Influence of the Heterocyclic Side Ring on Orientation During Nitrations of 1,2-Alkylenedioxy-annelated Benzenes and Their Mononitro Derivatives

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Nitration of 1,2-alkylenedioxybenzenes **1** furnished the respective nitro derivatives **3** and **4** in the relative ratios: **4a**:**3a**/100:trace, **4b**:**3b**/98:2.4, **4c**:**3c**/86:14, **4e**:**3e**/91:9 and **4f**:**3f**/99:1.3. Nitration of **4** gave **5a**:**6a**:**8a**/0:0:100, **5b**:**6b**:**8b**/7.7:3.2:89, **5c**:**6c**:**8c**/23:12:65, **5d**:**6d**:**8d**/14:74:12, **5e**:**6e**:**8e**/27:18:55 and **5f**:**6f**:**8f**/23:7.0:70. Nitration of the isomeric **3** afforded the dinitro products **5**, **6** and **7** in the following relative ratios: **5a**:**6a**:**7a**/92:8:0, **5b**:**6b**:**7b**/80:20:0, **5c**:**6c**:**7c**/69:20:11, **5d**:**6d**:**7d**/45:19:36, **5e**:**6e**:**7e**/37:57:5.9 and **5f**:**6f**:**7f**/64:36:0. Nitration of 3-nitro-1,2-dimethoxybenzene (**9**) furnished: **10**:**11**/63:37. Orientation as a function of the heterocyclic ring-size is discussed.

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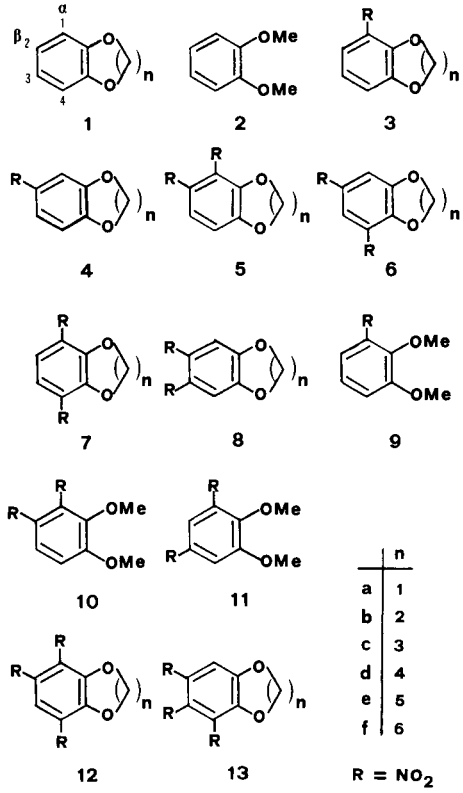
The 1,2-alkylenedioxy derivatives **1** provide fertile grounds for various mechanistic studies concerning electrophilic aromatic substitution (nitration in this case) [1-14], dedeuteration [15], detritiation [16], hydrolysis [17] and solvolytic reactions [18]. It is particularly intriguing to determine how variation in size of the 1,2-alkylenedioxy ring affects the outcome of these reactions. Inductive [13,17,18], resonance [8,13,16-19], conformational [12,13,16-19] and steric [13,17] effects, C_{aryl}-O-C_{alkyl} bond angle deformations [8,12,13,16,17,19], "built-in-solvation" [18], the Mills-Nixon effect [8,11,13,14,16,20], the Streitwieser-Finnegan rehybridization effect [16,21] and quasi-aromaticity [13] have been invoked to rationalize reactivity, orientation and some physical properties in these systems. To what extent one or more of these effects influence the transition state of a particular transformation, is a function of the heterocyclic ring-size firstly, and the type of reaction secondly.

Until recently, the bulk of the work has been carried out on the five- and six-membered heterocycles **1a** [1-5,8,12, 13,16-19] and **1b** [6-10,12,13,16-19,22] as well as on the acyclic analogue **2** [4,13,15-19,23,24]. Some reports included the seven-membered heterocycle **1c** [11-13,17-19], the nine-membered system **1e** [12,18] and one paper dealt with the eight-membered heterocycle **1d** [12]. Recently, we have reported that nitration of **1d** furnished the mononitro products **3d** and **4d** in the highest Ar-1 (Ar-α): Ar-2(Ar-β) ratio (23:77) observed in nitrations concerning the systems of type **1**. Furthermore, dinitration of **1d** afforded **6d** as the major reaction product, not previously obtained by direct nitration of these systems [14]. These results cast some doubt on some rules and generalizations previously expressed concerning electrophilic aromatic substitution of **1** or **4** [13], thus we decided to investigate the nitration products of the systems **1a-f**, **3a-f**, **4a-f** and **9**. Although nitration of some of these has been reported (see above), in our reinvestigation we have observed differences of a degree (different isomeric ratios) and of a kind (products not previously reported) both.



Nitrations of the 1,2-alkylenedioxybenzenes **1** were carried out under similar conditions employing an excess of concentrated nitric acid at 20-30° (1 hour). The isomeric mononitro products **3** and **4** were inseparable by either tlc or column chromatography; they did however separate by gc. The results are presented in Table 1 and plotted in Figure 1. We note that previous papers on nitration of **1a** [1-4], **1b** [6-9] and **1c** [11,12] report the Ar-2 products **4a-c** exclusively.

Inspection of Figure 1 reveals predominantly Ar-2 substitution as previously ascertained [1-14]. A new feature, however, is that Ar-1 selectivity increases progressively from the five- to the seven-membered heterocycles **1a-c**

Table 1
Nitration Products of **1**

Starting Compound	Isolated Yields, %	Relative Yields, % (by gc) 3	4
a	96	trace	100
b	98	2.4	98
c	88	14	86
d [a]	86	23	77
e	87	9	91
f	95	1.3	99

[a] Ref 14.

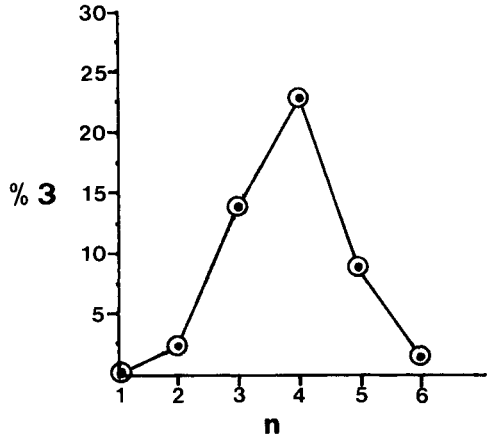


Figure 1. Relative yields, % of product **3** from nitration of **1** as a function of ring-size.

and it reaches a maximum value of 23% with the eight-membered system **1d** after which it falls again in the nine- and ten-membered heterocycles **1e,f**. The homologous derivatives **1** can be grouped into two categories: those with very low Ar-1 selectivity (**1a,b,f**) and those with relatively enhanced (**1c-e**). An attempt to increase the Ar-1:Ar-2 ratio by using a more reactive nitrating agent such as nitronium trifluoromethanesulfonate [25] was unsuccessful, as nitration of **1f** (a heterocycle with very low Ar-1 selectivity) gave identical results as those obtained above during conventional nitration.

Ar-1 and Ar-2 reactivity-selectivity in **1a**, **1b** and in veratrole (**2**) has been rationalized in terms of operation of the electron-releasing effect of the alkoxy oxygens (provided they are coplanar or nearly-coplanar with the benzene ring), conformational effects [8,13,16,18], the Mills-Nixon effect [8,16,13], rehybridization [16] and quasiaromaticity [13]. We have previously ascribed the enhanced Ar-1 selectivity of **1d** to the following two factors: a) Deviation of the alkoxy oxygen atoms from coplanarity with the benzene nucleus and b) supressed Mills-Nixon effect thus deactivating the Ar-1 position less in **1d** as compared to **1a** [14]. These two reasons are now invoked to rationalize the increased Ar-1 selectivity in the seven- and nine-membered rings **1c** and **1e** (although for **1e**, reason (a) may not be as effective since the heterocyclic ring may tend to reach near-coplanarity with the benzene ring due to its greater flexibility or due to a "built-in-solvation" effect [18]). Indeed, in these medium sized rings the strain imposed by fixation of the double bond at the carbon atoms common to the two rings should be insignificant so as to deactivate the Ar-1 position to a great extent. Moreover, the stabilizing factor due to the *para*-quinoidal resonance structures [16] should be decreased in **1c** (and to a lesser extent in **1e**) as compared to **1a** or **1b** due to less effective n-π conjugation thus deactivating the Ar-2 position more in **1c-e** than in **1a,b**. This factor (n-π conjugation) becomes important again in the ten-membered heterocycle **1f**, the selectivity of which approaches that of **1a**. This could be a consequence of the heterocyclic side ring to become nearly-coplanar with the benzene ring (due to its greater conformational mobility or perhaps due to "built-in-solvation") in the transition state of nitration, particularly since the incoming electrophile is electron-withdrawing [13] thus promoting Ar-2 substitution.

Further nitration of the Ar-2 mononitro derivatives **4** (with one Ar-β and two Ar-α positions available) under more drastic conditions (fuming nitric acid) furnished the 1,2-(**5**), 1,3-(**6**) and 2,3-(**8**) dinitro products as shown in Table 2 and Figure 2. With respect to the nitration of the eight-membered heterocycle **4d**, similar distribution of products has been previously obtained on dinitration of the parent compound **1d** [14]. Previous papers on nitration of **4b** do not report obtention of the products **5b** and **6b** [7,10].

