Diazapolycyclic Compounds. XXVII. On the Selective Hydrogenation of Benzo[g]phthalazine-1,4-dione and 5-Methoxybenzo[g]phthalazine-1,4-dione Adducts

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A number of diazapolycyclic structures obtained by cycloaddition reaction of benzo[g]phthalazine-1,4-dione with several 1,3-dienes have been catalytically hydrogenated on palladium over charcoal. In a first step the double bond formed in the cycloaddition was reduced, except in the case of tetrasubstitution. The use of longer reaction times led to the selective reduction of the terminal aromatic rings, although the presence of the 5-methoxy substituent favored tetrahydropyridazine ring opening and prevented aromatic ring reduction. The stereochemical features of new compounds obtained are commented on the basis of X-ray and nmr data.

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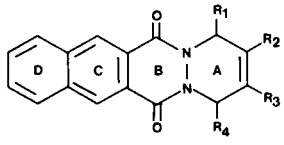
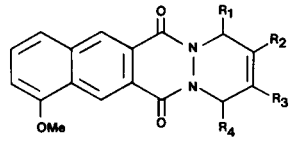
In the course of our studies on the synthesis of benzo[g]-phthalazine derivatives like **1** and **2**, usually accomplished by 4 + 2 cycloaddition of diazaquinones with diverse 1,3-dienes [1-3], we have been dealing with the systematic analysis of stereochemical and conformational features at the ring A moiety of these diazatetracyclic compounds. The regio- and stereoselectivity of electrophilic additions to the double bond at ring A have also been investigated [4-6], and epoxidation has shown to be a suitable procedure for the introduction of new substituents in the molecule [7].

With the aim of preparing monohydroxy derivatives *via* the catalytic hydrogenation of the aforementioned epoxides [8], we tried the reduction of epoxide **3** over palladium on charcoal in chloroform solution. This reaction regioselectively afforded chlorohydrin **4** as the only isolated product (Scheme 1). The oxirane ring opening in chloroform was not an unexpected reaction, but it was accompanied by the more surprising selective hydrogenation of the terminal aromatic ring D. In previous work we had already assessed the catalytic hydrogenation of the double bond at ring A of phthalazine-1,4-dione adducts in ethanol solution and on palladium over charcoal [9-10], and in every case the aromatic rings remained unaffected. On the other hand, not many references can be found in the recent literature concerning the selective reduction of aromatic rings in structures related to these compounds, and only those concerning the hydrogenation of the less deactivated terminal ring in antracenophanes [11] should properly be cited.

Scheme 1



1



2

1a : $R_1 = R_2 = R_3 = R_4 = H$

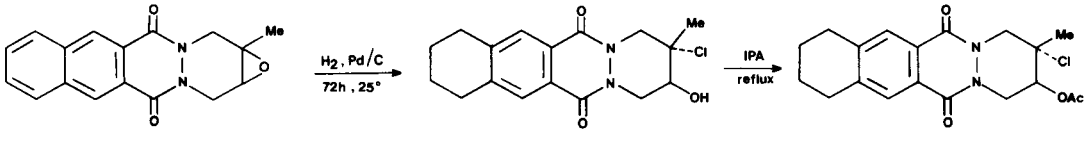
1b : $R_1 = R_4 = H$, $R_2 = R_3 = Me$

1c : $R_1 = R_3 = R_4 = H$, $R_2 = Me$

1d : $R_1 = R_4 = Ph$, $R_2 = R_3 = H$

2b : $R_1 = R_4 = H$, $R_2 = R_3 = Me$

2d : $R_1 = R_4 = Ph$, $R_2 = R_3 = H$



3 4 5

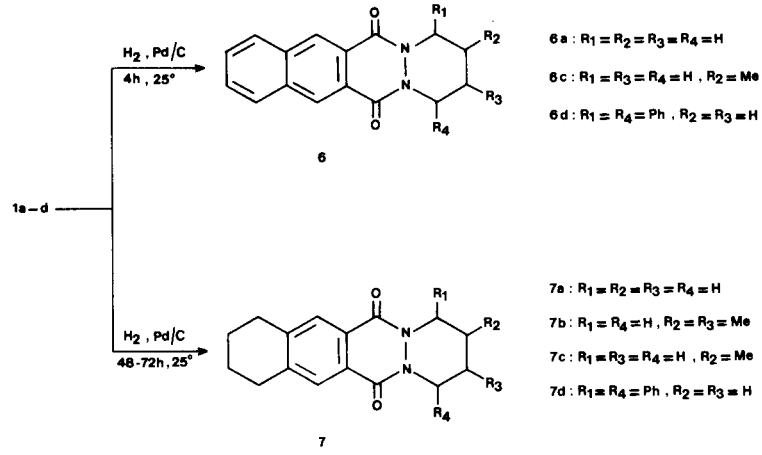
Therefore, this paper deals with the catalytic hydrogenation of a series of adducts in order to test the overall reproducibility of ring D reduction in other substrates. It should be of interest because the selective introduction of substituents at rings C and D could be made more easily and, furthermore, because the planarity of the molecule diminishes, and this fact could affect the biological properties of these diazapolycyclic compounds. For this last reason, stereochemical features of the hydrogenated derivatives obtained will be also worthy of a comment along the following lines.

