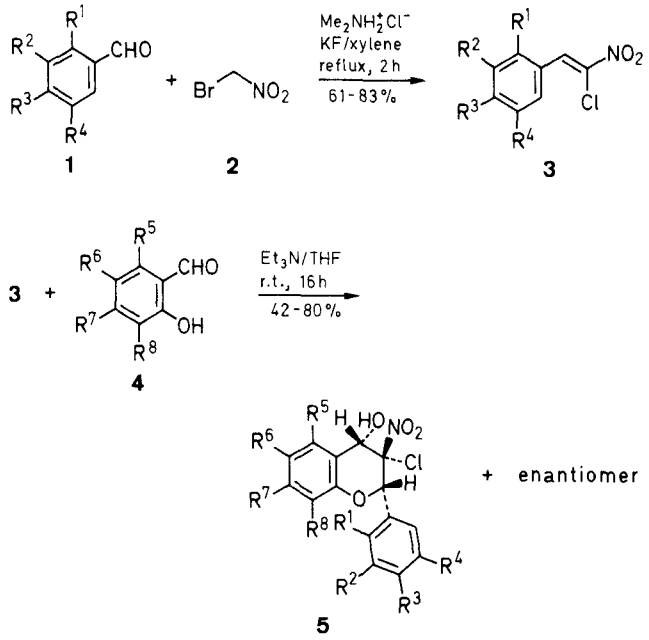
The novel title compounds **5** are prepared by a simple and efficient two-step procedure starting from substituted benzaldehydes **1**. A convenient route to the (2-chloro-2-nitroethenyl)benzenes **3** required as intermediates in the synthesis is reported.

In a previous paper,[1] we described the preparation of 2-(2-chloro-2-nitroethenyl)phenols. This novel class of compounds proved useful intermediates in the synthesis of 2-nitro-2,3-dihydrobenzofurans.[2] In continuation of our work on the synthetic applications of (2-chloro-2-nitroethenyl)benzenes **3**, we report here their use in the synthesis of six-membered oxygen-containing benzo-annulated heterocycles. We have found that, on treat-

ment with *o*-hydroxybenzaldehydes **4** in the presence of triethylamine in tetrahydrofuran at room temperature, (2-chloro-2-nitroethenyl)benzenes **3** are stereoselectively converted into the hitherto unknown 3-chloro-3,4-dihydro-4-hydroxy-3-nitro-2-phenyl-2*H*-1-benzopyrans **5**. Among the four possible diastereoisomers, only the relative configuration 2*S**, 3*S**, 4*S** is obtained.

The scope of this chemical process has been investigated with a number of substrates, including compounds bearing either electron-withdrawing groups or electron-donating groups in various positions, and was found to be very broad. However, the attempted condensations involving 2-(2-chloro-2-nitroethenyl)phenols[1] were unsuccessful.



1,3	R^1	R^2	R^3	R^4
a	H	H	H	H
b	Cl	H	H	H
c	H	Cl	H	H
d	H	H	Cl	H
e	NO_2	H	H	H
f	H	NO_2	H	H
g	H	H	NO_2	H
h	OMe	H	H	H
i	H	OMe	H	H
j	H	H	OMe	H
k	H	OMe	OMe	OMe
l	CH_3	H	H	H
m	H	H	$-(CH=CH)_2-$	

4	R^5	R^6	R^7	R^8
a	H	H	H	H
b	OMe	H	H	H
c	H	OMe	H	H
d	H	H	OMe	H
e	H	H	H	OMe
f	H	Br	H	Br
g	H	Cl	H	H
h	H	NO_2	H	H

Of the (2-chloro-2-nitroethenyl)benzenes **3** required for the reaction, some of which have been reported to show various interesting biological properties,[3-9] only two have been previously described, **3a**[10] and **3g**,[11] obtained in ungiven or very low yields by special procedures.

The lack of a reliable method prompted us to synthesize compounds **3** by modifying the procedure previously reported for 2-(2-chloro-2-nitroethenyl)phenols.[1] In the present case, it is particularly important to perform the condensation between substituted benzaldehydes **1** and bromonitromethane **(2)** at higher temperatures and in the presence of a large excess of dimethylammonium chloride in order to avoid the formation of the corresponding bromo derivatives as side-products.