Comparison of the results in Figures 1 and 2 shows similarities (in the qualitative sense) in orientation between the homologous series **1** and **4**. As in nitration of **1**, Ar-β substitution in **4** (reflected in product **8**) decreases with an increase in ring-size until it reaches a minimum value in the eight-membered heterocycle **4d**, after which it

Table 2
Nitration Products of **4**

Starting Compound	Isolated Yields, %	Relative Yields, % 5	6	8 [a]
a	92	0	0	100
b	93	7.7	3.2	89
c	94	23	12	65
d	89	14	74	12
e	99	27	18	55
f	100	23	7.0	70

[a] Separated by column chromatography.

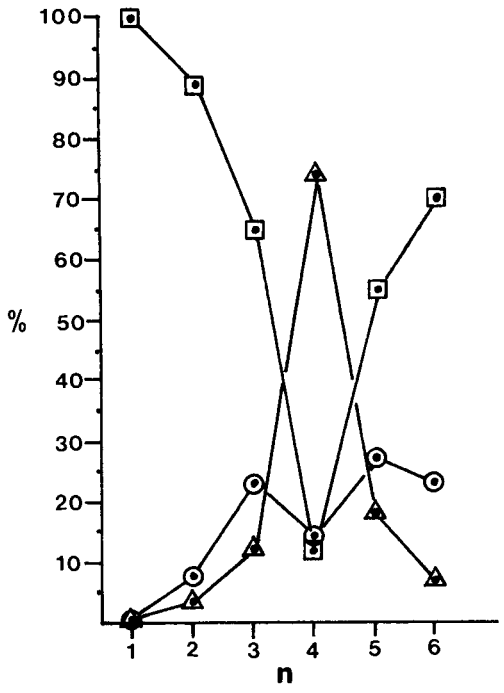


Figure 2. Relative yields, % of products **5** (⊙), **6** (△) and **8** (⊡) from nitration of **4** as a function of ring-size.

increases again in the nine- and ten-membered derivatives. Similarly, Ar-α substitution (sum of the products **5** and **6**) follows the pattern of products **3** during nitration of **1** (Figure 1). The diversity between the two series is that in the nitration of **4**, the quantitative differences among the members of this series are more pronounced compared to those in **1** (*i.e.*, for **4**, **8a**:**8b**:**8c**.../100:89:65..., whereas for **1**, **4a**:**4b**:**4c**.../100:98:86...).

It is interesting to compare the selectivity of the two Ar-α positions, *i.e.*, Ar-1 (products **5**) and Ar-4 (products **6**) with respect to ring-size during nitration of **4**. If one excludes the eight-membered compound **4d**, there is a steady increase in both Ar-1 and Ar-4 substitution in going from the five- (**4a**) to the nine-membered (**4e**) heterocycle, after which there is a small drop in the ten-membered system **4f**. In addition, the Ar-1 position is slightly preferred to Ar-4, except in **4d**, where substitution at the Ar-4 position preponderates over substitution at either Ar-1 or Ar-3 (Ar-β) positions. Thus, selectivity follows the order: Ar-3 > > Ar-1 > Ar-4 for the derivatives **4** at the exclusion, of course, of **4d**. The greater Ar-3 selectivity in **4a-c,e,f** may be rationalized in terms of the factors discussed above. The unique behavior of **4d** could be a consequence of the extreme deviation of the alkoxy oxygens from coplanarity with the benzene ring due to severe transannular interactions thus making a *para*-quinoidal resonance structure [16] (which has a stabilizing effect for Ar-3 substitution in the other heterocycles) less effective.

It has been previously asserted that in electrophilic aromatic substitutions of compounds **1** and **2** "almost only *p*-derivatives with respect to the alkoxy-groups are formed independent of the types of the first and the second substituents" [13]. Our results indicate this to be the case for **4a,b** and **2** [26]. However, in **4c-f**, nitration at the positions *ortho* to the alkoxy groups (Ar-α positions) ranges from 30 to 88% (sum of **5** and **6**) and we feel that these are considerable quantities.

Table 3

Nitration Products of **3**

Starting Compound	Isolated Yields, %	Relative Yields, % 5	6	7 [a]
a	80 (74)	92 (100)	8 (0)	0 (0)
b	73	80 (85)	20 (15)	0 (0)
c	93	69 (90)	20 (10)	11 (0)
d	99	45	19	36
e	93	37	57	5.9
f	74	64	36	0

[a] Separated by column chromatography. The values in parentheses are from ref 13.

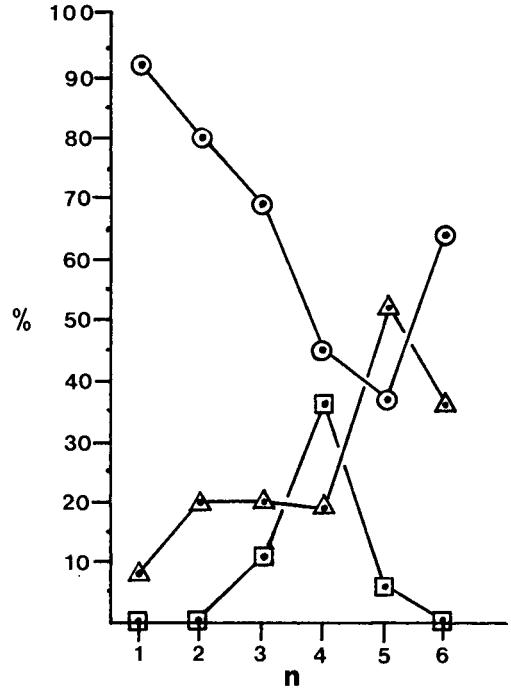


Figure 3. Relative yields, % of products **5** (⊙), **6** (△) and **7** (⊡) from nitration of **3** as a function of ring-size.

The mononitro derivatives **3** offer two Ar-β positions and one Ar-α for aromatic substitution. Nitration of **3** afforded the results shown in Table 3 and Figure 3. Some data from the literature [13] are also listed for comparison. It is observed that the products **6a** and **7c** have not been previously reported at all [13]. Moreover, we have repeated the nitration of the acyclic analogue **9** which gave the dinitro derivatives **10** (63%) and **11** (37%) in 86% isolated yield. In contrast, only isomer **10** (100%) is reported in the literature [13].

From Figure 3, the influence of the heterocyclic side ring is obvious again, as it can be seen by the progressive decrease in the relative yield of product **5** from the five- to the nine-membered ring. We note that the behavior of the ten-membered compound **3f** is similar to that of the acyclic derivative **9**. Also noteworthy is the shape of the curve of product **7** which is qualitatively similar to those of products **6** (Figure 2) and **3** (Figure 1), all for Ar-α substitution.

In reference to the electrophilic aromatic substitution of compounds of type **3** (R = any group), Daukšas and coworkers [13] have stated that only products of the type **5** and **6** (not **7**) are formed "as a rule". In nitration specifically, isomer **6** is favored if R is electron-donating, while isomer **5** predominates if R is electron-withdrawing. We have found this to be the case, in general, with the exception of **3e** where isomer **6e** is the major product (Table 3). Furthermore, we have obtained, in addition, isomer **7** in three cases (**3c-e**), in one of which (**3d**) in a considerable quantity (36%).

We have also nitrated the dinitro derivatives **5d** and **6d** with fuming nitric acid in order to determine the effect of a second nitro group. The former furnished the trinitro product **12d** exclusively in 68% yield, whereas **6d** afforded both **12d** (77%) and **13d** (23%) in 87% yield. Analogous results have been obtained by Heertjes and coworkers [22c] during nitration of **5b**. It seems that orientation at the two vacant aryl positions is not controlled as much by the heterocyclic side ring in these cases, as by the electronic and steric effects of the two nitro substituents.

Orientation during nitration of **1**, **3** and **4** is strongly influenced by the size of the heterocyclic side ring and to a lesser extent by the benzene ring substituent. Electronic, conformational and strain effects are involved to various degrees (according to ring-size) in determining the outcome of these electrophilic substitutions. Our observations necessitate a cautionary note that unless a homologous series is studied in more detail, generalizations as those found in the literature [13] should be avoided.

EXPERIMENTAL

General.

As previously described [14] with the following modifications and additions: The melting points were determined on a Gallenkamp or Kofler hot-stage apparatus. The ir spectra (chloroform solution) were obtained on a Perkin-Elmer Model 297 or 1310 or 1430 infrared spectrophotometer. The chromatographic fractions (gc or column chromatography) are listed in the order of increasing elution. All the crude solids were recrystallized from boiling ethanol (95%). Acetic acid refers to glacial acetic acid. Ether refers to ethyl ether. Exceptions are noted.

1,2-Dimethoxybenzene (Veratrole) (**2**) and 1,2-Alkylenedioxybenzenes (**1**).

Veratrole (**2**), benzo[1,3]dioxole (**1a**) and 2,3-dihydrobenzo[1,4]-dioxin (**1b**) were commercial samples from Fluka AG. 3,4-Dihydro-2*H*-benzo[*b*][1,4]dioxepin (**1c**) was prepared by the two methods described in the literature [19,27].