The catalytic hydrogenation of the benzo[*g*]phthalazine-1,4-dione adducts with 1,3-butadiene, isoprene, 2,3-dimethyl-1,3-butadiene and 1,4-diphenyl-1,3-butadiene (**1a-d**) was performed on palladium over charcoal in chloroform solution. Temperature, pressure and reaction times were as stated in the experimental. Results obtained are summarized in Scheme 2.

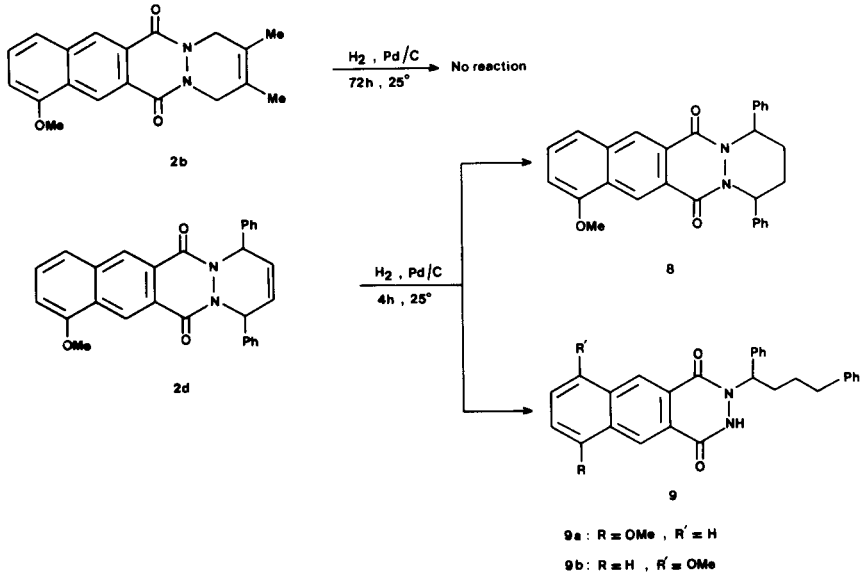
When the reactions were carried out during a period of 4 hours, only the double bond at the ring A moiety was reduced to give **6a**, **6c** and **6d** in nearly quantitative yields. Adduct **1b** could not be hydrogenated under these conditions and was recovered unchanged, probably owing to the steric hindrance originated by tetrasubstitution at the double bond. However, when reaction time was raised to 48 hours, the terminal aromatic ring was also reduced to give compounds **7a** and **7c**. In order to obtain **7b** and **7d** it was necessary to increase the reaction time until 72 hours.

In a parallel way, the reduction of 5-methoxybenzo[*g*]-phthalazine-1,4-dione adducts with 2,3-dimethyl-1,3-butadiene (**2b**) and 1,4-diphenyl-1,3-butadiene (**2d**) was also observed (Scheme 3). Compound **2b** was shown to be less reactive than **1b**, since it was recovered unchanged after 72 hours of reaction. In fact, the electron-donating methoxy group should reduce the withdrawing effect of the car-

Scheme 2



Scheme 3



bonyls on the aromatic moiety, and consequently ring D must be less deactivated in adducts **2** than in the **1** series.

From these results it is confirmed that selective reduction of the terminal aromatic ring can be easily achieved, and that shorter reaction times allow hydrogenation of the isolated double bond without modifications at the aromatic moiety if desired. A limitation is that electron-donating substitution at the aromatic ring seems to prevent reduction, although other substituents should be tested before any conclusion is stated.