The sole *Z* structure for compounds **3** as well as the stereochemistry of the prepared title compounds **5** have been ascertained by X-ray crystallography by examining the case of (2-chloro-2-nitroethenyl)benzene **(3a)** and that of the chloro derivative **(5da)**, respectively, selected as representative of their class of products.

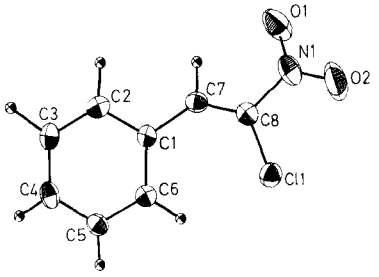


Figure 1. ORTEP perspective diagram of **3a** with thermal ellipsoids at 30% probability.

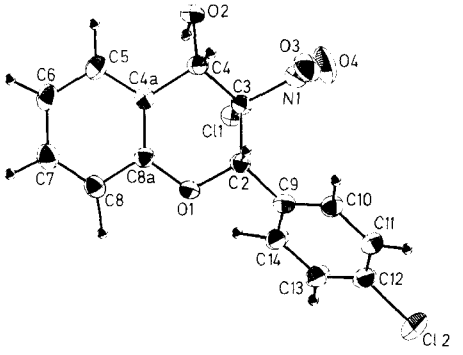


Figure 2. ORTEP perspective diagram of **5da** with thermal ellipsoids at 30% probability.

The (*Z*)-form determined for compounds **3** in the present work is in good agreement with the conclusions of the ^{1}H-NMR analysis based on the comparison of the chemical shifts (Table 1) with those published for (*Z*)- and (*E*)-(2-chloro-2-nitroethenyl)benzene **(3a)**.[12]

The unusually large $^3J_{H,OH}$ coupling constants observed in almost all of the ^{1}H-NMR spectra of compounds **5** (Table 2) is indicative of predominantly antiperiplanar conformations.[13-18] In this context, it is noteworthy that such a conformation exists clearly in the crystal of **5da**

Table 1. (2-Chloro-2-nitroethenyl)benzenes **3** Prepared

Product	Yield[a] (%)	mp (°C) (Solvent)	Molecular Formula[b] or Lit. mp (°C)	^{1}H-NMR ($CDCl_3$/TMS) δ, J(Hz)
3a	79	48.5–49.5 (pentane)	48–49[10]	7.38–7.63 (m, 3H). 7.73–7.98 (m, 2H), 8.36 (s, 1H)
3b	76	53.5–54.5 (pentane)	$C_8H_5Cl_2NO_2$ (218.0)	7.27–7.62 (m, 3H), 7.85–8.08 (m, 1H), 8.67 (s, 1H)
3c	70	45–46 (pentane)	$C_8H_5Cl_2NO_2$ (218.0)	7.30–7.80 (m, 3H), 7.85 (br. s, 1H), 8.30 (s, 1H)
3d	82	107–108.5 (heptane)	$C_8H_5Cl_2NO_2$ (218.0)	7.48 (d, 2H, J = 9.0), 7.82 (d, 2H, J = 9.0), 8.34 (s, 1H)
3e	70	85–86 (benzene/hexane)	$C_8H_5ClN_2O_4$ (228.6)	7.57–7.92 (m, 3H), 8.18–8.40 (m, 1H), 8.70 (s, 1H)
3f	61	111–112 (benzene/cyclohexane)	$C_8H_5ClN_2O_4$ (228.6)	7.70 (t, 1H, J = 8.0), 8.13 (ddd, 1H, J = 1.2, 1.8, 8.0), 8.37 (ddd, 1H, J = 1.2, 2.4, 8.0), 8.42 (s, 1H), 8.73 (dd, 1H, J = 1.8, 2.4)
3g	65	150–151.5 (benzene/cyclohexane)	150–153[11]	8.00 (d, 2H, J = 9.0), 8.35 (d, 2H, J = 9.0), 8.41 (s. 1H)
3h	73	60–61 (hexane)	$C_9H_8ClNO_3$ (213.6)	3.91 (s, 3H), 6.95 (br d, 1H, J = 8.4), 7.03 (br t, 1H, J = 7.8), 7.46 (dt, 1H, J = 1.8, 8.4), 8.04 (dd, 1H, J = 1.8, 7.8), 8.78 (s, 1H)
3i	75	56–57 (hexane)	$C_9H_8ClNO_3$ (213.6)	3.86 (s, 3H), 6.93–7.17 (m, 1H), 7.32–7.49 (m, 3H), 8.34 (s, 1H)
3j	79	74–75 (hexane)	$C_9H_8ClNO_3$ (213.6)	3.87 (s, 3H), 6.99 (d, 2H, J = 9.2), 7.86 (d, 2H, J = 9.2), 8.35 (s, 1H)
3k	82	124–125 (heptane)	$C_{11}H_{12}ClNO_5$ (273.7)	3.93 (s, 6H), 3.96 (s, 3H), 7.13 (s, 2H), 8.32 (s, 1H)
3l	72	41.5–42.5 (pentane)	$C_9H_8ClNO_2$ (197.6)	2.41 (s, 3H), 7.16–7.49 (m, 3H), 7.70–7.93 (m, 1H), 8.53 (s, 1H)
3m	83	116–117 (cyclohexane)	$C_{12}H_8ClNO_2$ (233.7)	7.41–8.02 (m, 6H), 8.32 (br s, 1H), 8.51 (s, 1H)