3,4,5,6-Tetrahydro-2*H*-benzo[*b*][1,4]dioxonin (**1e**) was prepared according to a slightly modified Ziegler procedure as described for the preparation of **1d** [14]. The reaction was carried out three times, each time using 9.42 g (36.4 mmoles) of 2-(5-bromopentoxy)phenol [27] (a total of 9.42 x 3 = 28.3 g, 109 mmoles were used). The combined residues were distilled to furnish **1e** (18.9 g, 97%) as a colorless viscous oil, bp 133-137° (16 torr) (lit [27] bp 122° (10 torr)); ir (neat): ν 1591 (w), 1573 (w), 1487 (s), 1285 (m), 1242 (s), 1183 (m), 1095 (m), 1052 (m), 1001 (m), 904 (m), 749 (m) cm^{-1}; ^1H nmr: δ 1.82 (m, 6H), 4.21 (m, 4H), 6.91 (s, 4H); the mass spectrum was similar to that reported [28].

2,3,4,5,6,7-Hexahydrobenzo[*b*][1,4]dioxecin (**1f**) was prepared as above, according to the modified Ziegler procedure [14]. Thus, 2-(6-bromohexoxy)phenol [27] (a total of 9.94 x 3 = 29.8 g, 109 mmoles were used) afforded **1f** (18.8 g, 90%) as a colorless viscous oil, bp 154-158° (16 torr) (lit [27] bp 140° (10 torr)); ir (neat): ν 1598 (w), 1496 (s), 1454 (m), 1388 (w), 1262 (s), 1197 (m), 1110 (m), 1040 (m), 1016 (m), 969 (m), 762 (m), cm^{-1}; ^1H nmr: δ 1.80 (m, 8H), 4.08 (m, 4H), 6.95 (s, 4H); ms: m/z (% relative intensity) 192 ($M^{+\cdot}$, 31), 122 (4), 121 (20), 110 (100), 109 (5), 105 (6), 83 (19), 82 (8), 81 (13), 80 (7), 77 (9), 67 (11), 65 (11), 64 (8), 63 (9), 55 (73), 53 (12), 52 (23), 51 (13), 41 (48), 39 (26).

The purity of all samples (**1**, **2**) was >98% as shown by analytical gc.

3-Nitrocatechol and 3-Nitroveratrole (**9**).

3-Nitrocatechol was prepared according to the method cited in the literature [29]. However, since the isolation described is complicated, we modified it as follows: At the end of the reaction, ether was distilled at atmospheric pressure and the dark brown residue was subjected to column chromatography. The column was eluted with chloroform:ethyl acetate/3:1 (v:v) to give 3-nitrocatechol and 4-nitrocatechol.

3-Nitrocatechol was treated with dimethyl sulfate and sodium hydroxide as described in the literature [23a] to afford (after purification by column chromatography using benzene to elute the column) 3-nitroveratrole (**9**) in 29% yield. Analytical gc indicated >99% purity. The sample was identical in all respects to that recently described in the literature [30].

General Nitration Procedures.

Nitrations with excess concentrated nitric acid (d = 1.42) were carried out as previously described by us for **1d** [14]. The Ar-α 3-nitro-1,2-alkylenedioxybenzenes **3** had invariably a smaller gc retention time than their Ar-β isomers **4**.

Nitrations with fuming nitric acid (d = 1.52) were carried out according to the following procedure: To a suspension of the compound to be nitrated and acetic acid, was added dropwise excess fuming nitric acid at 25°. The mixture was stirred at 25° for 30 minutes and decanted into ice-water. The aqueous mixture was extracted three times with ether or dichloromethane and the combined extracts were neutralized with sodium carbonate (solid or 10% solution), dried and concentrated *in vacuo*.

4- and 5-Nitrobenzo[1,3]dioxoles **3a** and **4a**.

A. From Nitration of **1a**.

Benzo[1,3]dioxole (**1a**) (1.71 g, 14.0 mmoles) was treated with nitric acid (8.0 ml) at 0° and the mixture was stirred at 25°. Analytical gc of a statistical sample indicated this to be a mixture of **3a** (trace) and **4a** (*ca.* 100%). Isomer **3a** had identical gc retention time with that of an authentic sample. Decantation of the reaction mixture in water furnished **4a** as a yellow solid (2.18 g). Extraction of the mother liquor with ether afforded an additional 76 mg (96% total). The ether extract was enriched in isomer **3a**.

Compound **4a** had mp (pale-yellow needles) 146-147° (lit [3] mp 147°, lit [4] mp 146-149°, lit [31] mp 146-147°); ir [32a]: ν 1627 (w), 1604 (w), 1513 (s), 1501 (s), 1484 (s), 1335 (s), 1266 (s), 1235 (m), 1030 (m), 918 (s), 868 (m), 822 (m), 740 (m) cm^{-1}; ^1H nmr [32]: δ 6.11 (s, 2H), 6.83 (d, J = 8.5 Hz, 1H), 7.63 (d, J = 2 Hz, 1H), 7.86 (dd, J = 8.5, 2 Hz, 1H); ms: m/z (% relative intensity) 167 ($M^{+\cdot}$, 100), 166 (8), 151 (3), 137 (17), 121 (36), 120 (10), 107 (19), 91 (18), 79 (12), 65 (56), 63 (50), 62 (25), 61 (11), 53 (19), 51 (14), 50 (10).

B. Compound **3a** from 3-Nitrocatechol.

An authentic sample of **3a** was prepared according to a method described in the literature for the preparation of 2,3-methylenedioxybenzaldehyde [33]. A mixture of 3-nitrocatechol (932 mg, 6.01 mmoles), diiodomethane (4.50 ml, 15.0 g, 56.0 mmoles), anhydrous potassium carbonate (3.50 g, 25.3 mmoles) and cupric oxide (200 mg) in dimethylformamide (20 ml) was heated at 160-170° for 2 hours. The solvent was removed by atmospheric distillation and the residue was decanted into water (200 ml) and extracted with ether. The crude product was purified by column chromatography to obtain **3a** (394 mg, 39%), mp (yellow needles) 116-118° (lit [34] mp 118-119°); ^1H nmr: δ 6.20 (s, 2H), 6.84 (dd, J = 7.8, 7.6 Hz, 1H), 7.06 (dd, J = 7.8, 2 Hz, 1H), 7.57 (dd, J = 7.8, 2 Hz, 1H). A ^1H nmr (dimethyl sulfoxide-d_6) was similar to that reported [34b].

5- and 6-Nitro-2,3-dihydrobenzo[1,4]dioxins **3b** and **4b**.

A. From Nitration of **1b**.

Benzodioxin **1b** (1.91 g, 14.0 mmoles) and nitric acid (8.0 ml) afforded **4b** as a yellow solid (2.39 g). Extraction of the mother liquor with ether gave 100 mg more (98% total). The ether extract was enriched in isomer **3b**. Analytical gc of a statistical sample withdrawn at the end of the reaction and previous to decantation in water indicated a mixture of **3b** (2.4%) and **4b** (*ca.* 98%). Isomer **3b** had identical gc retention time with that of an authentic sample.

Compound **4b** had mp (pale-yellow needles or leaflets) 120-122° (lit [6-8] mp 121-122°); ^1H nmr: δ 4.29 (s, 4H), 6.90 (d, J = 9.5 Hz, 1H), 7.73 (m, 2H); ms: as reported [35].

B. Compound **3b** from 3-Nitrocatechol.

Preparation of **3b** has been described [36]. However, we obtained a better yield by using the following modified procedure: A mixture of 3-nitrocatechol (507 mg, 3.27 mmoles), 1,2-dibromoethane (4.30 g, 22.9 mmoles) and anhydrous potassium carbonate (1.36 g, 9.84 mmoles) in isoamyl alcohol (40 ml) was heated at reflux (145-155°) for 7 hours. More 1,2-dibromoethane (3.0 g, 16 mmoles) and anhydrous potassium carbonate (2.19 g, 15.8 mmoles) were added to the initial mixture and heating at reflux continued for 8 additional hours. The isoamyl alcohol was removed by distillation at atmospheric pressure and the mixture was decanted into water (100 ml) and extracted with dichloromethane. Column chromatography furnished **3b** (441 mg, 74%) as a pale-yellow solid, mp (crude) 58-60° (lit [36] mp 60-61°); ^1H nmr: δ 4.36 (s, 4H), 6.85 (dd, J = 8, 8 Hz, 1H), 7.09 (dd, J = 8, 2 Hz, 1H), 7.45 (dd, J = 8, 2 Hz, 1H).

6- and 7-Nitro-3,4-dihydro-2*H*-benzo[*b*][1,4]dioxepins **3c** and **4c**.

Nitration of benzodioxepin **1c** (2.10 g, 14.0 mmoles) was performed as described for **1b** using 8.0 ml of nitric acid to give mainly **4c** as an orange solid (2.27 g). Ether extraction of the mother liquor furnished 121 mg additionally of a viscous orange oil (88% total), shown to be mainly isomer **3c**, purified by preparative gc. Analytical gc of a statistical sample withdrawn before the work-up procedure indicated a mixture of **3c** (14%) and **4c** (86%).