The structural elucidation of the new diazapolycyclic derivatives obtained in these reactions was mainly made on the basis of ^1H and ^{13}C nmr data, which are displayed in Tables 1 and 2. We have also included the ^{13}C shifts of

Table 1

^1H NMR Data of the New Hydrogenated Derivatives [a]

Compound	H_{1e}	H_{1a}	H_{4e}	H_{4a}	H_{2e}	H_{2a}	H_{3e}	H_{3a}	H_7	H_{12}	H_8	H_9	H_{10}	H_{11}
4	4.69 (d)	4.06 (d)	4.58 (q)	4.20 (q)	—	—	4.15 (m)	—	7.73 (s)	7.83 (s)	2.85 (m)	1.81 (m)	1.81 (m)	2.85 (m)
5	4.75 (d)	3.80 (d)	4.65 (q)	4.10 (q)	—	—	5.28 (m)	—	7.90 (bs)	7.90 (bs)	2.88 (m)	1.60-2.20 (m)		2.88 (m)
6a	3.72 (m)	3.72 (m)	3.72 (m)	3.72 (m)	1.45 (m)	1.45 (m)	1.45 (m)	1.45 (m)	8.33 (s)	8.33 (s)	7.58 (m)	7.20 (m)	7.20 (m)	7.58 (m)
6c	4.82 (m)	3.09 (q)	4.77 (m)	3.54 (o)	—	2.15 (m)	2.00 (m)	1.55 (m)	8.86 (s)	8.86 (s)	8.06 (m)	7.66 (m)	7.66 (m)	8.06 (m)
6d	6.01 (t)		6.01 (t)			1.93-2.53 (bm)			8.83 (s)	8.83 (s)	8.04 (m)	7.61 (m)	7.61 (m)	8.04 (m)
7a	4.11 (m)	4.11 (m)	4.11 (m)	4.11 (m)	1.90 (m)	1.90 (m)	1.90 (m)	1.90 (m)	7.92 (s)	7.92 (s)	2.85 (m)	1.90 (m)	1.90 (m)	2.85 (m)
7b	4.05 (q)	3.85 (q)	4.05 (q)	3.85 (q)	—	2.15 (m)	—	2.15 (m)	7.91 (s)	7.91 (s)	2.93 (m)	1.78 (m)	1.78 (m)	2.93 (m)
7c	4.82 (m)	3.06 (q)	4.77 (m)	3.50 (o)	—	2.15 (m)	2.00 (m)	1.53 (m)	7.93 (s)	7.93 (s)	2.90 (m)	1.84 (m)	1.84 (m)	2.90 (m)
7d	6.02 (t)		6.02 (t)		2.40 (m)	2.13 (m)	2.40 (m)	2.13 (m)	7.98 (s)	7.98 (s)	2.90 (m)	1.82 (m)	1.82 (m)	2.90 (m)
8	6.02 (t)		6.02 (t)		2.40 (m)	2.13 (m)	2.40 (m)	2.13 (m)	9.26 (s)	8.73 (s)	—	7.55 (m)	6.90 (m)	7.55 (m)
9a [b]	6.37 (t)		2.68 (t)		2.25 (m)		1.73 (m)		9.05 (s)	8.92 (s)	—	7.52 (m)	6.93 (m)	7.52 (m)
9b [b]	6.37 (t)		2.68 (t)		2.25 (m)		1.73 (m)		8.54 (s)	9.45 (s)	—	7.52 (m)	6.93 (m)	7.52 (m)