[a] Yield of recrystallized product based on **1**.

[b] Satisfactory microanalyses obtained: C ±0.20, H ±0.12, N ±0.15.

Table 2. 3-Chloro-3,4-dihydro-4-hydroxy-3-nitro-2-phenyl-2*H*-1-benzopyrans **5** Prepared

Starting Materials	Product	Yield (%)[a] (Method)	mp (°C) (Solvent)	Molecular Formula[b]	^{1}H-NMR ($CDCl_3$/TMS) δ, J(Hz)
3a + **4a**	**5aa**	77 (A)	126–127.5 (hexane)	$C_{15}H_{12}ClNO_4$ (305.7)	2.45 (d, 1H, J = 12.0),[c] 5.77 (s, 1H), 6.03 (d, 1H, J = 12.0), 6.93–7.68 (m, 9H)
3b + **4a**	**5ba**	45 (A)	119.5–120.5 (hexane)	$C_{15}H_{11}Cl_2NO_4$ (340.2)	2.54 (d, 1H, J = 12.0),[c] 6.18 (d, 1H, J = 12.0), 6.32 (s, 1H), 6.88–7.50 (m, 6H), 7.61 (br d, 1H, J = 7.5), 7.92–8.10 (m, 1H)
3c + **4a**	**5ca**	80 (A)	120–122 (hexane)	$C_{15}H_{11}Cl_2NO_4$ (340.2)	2.45 (d, 1H, J = 12.0),[c] 5.74 (s, 1H), 5.99 (d, 1H, J = 12.0), 6.92–7.68 (m, 8H)
3d + **4a**	**5da**	73 (A)	151.5–152.5 (cyclohexane)	$C_{15}H_{11}Cl_2NO_4$ (340.2)	2.46 (d, 1H, J = 12.0),[c] 5.75 (s, 1H), 5.99 (d, 1H, J = 12.0), 6.88–7.67 (m, 8H)
3e + **4a**	**5ea**	41 (A)	166–167 (benzene/cyclohexane)	$C_{15}H_{11}ClN_2O_6$ (350.7)	2.67 (d, 1H, J = 10.8),[c] 6.03 (d, 1H, J = 10.8), 6.70 (s, 1H), 6.77–8.37 (m, 8H)
3f + **4a**	**5fa**	80 (A)	181–182 (benzene/cyclohexane)	$C_{15}H_{11}ClN_2O_6$ (350.7)	2.52 (d, 1H, J = 12.0),[c] 5.92 (s, 1H), 6.04 (d, 1H, J = 12.0), 6.95–7.85 (m, 6H), 8.23–8.57 (m, 2H)
3g + **4a**	**5ga**	69 (A)	175–176 (benzene/heptane)	$C_{15}H_{11}ClN_2O_6$ (350.7)	2.52 (d, 1H, J = 12.0),[c] 5.91 (s, 1H), 6.04 (d, 1H, J = 12.0), 6.92–7.68 (m, 4H), 7.67 (d, 2H, J = 9.0), 8.26 (d, 2H, J = 9.0)
3h + **4a**	**5ha**	49 (A)	170–170.5[d] (benzene/heptane)	$C_{16}H_{14}ClNO_5$ (335.7)	2.46 (d, 1H, J = 11.5),[c] 3.73 (s, 3H), 6.20 (d, 1H, J = 11.5), 6.26 (s, 1H), 6.78–7.51 (m, 6H), 7.60 (br d, 1H, J = 7.5), 7.82 (dd, 1H, J = 1.8, 7.5)
3i + **4a**	**5ia**	65 (A)	162–163 (benzene/cyclohexane)	$C_{16}H_{14}ClNO_5$ (335.7)	2.44 (d, 1H, J = 12.0),[c] 3.82 (s, 3H), 5.73 (s, 1H), 6.00 (d, 1H, J = 12.0), 6.85–7.45 (m, 7H), 7.58 (br d, 1H, J = 7.5)