Compound **3c** had ir (neat): ν 1603 (w), 1575 (w), 1530 (s), 1483 (m), 1355 (m), 1301 (s), 1264 (s), 1077 (m), 1038 (m), 988 (w), 821 (m), 798 (w), 740 (m) cm^{-1}; ^1H nmr: as reported [37]; ms: m/z (% relative intensity) 195 ($M^{+\cdot}$, 100), 179 (2), 167 (3), 166 (10), 155 (4), 149 (6), 121 (6), 120 (6), 109 (10), 107 (59), 93 (7), 91 (6), 81 (7), 79 (17), 77 (7), 69 (11), 65 (18), 63 (12), 55 (11), 53 (13), 51 (30), 41 (45).

Anal. Calcd. for $C_9H_9NO_4$: C, 55.39; H, 4.65; N, 7.18. Found: C, 55.18; H, 4.71; N, 6.79.

Compound **4c** had mp (pale-yellow leaflets) 108-109° (lit [11] mp 106-107°, lit [12] mp 108-109°); ir (potassium bromide): ν 1608 (vw), 1585 (m), 1504 (s), 1348 (s), 1328 (s), 1271 (s), 1130 (m), 1079 (m), 1058 (m), 988 (m), 965 (m), 905 (s), 837 (m), 809 (m), 748 (m) cm^{-1}; ^1H nmr: as reported [12]; ms: m/z (% relative intensity) 195 ($M^{+\cdot}$, 100), 167 (8), 166 (29), 137 (8), 125 (3), 121 (9), 120 (11), 107 (16), 91 (7), 79 (18), 77 (5), 65 (15), 63 (16), 55 (5), 53 (8), 51 (24), 41 (54).

8- and 9-Nitro-3,4,5,6-tetrahydro-2*H*-benzo[*b*][1,4]dioxonins **3e** and **4e**.

A. From Nitration of **1e**.

Benzodioxonin **1e** (2.49 g, 14.0 mmoles) was treated with nitric acid (8.0 ml) to afford a viscous orange oil (2.72 g, 87%) found by analytical gc to be a mixture of **3e** (9%) and **4e** (91%). The two isomers were separated by preparative gc. Isomer **3e** was identical in all respects with an authentic sample.

B. Compound **3e** from 3-Nitrocatechol.

The procedure for the preparation of **3b** was followed. Thus, a mixture of 3-nitrocatechol (631 mg, 4.07 mmoles), 1,5-dibromopentane (3.1 g, 13 mmoles + 2.0 g, 8.7 mmoles after 4 hours at reflux) and anhydrous potassium carbonate (3.0 g, 22 mmoles + 2.0 g, 14 mmoles after 4 hours at reflux) in isoamyl alcohol (30 ml) was heated at reflux (140-150°) for a total of 8 hours. Column chromatography of the residue (after work-up) using benzene to elute the column gave **3e** as a pale-yellow viscous oil (169 mg, 19%).

Compound **3e** had ir (neat): ν 1600 (w), 1528 (s), 1472 (m), 1358

(m), 1290 (m), 1252 (m), 1075 (w), 1001 (w), 975 (w), 900 (w), 808 (w), 735 (w) cm^{-1}; ^1H nmr: δ 1.87 (m, 6H), 4.30 (m, 4H), 6.98 (dd, J = 8, 8 Hz, 1H), 7.20 (dd, J = 8, 2 Hz, 1H), 7.41 (dd, J = 8, 2 Hz, 1H); ms: m/z (% relative intensity) 223 ($M^{+\cdot}$, 38), 166 (2), 155 (33), 121 (2), 120 (4), 109 (9), 107 (29), 93 (5), 79 (9), 69 (100), 68 (49), 67 (11), 65 (9), 63 (8), 55 (14), 53 (12), 51 (21), 41 (91).

Anal. Calcd. for $C_{11}H_{13}NO_4$: C, 59.19; H, 5.87; H, 6.27. Found: C, 59.40; H, 6.15; N, 6.36.

Compound **4e** had ir (neat): ν 1580 (m), 1514 (s), 1490 (s), 1343 (s), 1310 (s), 1283 (s), 1252 (s), 1079 (m), 1000 (m), 908 (m), 745 (m) cm^{-1}; ^1H nmr: δ 1.89 (m, 6H), 4.23 (m, 2H), 4.49 (m, 2H), 6.99 (d, J = 9.5 Hz, 1H), 7.68-7.98 with maxima at 7.79, 7.88 (m, 2H); ms: m/z (% relative intensity) 223 ($M^{+\cdot}$, 23), 195 (4), 166 (5), 155 (12), 121 (3), 120 (4), 109 (3), 107 (8), 79 (9), 69 (100), 68 (19), 67 (6), 65 (6), 63 (8), 55 (10), 53 (8), 51 (16), 41 (90).

Anal. Calcd. for $C_{11}H_{13}NO_4$: C, 59.19; H, 5.87; N, 6.27. Found: C, 58.88; H, 5.69; N, 6.21.

9- and 10-Nitro-2,3,4,5,6,7-hexahydrobenzo[b][1,4]dioxecins **3f** and **4f**.

A. From Nitration of **1f**.

Benzodioxecin **1f** (2.69 g, 14.0 mmoles) was treated with nitric acid (8.0 ml) to furnish a viscous orange liquid (3.15 g, 95%) found by analytical gc to be a mixture of **3f** (1.3%) and **4f** (*ca.* 99%). Both isomers had identical gc retention times with those of authentic samples (prepared below). Isomer **4f** was isolated by preparative gc as a pale-yellow viscous oil; it was identical in all respects with an authentic sample.

Nitration of **1f** was also carried out according to the procedure described in the literature for the preparation of mononitrotoluene [25]. Thus, benzodioxecin **1f** (961 mg, 5.00 mmoles) was added in one portion at -15° to nitronium trifluoromethanesulfonate, prepared at room temperature from trifluoromethanesulfonic acid (1.51 g, 10.1 mmoles) and fuming nitric acid (0.21 ml, 0.32 g, 5.1 mmoles) in dichloromethane (25 ml). The mixture was stirred at -15° for 30 minutes, decanted quickly into crushed ice and extracted with dichloromethane to obtain a dark brown oil (1.066 g). Analytical gc indicated starting **1f** (33%, 352 mg, 63% conversion to products) and the two mononitro products (714 mg, 95% based on converted **1f**) **3f** (1.0%) and **4f** (99%).

B. From Nitration of 2-(6-Bromohexoxy)phenol Followed by Ring Closure.

Nitration of 2-(6-bromohexoxy)phenol [27] (3.73 g, 13.7 mmoles) was carried out in ether (55 ml) using fuming nitric acid (0.60 ml, 0.91 g, 14 mmoles) to furnish a dark-red oil (4.20 g). A solution of this in isoamyl alcohol (100 ml) was added dropwise into a boiling mixture of anhydrous potassium carbonate (6.0 g, 43 mmoles) and isoamyl alcohol (750 ml) within 9 hours [27]. The mixture was heated at reflux for 2 more hours and it was worked-up as for the preparation of **3b** (procedure B) to furnish a dark-red oil separated by preparative gc to give **3f** (453 mg, 14%), **4f** (647 mg, 20%) and an unidentified oil (289 mg) of greater retention time.

Compound **3f** had mp (ethanol at 50°, nearly colorless leaflets) 77-78°; ir (carbon tetrachloride): ν 1603 (w), 1535 (s), 1528 (s), 1469 (s), 1448 (m), 1360 (s), 1272 (s), 1225 (s), 1185 (w), 1073 (m), 1023 (s), 976 (m), 938 (m), 894 (w), 836 (w), 819 (m) cm^{-1}; ^1H nmr: δ 1.79 (m, 8H), 4.24 (m, 4H), 7.06 (dd, J = 8, 7.5 Hz, 1H), 7.23 (dd, J = 8, 2.5 Hz, 1H), 7.45 (dd, J = 7.5, 2.5 Hz, 1H); ms: m/z (% relative intensity) 237 ($M^{+\cdot}$, 7), 155 (6), 122 (1) 121 (2), 120 (3), 109 (9), 107 (27), 93 (6), 83 (52), 82 (39), 81 (31), 79 (10), 77 (5), 67 (27), 65 (10), 63 (7), 55 (100), 53 (12), 51 (22), 41 (61).

Anal. Calcd. for $C_{12}H_{15}NO_4$: C, 60.75; H, 6.37; N, 5.90. Found: C, 60.68; H, 6.38; N, 5.81.

Compound **4f** had ir (neat): ν 1583 (m), 1515 (s), 1495 (s), 1467 (m), 1343 (s), 1278 (s), 1254 (s), 1195 (m), 1081 (m), 1006 (m), 970 (m), 907 (w), 798 (w), 743 (w) cm^{-1}; ^1H nmr: δ 1.69 (m, 8H), 4.19 (m, 4H), 7.06 (d, J = 9.5 Hz, 1H), 7.77-8.04 with maxima at 7.87, 7.95 (m, 2H); ms: m/z (% relative intensity) 237 ($M^{+\cdot}$, 30), 223 (2), 181 (2), 166 (6), 155 (19), 137 (2), 121 (3), 120 (5), 109 (4), 107 (4), 91 (4), 83 (51), 82 (22), 81 (10), 79 (8), 69 (6), 67 (14), 55 (100), 53 (8), 51 (12), 41 (50).