Compound	Coupling Constants and Other Relevant Data
4	δ_{Me} = 1.83 (s), $J_{1e,1a}$ = 14.5, $J_{3e,4e}$ = 5.0, $J_{3e,4a}$ = 2.0, $J_{4e,4a}$ = 14.0
5	δ_{Me} = 1.70 (s), δ_{AcO} = 2.12 (s), $J_{1e,1a}$ = 14.5, $J_{3e,4e}$ = 14.5, $J_{3e,4e}$ = 5.0, $J_{3e,4a}$ = 3.0, $J_{4e,4a}$ = 14.0
6a	$W_{1/2}(H_{1e}\text{-}H_{4a})$ = 9.0, $W_{1/2}(H_{2e}\text{-}H_{4a})$ = 9.0
6c	δ_{Me} = 1.13 (d), $J_{1a,1e}$ = 13.2, $J_{1a,2a}$ = 10.4, $J_{1e,2a}$ = 4.1, $J_{2a,Me}$ = 6.4, $J_{3a,4a}$ = 11.4, $J_{3a,4e}$ = 3.5, $J_{4a,4e}$ = 13.4
6d	δ_{Ph} = 7.20 (s), $J_{1,2a}$ = $J_{1,2e}$ = 6.0
7a	$W_{1/2}(H_{1e}\text{-}H_{4a})$ = 7.5, $W_{1/2}(H_8\text{-}H_{11})$ = 8.0
7b	δ_{Me} = 1.05 (d), $J_{Me,2}$ = $J_{Me,3}$ = 6.0, $J_{1e,1a}$ = 13.5, $J_{1a,2a}$ = 7.5, $J_{1e,2a}$ = 4.5, $W_{1/2}(H_8\text{-}H_{11})$ = 8.0
7c	δ_{Me} = 1.11 (d), $J_{Me,2}$ = 6.4, $J_{1a,1e}$ = 13.2, $J_{1a,2a}$ = 10.4, $J_{3a,4a}$ = 11.4, $J_{3e,4a}$ = 3.5, $J_{4a,4e}$ = 13.4, $W_{1/2}(H_8\text{-}H_{11})$ = 7.5
7d	$W_{1/2}(H_{2e})$ = 12.0, $W_{1/2}(H_{2a})$ = 12.0, $J_{1,2a}$ = $J_{1,2e}$ = 6.0
8	δ_{OMe} = 4.00 (s), δ_{Ph} = 7.15 (s), $J_{1,2a}$ = $J_{1,2e}$ = 6.0
9a [b]	$\delta_{Ph}(1)$ = 7.25 (s), $\delta_{Ph}(4)$ = 7.13 (s), δ_{OMe} = 4.00 (s), $J_{1,2}$ = 8.0; $J_{1,3}$ = 2.0, $J_{3,4}$ = 7.5
9b [b]	$\delta_{Ph}(1)$ = 7.25 (s), $\delta_{Ph}(4)$ = 7.13 (s), δ_{OMe} = 4.03 (s)

[a] Spectra measured in deuteriochloroform (internal TMS) solution. Most of the assignments have been confirmed by double resonance experiments. Shifts are given in ppm (δ scale). [b] In spite of ring-opening, the numbering used in the cyclic derivatives has been maintained in **9a** and **9b**, in order to facilitate comparisons.

Table 2

^{13}C NMR Data of Starting Compounds Hydrogenated Derivatives corresponding to the B, C and D rings [a]

Compound	C_6	C_{6a}	C_7	C_{7a}	C_8	C_9	C_{10}	C_{11}	C_{11a}	C_{12}	C_{12a}	C_{13}
1a	158.7	124.2	128.8	134.8	129.2	129.2	129.2	129.2	134.8	128.8	124.2	158.7
1b	158.1	124.6	128.8	134.9	129.3	129.1	129.1	129.3	134.9	128.8	124.6	158.1
1c	158.2	124.2	128.7	134.6	128.7	128.7	128.7	128.7	134.6	128.7	124.2	158.2
1d	158.3	124.5	128.9	135.0	129.5	129.4	129.4	129.5	135.0	128.9	124.5	158.3
2d	158.6	123.8	128.8	127.9	156.7	106.3	129.5	121.3	136.2	127.6	124.7	158.6
3	155.9	121.8	129.0	132.6	129.4	129.1	129.1	129.4	132.6	129.0	121.8	155.9
4	160.2	125.6	127.8	144.3	29.7	22.4	22.4	29.7	144.3	127.7	125.2	159.4
6a	159.0	124.5	128.8	134.8	129.3	129.1	129.1	129.3	134.8	128.8	124.5	159.0
6c	159.1	124.6	127.9	134.9	129.3	128.9	128.9	129.3	134.9	127.9	124.6	159.1
6d	159.4	124.6	128.9	135.0	129.3	129.3	129.3	129.3	135.0	128.9	124.6	159.4
7a	158.6	125.5	127.7	143.7	29.6	22.5	22.5	29.6	143.7	127.7	125.5	158.6
7b	159.3	126.7	127.9	143.9	29.7	22.6	22.6	29.7	143.9	127.9	126.7	159.3
7c	158.9	126.9	127.9	144.0	29.7	22.6	22.6	29.7	144.0	127.9	126.9	158.9
8	158.7	123.9	128.5	127.9	156.7	106.2	129.4	121.2	136.1	127.7	125.1	158.7

^{13}C NMR Data of Starting Compounds Hydrogenated Derivatives corresponding to the A ring