3j + **4a**	**5ja**	61 (A)	143–144 (benzene/heptane)	$C_{16}H_{14}ClNO_5$ (335.7)	2.45 (d, 1H, J = 12.0),[c] 3.81 (s, 3H), 5.71 (s, 1H), 6.00 (d, 1H, J = 12.0), 6.90 (d, 2H, J = 9.0), 7.40 (d, 2H, J = 9.0), 6.80–7.68 (m, 4H)
3k + **4a**	**5ka**	63 (A)	167–168 (benzene/hexane)	$C_{18}H_{18}ClNO_7$ (395.8)	2.57 (d, 1H, J = 11.7),[c] 3.86 (s, 9H), 5.70 (s, 1H), 6.01 (d, 1H, J = 11.7). 6.68 (s, 2H), 6.92–7.70 (m, 4H)
3l + **4a**	**5la**	44 (A)	111–112 (hexane)	$C_{16}H_{14}ClNO_4$ (319.7)	2.34 (s, 3H), 2.48 (d, 1H, J = 12.0),[c] 6.01 (s, 1H), 6.07 (d, 1H, J = 12.0), 6.84–7.47 (m, 6H), 7.59 (br d, 1H, J = 7.5), 7.77–8.01 (m, 1H)
3m + **4a**	**5ma**	70 (A)	157–158 (cyclohexane)	$C_{19}H_{14}ClNO_4$ (355.8)	2.45 (d, 1H, J = 12.0),[c] 5.93 (s, 1H), 6.06 (d, 1H, J = 12.0), 6.95–8.02 (m, 11H)
3d + **4b**	**5db**	42 (B)	174–175 (benzene/cyclohexane)	$C_{16}H_{13}Cl_2NO_5$ (370.2)	3.02 (d, 1H, J = 3.4),[c] 3.89 (s, 3H), 5.38 (d, 1H, J = 3.4), 5.88 (s, 1H), 6.55 (d, 1H, J = 8.5), 6.60 (d, 1*H*, J = 8.5), 7.27 (t, 1*H*, J = 8.5), 7.33 (br d, 2H, J = 8.8), 7.67 (br d, 2H, J = 8.8)
3d + **4c**	**5dc**	79 (B)	186–187 (benzene/heptane)	$C_{16}H_{13}Cl_2NO_5$ (370.2)	2.48 (d, 1H, J = 12.0),[c] 3.79 (s, 3H), 5.67 (s, 1H), 594 (d, 1H, J = 12.0), 6.83–7.12 (m, 3H), 7.37 (s, 4H)
3d + **4d**	**5dd**	59 (B)	181–183 (benzene/cyclohexane)	$C_{16}H_{13}Cl_2NO_5$ (370.2)	2.39 (d, 1H, J = 12.0),[c] 3.80 (s, 3H), 5.71 (s, 1H), 5.92 (d, 1H, J = 12.0), 6.50 (d, 1H, J = 2.4), 6.68 (dd, 1H, J = 2.4, 8.7), 7.37 (s, 4H), 7.43 (d, 1H, J = 8.7)
3d + **4e**	**5de**	70 (B)	206–207[e] (benzene/heptane)	$C_{16}H_{13}Cl_2NO_5$ (370.2)	2.44 (d, 1H, J = 12.0),[c] 3.85 (s, 3H), 5.71 (s, 1H), 5.96 (d, 1H, J = 12.0), 6.80–7.52 (m, 7H)
3d + **4f**	**5df**	74 (B)	190.5–191.5 (benzene/heptane)	$C_{15}H_9Br_2Cl_2NO_4$ (498.0)	2.50 (d, 1H, J = 12.0),[c] 5.80 (s, 1H), 5.95 (d, 1H, J = 12.0), 7.39 (s, 4H), 7.55–7.78 (m, 2H)