Anal. Calcd. for $C_{12}H_{15}NO_4$: C, 60.75; H, 6.37; N, 5.90. Found: C, 60.86; H, 6.33; N, 5.88.

4,5-, 4,6- and 5,6-Dinitrobenzo[1,3]dioxoles **5a**, **6a** and **8a**.

A. Products **5a** and **6a** from Nitration of **3a**.

4-Nitrobenzodioxole **3a** (393 mg, 2.35 mmoles) in acetic acid (3 ml) was treated with fuming nitric acid (1.5 ml). Column chromatography gave **6a** (32 mg, 6.4%), after which the column was eluted with dichloromethane to obtain **5a** (366 mg, 73%) as a pale-yellow solid.

Compound **5a** had mp (crude) 164-167° (lit [34b] mp 167-168°); ^1H nmr: δ 6.30 (s, 2H), 6.95 (d, J = 8.5 Hz, 1H), 7.70 (d, J = 8.5 Hz, 1H); ^1H nmr (dimethyl sulfoxide-d_6): as reported [34b].

Compound **6a** had mp (pale-yellow needles) 107-108°; ir (carbon tetrachloride): ν 1631 (w), 1621 (w), 1545 (s), 1473 (m), 1343 (s), 1253 (m), 1050 (m), 923 (w) cm^{-1}; ^1H nmr: δ 6.41 (s, 2H), 7.86 (d, J = 2 Hz, 1H), 8.60 (d, J = 2 Hz, 1H); ms: m/z (% relative intensity) 212 ($M^{+\cdot}$, 29), 196 (1), 182 (1), 166 (2), 152 (9), 136 (1), 124 (2), 120 (7), 106 (6), 105 (6), 94 (8), 90 (5), 80 (15), 78 (14), 77 (9), 69 (6), 66 (23), 64 (20), 63 (17), 62 (46), 61 (27), 53 (19), 50 (35), 46 (18), 44 (17), 30 (100).

Anal. Calcd. for $C_7H_4N_2O_6$: C, 39.64; H, 1.90; N, 13.21. Found: C, 39.80; H, 2.00; N, 13.31.

B. Product **8a** from Nitration of **4a**.

5-Nitrobenzodioxole **4a** (701 mg, 4.19 mmoles) in acetic acid (5 ml) reacted with fuming nitric acid (4.0 ml). Analytical gc, tlc and ^1H nmr indicated formation of a single dinitro product identified as **8a** (819 mg, 92%), mp (crude) 97-99° (lit [4] mp 98-100°); ^1H nmr: δ 6.24 (s, 2H), 7.27 (s, 2H).

5,6- 5,7- and 6,7-Dinitro-2,3-dihydrobenzo[1,4]dioxins **5b**, **6b** and **8b**.

A. Products **5b** and **6b** from Nitration of **3b**.

5-Nitrobenzodioxin **5b** (429 mg, 2.37 mmoles) in acetic acid (4 ml) was nitrated with fuming nitric acid (2.5 ml). Column chromatography using a mixture of petroleum ether:ethyl acetate /2:1 (v:v) to elute the column furnished **6b** (77 mg, 14%) followed by **5b** (313 mg, 58%).

Compound **5b** had mp (off-white needles) 184-186° (lit [22c] mp 185.6-186.1°); ^1H nmr: δ 4.41 (s, 4H), 7.06 (d, J = 9 Hz, 1H), 7.76 (d, J = 9 Hz, 1H).

Compound **6b** had mp (off-white needles) 142-143° (lit [22b] mp 145.5-145.7°, lit [38a] mp 147°); ^1H nmr [38a]: δ 4.33-4.59 with maxima at 4.37, 4.45, 4.47, 4.48 (m, 4H), 7.97 (d, J = 3 Hz, 1H), 8.40 (d, J = 3 Hz, 1H).

B. From Nitration of **4b**.

6-Nitrobenzodioxin **4b** (634 mg, 3.50 mmoles) in acetic acid (4 ml) was treated with fuming nitric acid (5.0 ml) to furnish a pale-yellow solid (763 mg). Column chromatography gave **6b** (24 mg, 3.0%) and a mixture of **5b** + **8b** (719 mg, 3.18 mmoles) as revealed by ^{1}H nmr. Repeated recrystallizations of the mixture **5b** + **8b** (from a different preparation-separation) afforded a pure sample of **8b** for characterization. In order to determine the yields of **5b** and **8b** in the above mixture, we nitrated it further with fuming nitric acid (3 ml). Column chromatography employing a mixture of petroleum ether: ethyl acetate /1:1 (v:v) to elute the column furnished the trinitro derivatives **12b** (68 mg, 8%), followed by **13b** (790 mg, 92%). Based on the fact that **5b** is converted to **12b** exclusively [22c], while **8b** gives **13b** [10b], the yields of **5b** and **8b** were determined to be 57 mg (7.2%, calcd. from **12b**) and 659 mg (83%, calcd. from **13b**), respectively.

Compound **8b** had mp (off-white needles) 131-133° (lit [7] mp 131-132°, lit [10a], mp 133-134°); ^{1}H nmr: δ 4.39 (s, 4H), 7.40 (s, 2H).

5,6,8-Trinitro-2,3-dihydrobenzo[1,4]dioxin (**12b**) had mp (pale yellow needles) 177-178° (lit [22c] mp 180.4-181°); ^{1}H nmr: δ 4.44-4.72 with maxima at 4.50, 4.58 (m, 4H), 8.46 (s, 1H).

5,6,7-Trinitro-2,3-dihydrobenzo[1,4]dioxin (**13b**) had mp (ethanol:acetone/3:2 (v:v), pale-yellow granular plates) 154-155° (lit [7,10] mp 155-156°); ^{1}H nmr: δ 4.51 (s, 4H), 7.74 (s, 1H).

6,7-, 6,8-, 6,9- and 7,8-Dinitro-3,4-dihydro-2*H*-benzo[b][1,4]dioxepins **5c**, **6c**, **7c** and **8c**.

A. Products **5c**, **6c** and **7c** from Nitration of **3c**.

6-Nitrobenzodioxepin **3c** (194 mg, 0.994 mmole) in acetic acid (2 ml) was treated with fuming nitric acid (1.5 ml) to give a pale-yellow solid which on column chromatography afforded **7c** (24 mg, 10%), followed by **6c** (44 mg, 18%) and **5c** (154 mg, 65%).

Compound **5c** had mp (off-white leaflets) 127-128°; ir (carbon tetrachloride): ν 1584 (m), 1561 (s), 1555 (s), 1542 (s), 1537 (s), 1487 (m), 1342 (s), 1318 (s), 1289 (m), 1269 (s), 1060 (m), 1047 (m), 1008 (w), 989 (m), 907 (w), 837 (w), 826 (w), 809 (w) cm^{-1}; ^{1}H nmr: δ 2.32 (qn, J = 6 Hz, 2H), 4.37 (t, J = 6 Hz, 2H), 4.44 (t, J = 6 Hz, 2H), 7.12 (d, J = 9 Hz, 1H), 7.81 (d, J = 9 Hz, 1H); ms: m/z (% relative intensity) 240 (M$^{+\cdot}$, 100), 224 (1), 211 (3), 166 (5), 152 (1), 148 (14), 136 (2), 124 (11), 120 (7), 119 (14), 108 (5), 106 (9), 96 (20), 94 (7), 91 (5), 80 (24), 78 (26), 77 (17), 66 (7), 62 (17), 52 (8), 50 (22), 46 (12), 42 (16), 41 (47).

Anal. Calcd. for $C_9H_8N_2O_6$: C, 45.01; H, 3.36; N, 11.66. Found: C, 45.38; H, 3.38; N, 11.88.

Compound **6c** had mp (off-white needles) 124-125° (lit [38b] mp 124-125.5°); ir: ν 1594 (w), 1543 (s), 1484 (m), 1344 (s), 1312 (m), 1292 (m), 1269 (m), 1067 (m), 1058 (m), 1008 (w), 963 (w), 808 (w), cm^{-1}; ^{1}H nmr [38b]: δ 2.36 (qn, J = 6 Hz, 2H), 4.40 (t, J = 6 Hz, 2H), 4.50 (t, J = 6 Hz, 2H), 8.00 (d, J = 3 Hz, 1H), 8.26 (d, J = 3 Hz, 1H); ms: m/z (% relative intensity) 240 (M$^{+\cdot}$, 100), 224 (1), 223 (2), 212 (2), 211 (7), 166 (2), 165 (5), 152 (11), 148 (6), 136 (1), 120 (2), 119 (2), 106 (5), 94 (5), 91 (4), 80 (6), 78 (10), 77 (6), 66 (14), 62 (9), 50 (19), 42 (33), 41 (37).

Anal. Calcd. for $C_9H_8N_2O_6$: C, 45.01; H, 3.36; N, 11.66. Found: C, 45.01; H, 3.30; N, 11.80.