Compound	C_1	C_2	C_3	C_4	
1a	44.5	120.7	120.7	44.5	
1b	48.3	121.4	121.4	48.3	δ_{Me} = 15.8
1c	47.7	134.6	114.9	44.4	δ_{Me} = 20.0
1d	57.7	125.2	125.2	57.7	δ_{Ph} ($C_{1'}$ = 139.2, $C_{2'}$ = 126.6, $C_{3'}$ = 128.5, $C_{4'}$ = 127.5)
2d	57.8	125.2	125.2	57.8	δ_{Me} = 55.8, δ_{Ph} ($C_{1'}$ = 139.3, $C_{2'}$ = 126.7, $C_{3'}$ = 128.6, $C_{4'}$ = 126.8)
3	54.2	43.2	46.3	54.2	δ_{Me} = 19.3
4	51.7	65.6	70.5	51.0	δ_{Me} = 24.6
6a	44.5	22.5	22.5	44.5	
6c	50.8	28.5	30.8	44.2	δ_{Me} = 18.5
6d	60.1	25.6	25.6	60.1	δ_{Ph} ($C_{1'}$ = 141.0, $C_{2'}$ = 125.3, $C_{3'}$ = 128.5, $C_{4'}$ 126.9)
7a	44.2	22.3	22.3	44.2	
7b	48.7	31.1	31.1	48.7	δ_{Me} = 12.9
7c	50.5	28.4	30.7	44.0	δ_{Me} = 18.5
8	60.0	25.7	25.7	60.0	δ_{Me} = 55.8, δ_{Ph} ($C_{1'}$ = 141.2, $C_{2'}$ 125.4, $C_{3'}$ = 128.5, $C_{4'}$ = 127.0)

[a] Spectra measured in deuteriochloroform (internal TMS) solution). Shifts are given in ppm (δ scale).

the starting compounds **1a-d** and **2d** because these data had not until now been published, and carbon signals in the hydrogenated derivatives have often been ascertained by comparison with those of the corresponding adducts. Structural features of all compounds synthesized have been gathered here together for easier comment.

Chlorohydrin **4** seems to be formed in a regiospecific way, and the orientation of substituents in the isomer obtained is in accordance with the usual rules concerning electrophilic opening of epoxides. The chemical shift of the methyl group in the ^1H nmr spectrum (1.83 ppm) should be evidence for the situation of the chloride atom, since the methyl signal appears at higher fields when a hydroxy group is attached to C_2 [12]. However, acetylation with isopropenyl acetate to give **5** was performed in order to confirm this assignment and, as expected, the C_3 methinic hydrogen of **5** was found to be deshielded about 1.13 ppm with respect to **4** [13]. Examination of the ^{13}C chemical shifts of C_2 and C_3 in **4** and **5** by means of the Shoolery rules led to the same results. As in other diazapolycyclic

epoxides [4], ring-opening takes place in a *trans*-diaxal way, since the C_3 methinic proton at 4.15 ppm is shown to be equatorially oriented on the basis of its coupling constants values with the vicinal methylene ($J_{H_{3e}-H_{4e}}$ = 5.0 Hz, $J_{H_{3e}-H_{4a}}$ = 2.0 Hz). In this case, $J_{ee} > J_{ea}$ because the reducing influence of the electronegative chlorine upon J_{vic} is greatest when it is transcoplanar to one of the coupling protons, H_{4a} [4]. Hydrogenation of the terminal aromatic ring of **4** is easily confirmed by the lack of aromatic signals at 8.16 and 7.75 ppm or 129.4 and 129.1 ppm in respectively the ^1H and ^{13}C spectra, and the appearance of the new aliphatic ones at 2.85 and 1.81 ppm or 29.7 and 22.4 ppm.

In a similar way, the reduction of the aromatic rings in series **7** can also be inferred by comparing the chemical shifts of adducts and derivatives in Table 2. We think that it is also interesting to comment on the stereochemical features of these compounds. As expected, stereochemistry and conformational arrangements at the terminal tetrahydropyridazine ring moiety are not affected by the hydrogenation of ring D. With regard to the orientation of substituents in derivatives **6** and **7**, remarks can be made as follows.

In **6c** and **7c**, the methyl group at C_2 exhibits the more stable equatorial orientation, as it is shown by the coupling constants between H_2 and the neighbouring methylene (4.1 and 10.4 Hz) in the ^1H nmr spectrum. In the dimethyl derivative **7b** the J values between the methinic protons and the vicinal methylene again correspond to a *trans*-diequatorial orientation for both methyl groups. Although *trans*-diaxial coupling is somewhat small (7.5 Hz), it is an usual value in heterocyclic systems [14]. The chemical shifts of these methylenic hydrogens (2.15 ppm), deshielded both by the C_2 and C_3 methyls also agree with the supposed axial disposition. For further confirmation, the ^{13}C shifts of the tetrahydropyridazine ring carbon atoms have been calculated for the methyl substituted compounds **6c**, **7b** and **7c** on the basis of those found in the unsubstituted adduct **6a**, taking into account the theoretical effect of equatorial substituents [15] (*i.e.* **6c**; theoretical values considering equatorial Me, C_1 = 53.9; C_2 = 28.5, C_3, = 31.5; C_4 = 44.5 ppm; theoretical values for axial Me, C_1 = 59.3, C_2 = 29.9, C_3 = 36.9, C_4 = 38.1 ppm; experimental, C_1 = 50.8, C_2 = 28.5, C_3 = 30.8, C_4 = 44.2 ppm).