Table 2. (continued)

Starting Materials	Product	Yield (%)[a] (Method)	mp (°C) (Solvent)	Molecular Formula[b]	^{1}H-NMR ($CDCl_3$/TMS) δ, J (Hz)
3d + 4g	**5dg**	75 (B)	187–188 (benzene/heptane)	$C_{15}H_{10}Cl_3NO_4$ (374.6)	2.50 (d, 1H, J = 12.0),[c] 5.72 (s, 1H), 5.95 (d, 1H, J = 12.0), 6.91 (d, 1H, J = 9.0), 7.26 (br d, 1H, J = 9.0), 7.36 (s, 4H), 7.50–7.60 (m, 1H)
3d + 4h	**5dh**	65 (B)	210–211 (benzene/heptane)	$C_{15}H_{10}Cl_2N_2O_6$ (385.2)	2.75 (br d, 1H, J = 12.0),[c] 5.87 (s, 1H), 6.03 (br d, 1H, J = 12.0), 7.10 (d, 1H, J = 9.0), 7.37 (s, 4H), 8.20 (dd, 1H, J = 2.8, 9.0), 8.50 (br d, 1H, J = 2.8)

[a] Yield of recrystallized product based on **3**.
[b] Satisfactory microanalyses obtained: C ± 0.24, H ± 0.10, N ± 0.17.
[c] Exchangeable with D_2O.
[d] Allotropic change at 163–166°.
[e] Allotropic change at 194–198 °C.

where a hydrogen bond between the hydroxyl proton and the vicinal chlorine atom is evidenced by X-ray analysis (length = 2.44 Å). The markedly lower $^3J_{H,OH}$ coupling measured for **5db** is due to the presence of a methoxy group in 5-position which significantly affects the geometry of the molecule; probably because of specific hydrogen bonding involving the hydroxyl proton and the oxygen atom of the methoxy group.

The benzopyran derivatives **5** are sensitive to aqueous bases, which induce a reverse reaction and yield the starting materials quantitatively.

Melting points were determined on a Kofler hot stage apparatus and are uncorrected. Microanalyses were performed by the Service d'Analyses du CNRS, Vernaison. ^{1}H-NMR spectra were recorded at 90 MHz using a Varian EM 390 spectrometer. 2-Hydroxy-6-methoxybenzaldehyde (**4b**) was prepared according to a previously described procedure.[19,20] All other substituted 2-hydroxybenzaldehydes **4** are commercially available.

(2-Chloro-2-nitroethenyl)benzenes 3a–m; General Procedure:
The appropriate aldehyde **1a–m** (0.1 mol), dimethylammonium chloride (73.4 g, 0.9 mol), xylene (250 mL), bromonitromethane (**2**; 26.30 g, 0.188 mol), and KF (870 mg, 15 mmol) are placed in a 500 mL Erlenmeyer flask fitted with a Dean Stark apparatus (capacity about 20 mL). The mixture is vigorously refluxed with stirring for 2 h, then allowed to cool to r.t. The volatiles are removed *in vacuo* using a rotary evaporator to leave a residue, which is partitioned between H_2O (100 mL) and CH_2Cl_2 (300 mL). The organic phase is separated and the aqueous layer is extracted with CH_2Cl_2 (3 × 100 mL). The combined organic extracts are dried ($MgSO_4$), filtered, then evaporated under reduced pressure to give a crude material, which is chromatographed on a silica gel column (400 g, 200–400 mesh, eluent CH_2Cl_2). Evaporation of the solvent followed by recrystallization affords analytically pure compounds **3a–m** (Table 1).

3-Chloro-3,4-dihydro-4-hydroxy-3-nitro-2-phenyl-2*H*-1-benzopyrans 5; General Procedure:
Method A, *for 3-chloro-3,4-dihydro-4-hydroxy-3-nitro-2-phenyl-2H-1-benzopyrans* **5aa–ma:** The appropriate (2-chloro-2-nitroethenyl)benzene **3a–m** (20 mmol) is placed in a 100 mL round-bottomed flask fitted with a drying tube and dissolved in a mixture of dry THF (20 mL) and salicylaldehyde (**4a**; 12 mL). Anhydrous Et_3N (1.5 mL) is added and the solution is magnetically stirred at r.t. for 16 h. The volatiles are then removed on a rotary-evaporator under reduced pressure (0.7 Torr) at 45 °C in order to remove the most of unreacted salicylaldehyde (excessive heating must be avoided). The crude material is directly chromatographed over a silica gel column [300 g, 200–400 mesh, eluent CH_2Cl_2/hexane (75:25), then pure CH_2Cl_2]. Removal of the solvents *in vacuo* followed by recrystallization yields analytically pure products **5aa–ma** (Table 2).