Compound **7c** had mp (ethanol at 60°, off-white needles) 96-98°; ir: ν 1607 (w), 1579 (w), 1547 (s), 1476 (m), 1452 (m), 1367 (m), 1352 (s), 1297 (s), 1276 (m), 1256 (s), 1052 (m), 1001 (w), 968 (w), 817 (s), cm^{-1}; ^{1}H nmr: δ 2.34 (qn, J = 6 Hz, 2H), 4.40 (t, J = 6 Hz, 4H), 7.40 (s, 2H); ms: m/z (% relative intensity) 240 (M$^{+\cdot}$, 100), 224 (2), 223 (2), 212 (2), 211 (6), 182 (2), 181 (2), 180 (3), 165 (4), 152 (2), 136 (8), 120 (4), 119 (4), 110 (6), 108 (6), 105 (11), 96 (6), 94 (8), 91 (5), 80 (12), 78 (11), 77 (11), 64 (14), 57 (14), 53 (15), 50 (9), 43 (15), 42 (12), 41 (43).

Anal. Calcd. for $C_9H_8N_2O_6$: C, 45.01; H, 3.36; N, 11.66. Found: C, 45.10; H, 3.26; N, 11.86.

B. Products **5c**, **6c** and **8c** from Nitration of **4c**.

7-Nitrobenzodioxepin **4c** (460 mg, 2.36 mmoles) in acetic acid (5 ml) was treated with fuming nitric acid (4.0 ml). Column chromatography furnished **6c** (63 mg, 11%) followed by an off-white solid, shown by ^{1}H nmr to be a mixture of **5c** + **8c** (480 mg). Fractional recrystallization of this with *para*-dioxane afforded a crystalline **8c**: *para*-dioxane/2:1 complex (144 mg, 0.253 mmole) and a mixture of **5c** + **8c** (358 mg) as shown by ^{1}H nmr. The complex was decomposed by refluxing in toluene for 1 hour to furnish pure **8c** (117 mg, 96%). Following previous considerations (see nitration of the mixture **5b** + **8b** above), the mixture of **5c** + **8c** (358 mg, 1.49 mmoles) reacted with fuming nitric acid (2 ml), followed by column chromatographic separation of the two products. Elution of the column with petroleum ether: ethyl acetate/1:1 (v:v) afforded the trinitro derivatives **12c** (146 mg, 34%) followed by **13c** (270 mg, 64%) as pale-yellow solids. From these, the total yields of **5c** and **8c** from nitration of **4c** were calculated to be 123 mg (22%) and 117 + 227 = 344 mg (61%), respectively. Differentiation between **12c** and **13c** was based on the aromatic proton chemical shifts (as previously, determined for **12d** and **13d** [14]). Thus, for **12c**: δ 8.34 (s, 1H) and for **13c**: δ 7.75 (s, 1H) [39].

The **8c**:*para*-dioxane/2:1 complex had mp (not recrystallized, colorless granular plates) 91-97° (variable); ir: ν 1585 (m), 1546 (s), 1497 (s), 1358 (s), 1328 (s), 1294 (s), 1273 (s), 1254 (m), 1174 (w), 1121 (s), 1057 (m), 985 (m), 899 (m), 888 (m), 874 (s), 850 (m), 826 (m) cm^{-1}; ^{1}H nmr: δ 2.31 (qn, J = 6 Hz, 4H), 3.67 (s, 8H), 4.41 (t, J = 6 Hz, 8H), 7.45 (s, 4H); ms: m/z (% relative intensity) 568 (M$^{+\cdot}$, absent), 240 (96), 224 (1), 211 (10), 165 (3), 152 (5), 148 (14), 124 (7), 120 (12), 119 (28), 96 (9), 88 (100), 80 (10), 78 (12), 77 (9), 69 (25), 67 (11), 62 (26), 58 (76), 57 (25), 55 (15), 53 (19), 50 (48), 43 (57), 42 (32), 41 (87). The elemental analysis for $C_{22}H_{24}N_4O_{14}$ was incorrect, however, the technique for volatile solids was not employed.

Compound **8c** had mp (off-white needles) 112-113°; ir (carbon tetrachloride): ν 1585 (m), 1546 (s), 1497 (s), 1358 (s), 1328 (s), 1294 (s), 1272 (s), 1175 (w), 1058 (m), 984 (m), 899 (m), 850 (m), 826 (m) cm^{-1}; ^{1}H nmr: δ 2.31 (qn, J = 6 Hz, 2H), 4.42 (t, J = 6 Hz, 4H), 7.45 (s, 2H); ms: m/z (% relative intensity) 240 (M$^{+\cdot}$, 100), 224 (1), 211 (8), 165 (3), 152 (5), 148 (12), 124 (6), 120 (10), 119 (29), 108 (4), 96 (5), 95 (6), 80 (5), 78 (7), 77 (8), 69 (23), 67 (9), 62 (29), 55 (11), 53 (15), 50 (47), 46 (34), 42 (18), 41 (65).

Anal. Calcd. for $C_9H_8N_2O_6$: C, 45.01; H, 3.36; N, 11.66. Found: C, 44.88; H, 3.33; N, 11.86.

7,8-, 7,9-, 7,10- and 8,9-Dinitro-2,3,4,5-tetrahydrobenzo[b][1,4]-dioxocins **5d**, **6d**, **7d** and **8d**.

A. Products **5d**, **6d** and **7d** from Nitration of **3d**.

7-Nitrobenzodioxocin **3d** [14] (48 mg, 0.23 mmole) in acetic acid (1 ml) was treated with fuming nitric acid (1.0 ml). Column chromatography furnished **7d** (21 mg, 36%), **6d** (11 mg, 19%) and **5d** (26 mg, 45%) all previously characterized [14].

B. Products **5d**, **6d** and **8d** from Nitration of **4d**.

8-Nitrobenzodioxocin **4d** [14] (200 mg, 0.956 mmole) was treated with fuming nitric acid (0.20 ml) at 0-10° (1 hour). Column chromatography gave **6d** (160 mg, 61%) and a mixture of **5d** + **8d**. Column chromatography (long column) of **5d** + **8d** was repeated using benzene this time to elute the column, to afford **5d** (30 mg, 12%) and **8d** (26 mg, 11%). The compounds have been characterized previously [14].

7,8,9-, and 7,8,10-Trinitro-2,3,4,5-tetrahydrobenzo[b][1,4]dioxocins **13d** and **12d**.

A. Product **12d** from Nitration of **5d**.

7,8-Dinitrobenzodioxocin **5d** (5.0 mg, 0.020 mmole) and fuming nitric acid (0.170 ml) afforded **12d** (*ca.* 4.0 mg, 68%), exclusively [14].

B. Products **12d** and **13d** from Nitration of **6d**.

7,9-Dinitrobenzodioxocin **6d** (254 mg, 0.999 mmole) and fuming nitric acid (2.5 ml) gave a pale-yellow mixture which on column chromatography furnished **12d** (201 mg, 67%) and **13d** (61 mg, 20%). Characterization of these compounds has been reported [14].

8,9-, 8,10-, 8,11- and 9,10-Dinitro-3,4,5,6-tetrahydro-2*H*-benzo[*b*]-[1,4]dioxonins **5e**, **6e**, **7e** and **8e**.

A. Products **5e**, **6e** and **7e** from Nitration of **3e**.

8-Nitrobenzodioxonin **3e** (183 mg, 0.820 mmole) in acetic acid (2 ml) was reacted with fuming nitric acid (1.7 ml). The mixture was separated by column chromatography to obtain **7e** (12 mg, 5.5%), **6e** (116 mg, 53%) and **5e** (76 mg, 35%).

Compound **5e** had mp (off-white granular plates) 106-107°; ir: ν 1582 (s), 1563 (s), 1553 (s), 1537 (s), 1487 (s), 1345 (s), 1311 (s), 1260 (s), 1016 (m), 980 (m), 877 (m), 842 (w) cm^{-1}; ^1H nmr: δ 1.88 (m, 6H), 4.30 (t, J = 5 Hz, 2H), 4.49 (t, J = 5 Hz, 2H), 7.20 (d, J = 9 Hz, 1H), 7.91 (d, J = 9 Hz, 1H); ms: m/z (% relative intensity) 268 ($M^{+\cdot}$, 5), 223 (2), 205 (2), 200 (1), 165 (1), 155 (1), 120 (2), 119 (3), 105 (4), 78 (7), 77 (8), 69 (100), 68 (18), 67 (11), 57 (11), 55 (15), 43 (15), 41 (93).

Anal. Calcd. for $C_{11}H_{12}N_2O_6$: C, 49.26; H, 4.51; N, 10.44. Found: C, 49.24; H, 4.51; N, 10.55.

Compound **6e** (pale-yellow oil) had ir (neat): ν 1593 (m), 1543 (s), 1533 (s), 1342 (s), 1298 (s), 1257 (m), 1233 (w), 1065 (m), 1014 (m), 978 (m), 905 (m), cm^{-1}; ^1H nmr: δ 1.93 (m, 6H), 4.32 (m, 2H), 4.62 (m, 2H), 8.06 (d, J = 3 Hz, 1H), 8.31 (d, J = 3 Hz, 1H); ms: m/z (% relative intensity) 268 ($M^{+\cdot}$, 2), 120 (1), 119 (2), 105 (4), 99 (4), 91 (5), 89 (6), 75 (8), 73 (9), 71 (10), 69 (21), 59 (9), 58 (10), 57 (26), 55 (29), 43 (100), 41 (41).

Anal. Calcd. for $C_{11}H_{12}N_2O_6$: C, 49.26; H, 4.51; N, 10.44. Found: C, 48.99; H, 4.41; N, 10.32.