In order to improve our knowledge about the stereochemical features at the tetrahydropyridazine ring moiety, X-rays data were obtained for hydrogenated compounds **6a** and **6c** [16]. A typical Chair-like conformation has been found in both cases for ring A, whereas diazaquinonic ring B is clearly less planar in **6c** than in **6a**. In **6c**, equatorial H_1 exhibits a more coplanar orientation with respect to the neighbouring carbonyl group than the homologous H_4 does, and this fact agrees with evidence obtained from the ^1H chemical shifts differences between the two pairs of methylenic protons at C_1 and C_4 ($\Delta\delta$ H_{1e}-H_{1a} = 1.8 ppm, $\Delta\delta H_{4e}$-H_{4a} = 1.2 ppm). This seems to be an usual feature of adducts derivatives with substituents attached to C_2 [4], in which this substitution increases the coplanarity between the N-C_1-C_2- fragment and ring B. On the other hand, the equatorial orientation of the C_2-methyl at **6c** is confirmed and the amidic nitrogen atoms show a clear deformation with respect to sp^2 hybridization. In short, X-ray data agree with those obtained from nmr spectra.

In the case of the 1,4-diphenylderivatives **6d** and **7d**, ^1H vicinal coupling constants between methinic and both methylenic protons are identical, with a value of 6.0 Hz. A simple interpretation of these data is that phenyl groups addopt an intermediate orientation between axial and equatorial positions, so minimizing steric hindrance with both the neighbouring carbonyls at ring B and the axial hydrogens at ring A.

Turning now towards the 8-methoxy derivatives, the tetracyclic hydrogenation product **8** shows spectroscopical features with respect to the tetrahydropyridazine ring which are very close to those mentioned above for **6d** and **7d**, indicating a similar arrangement of the phenyl substituents. The rather complicated assignment of signals corresponding to the carbon atoms at the aromatic rings moiety in the ^{13}C spectra of **2d** and **8** was made by comparison with the related signals at the non-methoxylated adduct **1d**, taking into account the shift effects due to the methoxy group, according to the Shoolery rules.

The ir spectra of the isomeric opening products **9a** and **9b** present a wide NH absorption in the range of 2500-3300 cm^{-1} when registered in chloroform solution. This signal clearly diminished when spectra are registered in the solid state (potassium bromide), whereas a strong OH absorption appears at 3440 cm^{-1} together with another new signal at 1570 cm^{-1}, assignable to C=N. These data might support the idea that the amidic form predominates in solution, while the imidic one does in the solid state.

When comparing the ^1H nmr spectra of **9a** and **9b** with that one of **2d**, ring opening is confirmed by the strong shielding experimented by one of the methinic hydrogens (from 6.02 to 2.86 ppm) whereas the other one remains unaffected. Additional evidence is provided by the fact that the two phenyl groups are not any more equivalent, and methylenic protons at C_2 and C_3 are upfield shifted, losing the previous differentiation between the geminal hydrogens. Spectra of **9a** and **9b** display symmetrical patterns, except in the case of the aromatic protons at ring C, H_7 and H_{12}. In isomer **9a**, $\Delta\delta_{H_{12}-H_7}$ = 0.91 ppm, in **9b**, $\Delta\delta_{H_{12}-H_7}$ = 0.13 ppm. This fact allows stuctural identification of both compounds, since H_{12} should be highly deshielded in **9b** because of its coplanarity both with the methoxy group and the neighbouring carbonyl. In con-

trast, H_7 is not affected by the methoxy substituent, and the neighbouring carbonyl has a substantial contribution of the enolic form. The situation is quite different in isomer **9a**, where the deshielding effect of the methoxy group on H_7 and H_{12} is just inverted. In consequence, chemical shifts differences between these two protons must be greater in the case of **9b**.