Table 3. Bond Lengths (Å) and Angles (deg) for **3a**

Atoms		Atoms	
Cl(1)–C(8)	1.698(6)	O(1)–N(1)	1.203(7)
O(2)–N(1)	1.199(6)	N(1)–C(8)	1.473(6)
C(1)–C(2)	1.388(7)	C(1)–C(6)	1.403(6)
C(1)–C(7)	1.457(7)	C(2)–C(3)	1.383(8)
C(3)–C(4)	1.371(8)	C(4)–C(5)	1.373(8)
C(5)–C(6)	1.375(7)	C(7)–C(8)	1.330(7)
O(2)–N(1)–O(1)	123.7(6)	C(8)–N(1)–O(1)	118.4(6)
C(8)–N(1)–O(2)	117.9(6)	C(6)–C(1)–C(2)	118.6(5)
C(7)–C(1)–C(2)	118.1(4)	C(7)–C(1)–C(6)	123.2(5)
C(3)–C(2)–C(1)	120.9(5)	C(4)–C(3)–C(2)	119.4(5)
C(5)–C(4)–C(3)	120.7(5)	C(6)–C(5)–C(4)	120.6(5)
C(5)–C(6)–C(1)	119.8(5)	C(8)–C(7)–C(1)	131.6(5)
N(1)–C(8)–Cl(1)	113.6(4)	C(7)–C(8)–Cl(1)	127.6(4)
C(7)–C(8)–N(1)	118.8(5)		

Table 4. Bond Lengths (Å) and Angles (deg) for **5da**

Atoms		Atoms	
Cl(1) –C(3)	1.801(4)	Cl(2) –C(12)	1.741(4)
O(1) –C(2)	1.431(5)	O(1) –C(8a)	1.377(5)
O(2) –C(4)	1.403(5)	O(3) –N(1)	1.211(5)
O(4) –N(1)	1.186(5)	N(1) –C(3)	1.530(5)
C(2) –C(3)	1.542(5)	C(2) –C(9)	1.511(5)
C(3) –C(4)	1.537(5)	C(4) –C(4a)	1.504(6)
C(4a)–C(5)	1.394(6)	C(4a)–C(8a)	1.384(5)
C(5) –C(6)	1.393(6)	C(6) –C(7)	1.371(7)
C(7) –C(8)	1.385(7)	C(8) –C(8a)	1.380(6)
C(9) –C(14)	1.382(6)	C(9) –C(10)	1.382(6)
C(11)–C(12)	1.368(6)	C(10)–C(11)	1.378(6)
C(13)–C(14)	1.385(6)	C(12)–C(13)	1.375(7)
C(8a)–O(1) –C(2)	117.8(3)	O(4) –N(1) –O(3)	124.8(4)
C(3) –N(1) –O(3)	114.9(4)	C(3) –N(1) –O(4)	120.3(4)
C(3) –C(2) –O(1)	109.1(3)	C(9) –C(2) –O(1)	108.1(3)
C(9) –C(2) –C(3)	114.1(3)	N(1) –C(3) –Cl(1)	109.3(3)
C(2) –C(3) –Cl(1)	111.4(3)	C(2) –C(3) –N(1)	108.1(3)
C(4) –C(3) –Cl(1)	110.5(3)	C(4) –C(3) –N(1)	107.8(3)
C(4) –C(3) –C(2)	109.6(3)	C(3) –C(4) –O(2)	112.4(3)
C(4a)–C(4) –O(2)	111.8(3)	C(4a)–C(4) –C(3)	109.0(3)
C(5) –C(4a)–C(4)	119.9(4)	C(8a)–C(4a)–C(4)	121.2(3)
C(8a)–C(4a)–C(5)	118.8(4)	C(6) –C(5) –C(4a)	120.3(4)
C(7) –C(6) –C(5)	119.9(4)	C(8) –C(7) –C(6)	120.2(4)
C(8a)–C(8) –C(7)	119.9(4)	C(4a)–C(8a)–O(1)	123.0(3)
C(8) –C(8a)–O(1)	116.2(3)	C(8) –C(8a)–C(4a)	120.8(4)
C(14)–C(9) –C(2)	121.0(4)	C(10)–C(9) –C(2)	120.2(4)
C(10)–C(9) –C(14)	118.8(4)	C(13)–C(14)–C(9)	121.0(4)
C(10)–C(11)–C(12)	119.6(4)	C(11)–C(10)–C(9)	120.6(4)
C(12)–C(13)–C(14)	118.7(4)	C(13)–C(12)–Cl(2)	119.2(3)
C(11)–C(12)–Cl(2)	119.5(4)	C(11)–C(12)–C(13)	121.2(4)