Compound **7e** (pale-yellow semisolid) had ir (carbon tetrachloride): ν 1636 (w), 1606 (w), 1540 (s), 1471 (w), 1444 (w), 1353 (m), 1284 (m), 1249 (m), 1078 (w), 997 (w), 891 (w) cm^{-1}; ^1H nmr: δ 1.92 (m, 6H), 4.38 (m, 4H), 7.48 (s, 2H).

Anal. Calcd. for $C_{11}H_{12}N_2O_6$: C, 49.26; H, 4.51; N, 10.44. Found: C, 49.33; H, 4.51; N, 10.38.

B. Products **5e**, **6e** and **8e** from Nitration of **4e**.

9-Nitrobenzodioxonin **4e** (517 mg, 2.32 mmoles) and fuming nitric acid (0.40 ml) gave a mixture, separated by column chromatography to yield **6e** (110 mg, 18%), **8e** (339 mg, 55%) and **5e** (169 mg, 27%).

Compound **8e** had mp (ethanol at 70°, pale-yellow needles) 80-81°; ir: ν 1588 (m), 1549 (s), 1537 (s), 1498 (m), 1358 (s), 1323 (s), 1294 (s), 1260 (m), 1190 (w), 1047 (m), 986 (w), 966 (w), 904 (w), 855 (m) cm^{-1}; ^1H nmr: δ 1.83 (m, 6H), 4.45 (m, 4H), 7.49 (s, 2H); ms: m/z (% relative intensity) 268 ($M^{+\cdot}$, 9), 238 (3), 223 (3), 211 (1), 205 (3), 170 (3), 165 (2), 155 (3), 120 (3), 119 (7), 105 (5), 91 (4), 77 (7), 71 (5), 69 (100), 68 (9), 67 (9), 57 (12), 55 (16), 43 (14), 41 (85).

Anal. Calcd. for $C_{11}H_{12}N_2O_6$: C, 49.26; H, 4.51; N, 10.44. Found: C, 49.19; H, 4.53; N, 10.59.

8,9,10-Trinitro-3,4,5,6-tetrahydro-2*H*-benzo[b][1,4]dioxonin (**13e**).

9,10-Dinitrobenzodioxonin **8e** was converted to **13e** with fuming nitric acid, mp (pale-yellow granules) 128-129°; ir: ν 1569 (s), 1553 (s), 1485 (m), 1353 (s), 1336 (s), 1315 (s), 1061 (w), 979 (w), 863 (m) cm^{-1}; ^1H nmr: δ 1.88 (m, 6H), 4.41 (t, J = 5 Hz, 2H), 4.62 (t, J = 5 Hz, 2H), 7.83 (s, 1H); ms: m/z (% relative intensity) 313 ($M^{+\cdot}$, 17), 283 (1), 271 (2), 268 (1), 256 (1), 223 (1), 215 (1), 205 (1), 165 (1), 164 (2), 155 (1), 119 (2), 105 (2), 77 (11), 69 (100), 68 (12), 67 (11), 57 (6), 55 (11), 53 (6), 41 (70).

Anal. Calcd. for $C_{11}H_{11}N_3O_8$: C, 42.18; H, 3.54; N, 13.42. Found: C, 42.08; H, 3.32; N, 13.42.

9,10-, 9,11- and 10,11-Dinitro-2,3,4,5,6,7-hexahydrobenzo[b][1,4]-dioxecins **5f**, **6f** and **8f**.

A. Products **5f** and **6f** from Nitration of **3f**.

9-Nitrobenzodioxecin **3f** (250 mg, 1.05 mmoles) in acetic acid (2 ml) was treated with fuming nitric acid (0.90 ml), followed by column chromatography to give **6f** (80 mg, 27%) and **5f** (140 mg, 47%).

Compound **5f** had mp (pale-yellow needles) 119-120°; ir: ν 1583 (m), 1563 (s), 1553 (s), 1536 (s), 1495 (m), 1468 (m), 1371 (m), 1343 (s), 1292 (s), 1277 (s), 1261 (w), 1019 (m), 1006 (m), 924 (w), 884 (w), 851 (m), 830 (w) cm^{-1}; ^1H nmr: δ 1.76 (m, 8H), 4.16 (t, J = 5 Hz, 2H), 4.31 (t, J = 5 Hz, 2H), 7.15 (d, J = 9 Hz, 1H), 8.00 (d, J = 9 Hz, 1H); ms: m/z (% relative intensity) 282 ($M^{+\cdot}$, 8), 226 (1), 223 (1), 200 (1), 120 (2), 119 (3), 106 (2), 83 (44), 82 (18), 81 (38), 69 (2), 67 (11), 55 (100), 54 (5), 53 (5), 43 (8), 41 (51).

Anal. Calcd. for $C_{12}H_{14}N_2O_6$: C, 51.07; H, 5.00; N, 9.92. Found: C, 51.19; H, 5.10; N, 10.05.

Compound **6f** had mp (white needles) 95-96°; ir: ν 1595 (w), 1545 (s), 1535 (s), 1346 (s), 1278 (m), 1090 (w), 1027 (w), 940 (w), 890 (w) cm^{-1}; ^1H nmr: δ 1.78 (m, 8H), 4.28 (m, 4H), 8.03 (d, J = 3 Hz, 1H), 8.34 (d, J = 3 Hz, 1H); ms: m/z (% relative intensity) 282 ($M^{+\cdot}$, 15), 226 (2), 211 (1), 200 (2), 197 (1), 165 (2), 135 (3), 120 (2), 119 (2), 105 (2), 94 (5), 92 (7), 83 (46), 82 (23), 81 (37), 77 (5), 69 (6), 67 (17), 57 (4), 55 (100), 53 (8), 50 (17), 43 (9), 41 (47).

Anal. Calcd. for $C_{12}H_{14}N_2O_6$: C, 51.07; H, 5.00; N, 9.92. Found: C, 50.93; H, 5.00; N, 9.98.

B. From Nitration of **4f**.

10-Nitrobenzodioxecin **4f** (1.05 g, 4.43 mmoles) was treated with fuming nitric acid (0.50 ml). Column chromatography (long column) afforded a mixture of starting **4f** + **6f** (318 mg), followed by pure **8f** (673 mg, 70% based on converted **4f**) and pure **5f** (221 mg, 23% based on converted **4f**). The mixture **4f** + **6f** was separated further by column chromatography (long column) using benzene to elute the column to give **6f** (67 mg, 7.0% based on converted **4f**) as the first fraction, followed by starting **4f** (242 mg, 77% conversion). Using a greater quantity of fuming nitric acid to obtain 100% conversion of **4f** to the products, resulted in formation of the trinitro by-product **13f**.

Compound **8f** had mp (ethanol at 70°, pale-yellow needles) 76-77°; ir: ν 1593 (w), 1548 (s), 1537 (s), 1503 (m), 1358 (s), 1292 (s), 1276 (m), 1194 (w), 1006 (m), 922 (w), 851 (w) cm^{-1}; ^1H nmr: δ 1.74 (m, 8H), 4.28 (m, 4H), 7.52 (s, 2H); ms: m/z (% relative intensity) 282 ($M^{+\cdot}$, 29), 252 (2), 236 (2), 226 (2), 223 (2), 211 (3), 206 (1), 205 (1), 200 (1), 165 (2), 155 (3), 120 (3), 119 (6), 105 (3), 95 (5), 83 (46), 82 (12), 81 (19), 69 (11), 67 (12), 57 (10), 55 (100), 53 (7), 50 (8), 43 (16), 41 (51).

Anal. Calcd. for $C_{12}H_{14}N_2O_6$: C, 51.07; H, 5.00; N, 9.92. Found: C, 50.94; H, 4.88; N, 9.78.

9,10,11-Trinitro-2,3,4,5,6,7-hexahydrobenzo[*b*][1,4]dioxecin (**13f**).

10,11-Dinitrobenzodioxecin **8f** was converted to **13f** with fuming nitric acid, mp (off-white needles) 135-136°; ir: ν 1564 (s), 1552 (s), 1493 (w), 1467 (w), 1367 (m), 1352 (m), 1339 (m), 1300 (m), 1072 (w), 1012 (w), 922 (w), 869 (w), 842 (w) cm^{-1}; ^1H nmr: δ 1.79 (m, 8H), 4.33 (m, 4H), 7.74 (s, 1H); ms: m/z (% relative intensity) 327 ($M^{+\cdot}$, 17), 297 (2), 285 (2), 271 (2), 223 (3), 215 (3), 205 (3), 167 (16), 166 (8), 165 (18), 155 (5), 139 (11), 119 (4), 105 (15), 95 (8), 83 (42), 82 (17), 81 (44), 77 (28), 69 (16), 67 (17), 57 (21), 55 (100), 53 (11), 51 (14), 50 (13), 43 (40), 41 (76).

Anal. Calcd. for $C_{12}H_{13}N_3O_8$: C, 44.04; H, 4.00; N, 12.84. Found: C, 43.85; H, 4.06; N, 12.84.

3,4- and 3,5-Dinitroveratroles **10** and **11**.

3-Nitroveratrole (**9**) (287 mg, 1.57 mmoles) in acetic acid (2 ml) was treated with fuming nitric acid (1.0 ml). Column chromatography using petroleum ether:ethyl acetate/1:1 (v:v) to elute the column furnished **11** (113 mg, 32%) followed by **10** (196 mg, 55%).