EXPERIMENTAL

Melting points are uncorrected, and were determined in open capillary tubes on a Köfler hot-stage apparatus. The ^1H and ^{13}C nmr spectra were recorded on Varian EM-390 and Varian XL-300 spectrometers operating at 90 and 300 MHz, with TMS as internal standard. Mass spectra were recorded on a Hitachi Perkin-Elmer RMV-6MG at 70 eV. The ir spectra were obtained on a Perkin-Elmer 257 spectrometer. Analytical tlc was performed on aluminium sheets coated with a 0.2 mm layer of silica gel 60 F_{254} (Merck). Chromatographic separations were performed either on columns using the flash chromatography technique on silica gel 60 (Merck), 200-400 mesh, or by preparative layer chromatography on 20 × 20 cm glass plates coated with a 2 mm layer of silica gel PF_{254} (Merck).

Adducts **1a-d** [1,2], **2b**, **2d** [3] and epoxide **3** [4] were obtained as described in previous papers.

General Procedure for Hydrogenation.

To a solution of 0.9-3.0 mmoles of the starting adduct in 50 ml of dry chloroform, a catalytic amount of palladium on charcoal (10%) was added. Then, the vigorously stirred suspension was hydrogenated at room temperature and under a pressure of 45-65 psi during a variable period of time. Once the theoretical amount of hydrogen had been consumed, the catalyst was filtered off and the solvent evaporated *in vacuo*. After that, the resulting residue was purified as stated in every case.

2-Chloro-3-hydroxy-2-methyl-6,13-dioxo-1,2,3,4,6,13-hexahydrobenzo[*g*]pyridazine[1,2-*b*]phthalazine (**4**).

This compound was prepared as described in the general procedure from 0.5 g (1.27 mmoles) of epoxide **3** (65 psi, 72 hours). The resulting residue was repeatedly washed with boiling *n*-hexane. The remaining insoluble solid was then analyzed by tlc on silica gel and with chloroform/benzene/ethyl acetate (1/1/1) as the eluent, showing to be a pure compound with Rf = 0.36, which was identified as chlorohydrin **4**; 0.24 g were obtained (42% yield), mp 212-214°; ir (potassium bromide): ν max 3430 (OH), 2940, 1635 (C=O), 1610, 1450, 1370, 1285, 1070 (C=O), 940, 725 cm^{-1}; ms: m/e (% relative abundance) 336 (17, $M^+ + 2$), 334 (44, M^+), 259 (52), 214 (50), 158 (100).

Anal. Calcd. for $C_{17}H_{19}ClN_2O_3$: C, 60.98; H, 5.73; N, 8.36; Cl, 10.58. Found: C, 60.79; H, 5.74; N, 8.08; Cl, 10.24.

3-Acetoxy-2-chloro-2-methyl-6,13-dioxo-1,2,3,4,6,13-hexahydrobenzo-[*g*]pyridazine[1,2-*b*]phthalazine (**5**).

A solution of 0.35 g (1.0 mmoles) of **4** and 0.05 g of *p*-toluenesulphonyl chloride in 40 ml of isopropenyl acetate was refluxed for 7 hours. The reaction mixture was allowed to cool to room temperature and washed with 5% aqueous sodium bicarbonate (2 × 50 ml) and water. After drying over magnesium sulphate, solvent was evaporated *in vacuo*. The resulting oil was purified by flash column chromatography with benzene/ethyl acetate (3/1) as eluent to give 0.094 g of the acetylated derivative **5** (25% yield); mp 65-67°; ir (film): ν max 2940, 1745 (OAc), 1650 (C=O), 1615, 1435, 1375, 1210, 940, 760 cm^{-1}; ms: m/e (% relative abundance) 378 (7, $M^+ + 2$), 376 (18, M^+), 282 (21), 281 (100), 158 (23), 43 (41).

Anal. Calcd. for $C_{19}H_{21}ClN_2O_4$: C, 60.56; H, 5.57; N, 7.44; Cl, 9.41. Found: C, 60.39; H, 5.41; N, 7.15.

6,13-Dioxo-1,2,3,4,6,13-hexahydrobenzo[*g*]pyridazine [1,2-*b*]phthalazine (**6a**).

This compound was prepared as described in the general procedure from 0.5 g (1.8 mmoles) of adduct **1a** (65 psi, 4 hours). After usual work-up an oil was obtained which crystallised from ethanol to give 0.15 g. (32% yield) of **6a**, mp 200-202°; ir (potassium bromide): ν max 2940, 2640 (C=O), 1615, 1285, 920, 770, 760 cm^{-1}; ms: m/e (% relative abundance) 226 (54, M^+), 126 (100).