Method B, *for 3-Chloro-3,4-dihydro-4-hydroxy-3-nitro-2-phenyl-2H-1-benzopyrans* **5db–dh**: In a 50 mL round-bottomed flask equipped with a drying tube, the appropriate 2-hydroxybenzaldehyde **4b–h** (55 mmol) and 4-chloro-(2-chloro-2-nitroethenyl)benzene (**3d**; 2.18 g, 10 mmol) are dissolved in anhydrous THF (10 mL for **4b–f**, 20 mL for **4g** or 30 mL for **4h**). Anhydrous Et_3N (0.75 mL) is added, then the solution is magnetically stirred at r.t. for 16 h. Removal of the volatiles under reduced pressure (0.7 Torr) at 45 °C leaves a residue, which is taken up with a lukewarm solution (50 °C) of Girard's reagent T [prepared by dissolving the reagent (9.62 g, 55 mmol) in a mixture of EtOH/H_2O/AcOH (8:1:1, 75 mL)]. This reaction mixture is vigorously stirred for 1 h at r.t., then diluted with H_2O (75 mL) and CH_2Cl_2 (150 mL). If an insoluble material remains, it is suction-filtered and thoroughly rinsed with CH_2Cl_2 (3 × 50 mL). The combined organic extracts are dried ($MgSO_4$), filtered and concentrated *in vacuo* to give an aldehyde-free material, which is flash-chromatographed on silica gel (150 g, 200–400 mesh, eluent CH_2Cl_2). Evaporation of the solvent followed by recrystallization provides analytically pure compounds **5db–dh** (Table 2).

This method B allows the facile recovery of unreacted aldehydes after acidic hydrolysis of the hydrazone derivatives.

X-Ray Diffraction Studies of 3a and 5da:

Crystal Data:

3a: Orthorhombic space group Pbca; unit cell a = 19.562 (4), b = 11.365 (1), c = 7.390 (3) Å; V = 1643 (1) Å^3; μ = 4.2 cm^{-1}; D_{calc} = 1.48 g cm^{-3}; Z = 8.

5da: Monoclinic space group $P2_{1/c}$; unit cell a = 14.597 (3), b = 12.338 (2), c = 8.241 (2) Å; β = 91.52 (2)°; V = 1483.7 (6) Å^3; μ = 4.5 cm^{-1}; D_{calc} = 1.52 g cm^{-3}; Z = 4.

Parameters obtained from least squares refinement of twenty-five reflections in the 13–14° Θ range.

Data Collection: The crystals sizes were respectively 0.40 × 0.35 × 0.20 mm for **3a** and 0.40 × 0.30 × 0.30 mm for **5da**; Philips PW1100 diffractometer; Mo K_α radiations (λ = 0.71073 Å) and graphite monochromator; 1365 independent reflections for **3a** and 2414 for **5da** in the range 1.50 ≤ Θ ≤ 25° were measured; ω-2 Θ scan mode; scan width (1.0 + 0.34 tan Θ)°; no absorption correction as suggested by a flat psi-scan.

Structure Resolution and Refinement: Both structures were solved by direct methods and subsequent Fourier maps. Full matrix refinement with 826 reflections for **3a** and three blocks least squares refinement with 1609 reflections for **5da** [F ≥ 3σ(F)]. Hydrogen atoms were found on a difference map and refined with an overall isotropic thermal parameter. The refinements converged respectively at R = 0.048, $R_w = [\Sigma w(F)^2/\Sigma w F_o^2]^{1/2}$ = 0.047 for **3a** and at R = 0.052, R_w = 0.055 for **5da**. The largest shift/error ratio at this stage was less than 0.05. The final difference map showed no significant features.

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