Compound **10** had mp (crude) 89-91° (lit [29] mp 90.5°); ^1H nmr: δ 3.95 (s, 3H), 4.04 (s, 3H), 7.08 (d, J = 9 Hz, 1H), 8.00 (d, J = 9 Hz, 1H).

Compound **11** had mp (crude) 98-100° (lit [40] mp 101°); ^1H nmr: δ 4.03 (s, 3H), 4.07 (s, 3H), 7.94 (d, J = 2.5 Hz, 1H), 8.20 (d, J = 2.5 Hz, 1H).

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REFERENCES AND NOTES

[1] E. Mameli and E. Boi, *Atti. R. Accad. dei Lincei Roma*, [5], **15**, II, 101 (1906); also see: *Chem. Zentralbl.*, 1005 (1906, II).

[2] E. Mameli, *Gazz. Chim. Ital.*, **36**, II, 376 (1906).

[3] W. H. Perkin, Jr., R. Robinson and F. Thomas, *J. Chem. Soc.*, **95**, 1977 (1909).

[4] D. S. Wulfman and C. F. Cooper, *Synthesis*, 924 (1978).

[5] E. Mameli, *Gazz. Chim. Ital.*, **39**, II, 172, (1909).

[6] D. Vorländer, *Liebigs Ann. Chem.*, **280**, 205 (1894).

[7] P. M. Heertjes, E. A. M. F. Dahmen and T. G. Wierda, *Recl. Trav. Chim. Pays-Bas*, **60**, 569 (1941).

[8] H. D. Springall, G. C. Hampson, C. G. May and H. Spedding, *J. Chem. Soc.*, 1524 (1949).

[9] P. M. Heertjes and L. J. Revallier, *Recl. Trav. Chim. Pays-Bas*, **69**, 262 (1950).

[10a] B. N. Ghosh, *J. Chem. Soc.*, **107**, 1588 (1915); [b] G. M. Robinson and R. Robinson, *J. Chem. Soc.*, **111**, 929 (1917).

[11] R. B. Thompson and T. Symon, *J. Am. Oil Chem. Soc.*, **33**, 414 (1956).

[12] A. W. Archer, P. A. Claret and D. F. Hayman, *J. Chem. Soc. (B)*, 1231 (1971).

[13] V. K. Daukšas, G. V. Purvaneckas, E. B. Udrénaité, V. L. Gineityté and A. V. Barauskaité, *Heterocycles*, **15**, 1395 (1981) and references therein.

[14] I. M. Takakis and P. M. Hadjimihalakis, *J. Heterocyclic Chem.*, **27**, 177 (1990).

[15] A. I. Serebryanskaja, A. V. Eltsov and A. I. Shatenshtein, *Zh. Org. Khim.*, **3**, 358 (1967).

[16] J. H. Czernohorsky, K. E. Richards and E. J. Wright, *Aust. J. Chem.*, **25**, 1459 (1972).

[17] M. M. Byrne and N. H. P. Smith, *J. Chem. Soc. (B)*, 809 (1968).

[18] G. Baddeley and N. H. P. Smith, *J. Chem. Soc.*, 2516 (1961).

[19] R. C. Cass, S. E. Fletcher, C. T. Mortimer, P. G. Quincey and H. D. Springall, *J. Chem. Soc.*, 2595 (1958).

[20] W. H. Mills and I. G. Nixon, *J. Chem. Soc.*, 2510 (1930); P. C. Hiberty, G. Ohanessian and F. Delbecq, *J. Am. Chem. Soc.*, **107**, 3095 (1985).

[21] R. A. Finnegan, *J. Org. Chem.*, **30**, 1333 (1965); A. Streitwieser, Jr., G. R. Ziegler, P. C. Mowery, A. Lewis and R. G. Lawler, *J. Am. Chem. Soc.*, **90**, 1357 (1968).

[22a] P. M. Heertjes, A. A. Knape, H. Talsma and P. Andriesse, *J. Chem. Soc.*, 18 (1954); [b] P. M. Heertjes, A. A. Knape and H. Talsma, *J. Chem. Soc.*, 1868 (1954); [c] P. M. Heertjes, A. A. Nijman-Knape, H. Talsma and N. J. Faasen, *J. Chem. Soc.*, 1313 (1955).

[23a] H. Vermeulen, *Recl. Trav. Chim. Pays-Bas*, **25**, 12 (1906); [b] D. Cardwell and R. Robinson, *J. Chem. Soc.*, **107**, 255 (1915); M. P. De Lange, *Recl. Trav. Chim. Pays-Bas*, **45**, 19 (1926); E. P. Clark, *J. Am. Chem. Soc.*, **53**, 3431 (1931); S. H. Harper, *J. Chem. Soc.*, 593 (1942); [c] Ch. Moureu, *Bull. Soc. Chim. France*, [3] **15**, 646 (1895); [d] L. Weinberger and A. R. Day, *J. Org. Chem.*, **24**, 1451 (1959); H. Zellner and G. Zellner, *Helv. Chim. Acta*, **49**, 913 (1966); [e] F. Brüggemann, *J. Prakt. Chem.*, [2] **53**, 250 (1896); Ch. Moureu, *C. R. Acad. Sci.*, **125**, 31 (1897); A. H. Parijs, *Recl. Trav. Chim. Pays-Bas*, **49**, 45 (1930); N. L. Drake, H. D. Anspon, J. D. Draper, S. T. Haywood, J. V. Hook, S. Melamed, R. M. Peck, J. Sterling, Jr., E. W. Walton and A. Whiton, *J. Am. Chem. Soc.*, **68**, 1536 (1946); J. Ehrlich and M. T. Bogert, *J. Org. Chem.*, **12**, 522 (1947); [f] H. Vermeulen, *Recl. Trav. Chim. Pays-Bas*, **48**, 969 (1929); [g] T. G. H. Jones and R. Robinson, *J. Chem. Soc.*, **111**, 903 (1917); F. Pollecoff and R. Robinson, *J. Chem. Soc.*, **113**, 645 (1918); [h] J. Marquet, M. Moreno-Mañas, A. Vallribera, A. Virgili, J. Bertran, A. Gonzalez-Lafont and J. Ma Lluch, *Tetrahedron*, **43**, 351 (1987).

[24] P. B. D. De La Mare and C. A. Vernon, *J. Chem. Soc.*, 1764 (1951); G. M. Anderson III, P. A. Kollman, L. N. Domelsmith and K. N. Houk, *J. Am. Chem. Soc.*, **101**, 2344 (1979).

[25] C. L. Coon, W. G. Blucher and M. E. Hill, *J. Org. Chem.*, **38**, 4243 (1973).

[26] We have confirmed that nitration of veratrole (**2**) furnishes only 4-nitroveratrole [23a-d]. Further nitration of the latter afforded 4,5-dinitroveratrole [23d,f] exclusively; this was also obtained by dinitration of **2** [4,23c,e,h].

[27] A. Lüttringhaus and K. Ziegler, *Liebigs Ann. Chem.*, **528**, 155 (1937); K. Ziegler, A. Lüttringhaus and K. Wohlgemuth, *Liebigs Ann. Chem.*, **528**, 162 (1937).

[28] P. Vouros and K. Biemann, *Org. Mass Spectrom.*, **3**, 1317 (1970).

[29] D. H. Rosenblatt, J. Epstein and M. Levitch, *J. Am. Chem. Soc.*, **75**, 3277 (1953).

[30] N. J. Bunce and K. Labonte Stephenson, *Can. J. Chem.*, **67**, 220 (1989).

[31] H.-Minlon, *Chem. Ber.*, **70**, 951 (1937).

[32a] Y. Sasaki and H. Kurokawa, *Yakugaku Zasshi*, **85**, 857 (1965); also see: Chem. Abstr., **66**, 120604j (1967); [b] Y. Sasaki, M. Suzuki, T. Hibino and K. Karai, *Chem. Pharm. Bull.*, **15**, 599 (1967).

[33] S. McLean, M.-S. Lin and J. Whelan, *Can. J. Chem.*, **48**, 948 (1970).

[34a] A. Meisels and F. Sondheimer, *J. Am. Chem. Soc.*, **79**, 6328 (1957); [b] V. K. Daukšas, E. B. Udrénaité, V. L. Gineityté and G. G.

Komovnikova, *Khim. Geterotsikl. Soedin.*, 1183 (1979).

[35] J. H. Bowie and A. C. Ho, *Aust. J. Chem.*, **30**, 675 (1977).

[36] J. H. Bowie and A. C. Ho, *J. Chem. Soc., Perkin Trans 2*, 724 (1975).

[37] I. van Wijngaarden, C. G. Kruse, J. A. M. van der Heyden and M. Th. M. Tulp, *J. Med. Chem.*, **31**, 1934 (1988).

[38a] V. N. Knyazev, V. N. Drozd and A. A. Klimov, *Zh. Org. Khim.*, **12**, 2387 (1976); [b] V. N. Knyazev, V. N. Minov and V. N. Drozd, *Zh. Org. Khim.*, **12**, 844 (1976).

[39] Full data on **12c** and **13c** will be reported by one of us (P. M. H., *J. Heterocyclic Chem.*, submitted.

[40] J. J. Blaksma, *Recl. Trav. Chim. Pays-Bas*, **23**, 111 (1904).