Anal. Calcd. for $C_{16}H_{14}N_2O_2$: C, 72.17; H, 5.29; N, 10.51. Found: C, 71.87; H, 5.39; N, 10.46.

2-Methyl-6,13-dioxo-1,2,3,4,6,13-hexahydrobenzo[*g*]pyridazine[1,2-*b*]-phthalazine (**6c**).

This compound was prepared as described in the general procedure from 0.5 g (1.8 mmoles) of adduct **1c** (60 psi, 4 hours). A yellow solid was obtained which crystallized from *n*-hexane to give 0.22 g (44% yield) of **6c**, mp 148-150°; ir (potassium bromide): ν max 2940, 1640 (C=O), 1615, 1450, 1285, 935, 760, 750 cm^{-1}; ms: m/e (% relative abundance) 280 (100, M^+), 126 (85).

Anal. Calcd. for $C_{17}H_{16}N_2O_2$: C, 72.83; H, 5.75; N, 9.99. Found: C, 72.97; H, 6.03; N, 10.19.

1,4-Diphenyl-6,13-dioxo-1,2,3,4,6,13-hexahydrobenzo[*g*]pyridazine[1,2-*b*]-phthalazine (**6d**).

This compound was prepared as described in the general procedure from 0.3 g (1.2 mmoles) of adduct **1d** (55 psi, 4 hours). After usual work-up, the residue was crystallized from benzene/*n*-hexane to give 0.1 g (33% yield) of **6d**, mp 219-220°; ir (potassium bromide): ν max 2940, 1635 (C=O), 1622, 1500, 1455, 1265, 765 cm^{-1}; ms: m/e (% relative abundance) 418 (70, M^+), 301 (100), 126 (39).

Anal. Calcd. for $C_{28}H_{22}N_2O_2$: C, 80.36; H, 5.29; N, 6.69. Found: C, 80.09; H, 5.32; N, 6.59.

6,13-Dioxo-1,2,3,4,6,8,9,10,11,13-decahydrobenzo[*g*]pyridazine[1,2-*b*]-phthalazine (**7a**).

This compound was prepared as described in the general procedure from 0.8 g (3.0 mmoles) of adduct **1a** (65 psi, 48 hours). The resulting residue was purified by silica gel tlc using benzene/ethyl acetate (3/1) as the eluent. The fraction with Rf = 0.20 was crystallised from methanol to give 0.15 g (18% yield) of **7a**, mp 248-250°; ir (potassium bromide): ν 2940, 1640 (C=O), 1612, 1450, 1285, 935, 768, 760 cm^{-1}; ms: m/e (% relative abundance) 270 (61, M^+), 266 (71), 126 (100).

Anal. Calcd. for $C_{16}H_{18}N_2O_2$: C, 71.08; H, 6.71; N, 10.36. Found: C, 70.98; H, 6.64; N, 10.32.

2,3-Dimethyl-6,13-dioxo-1,2,3,4,6,8,9,10,11,13-decahydrobenzo[*g*]pyridazine[1,2-*b*]phthalazine (**7b**).

This compound was prepared as described in the general procedure from 0.5 g (1.7 mmoles) of adduct **1b** (60 psi, 72 hours). After usual work-up, the residue was crystallized from *n*-hexane to give 0.14 g (27% yield) of **7b**, mp 148-150°; ir (nujol): ν max 1630 (C=O), 1605, 1260, 1195, 928, 715 cm^{-1}; ms: m/e (% relative abundance) 298 (100, M^+), 229 (32), 158 (39).

Anal. Calcd. for $C_{18}H_{22}N_2O_2$: C, 72.45; H, 7.43; N, 9.38. Found: C, 72.67; H, 7.39; N, 9.29.

2-Methyl-6,13-dioxo-1,2,3,4,6,8,9,10,11,13-decahydrobenzo[*g*]pyridazine-[1,2-*b*]phthalazine (**7c**).

This compound was prepared as described in the general procedure from 0.6 g (2.2 mmoles) of adduct **1c** (70 psi, 43 hours). A white solid was obtained which crystallized from diethyl ether/petroleum ether to give 0.39 g (64% yield) of **7c**, mp 194-196°; ir (potassium bromide): ν max 2940, 1635 (C=O), 1612, 1450, 1280, 1210, 935, 725 cm^{-1}; ms: m/e (% relative abundance) 284 (100, M^+), 214 (40), 158 (60).

Anal. Calcd. for $C_{17}H_{20}N_2O_2$: C, 71.80; H, 7.08; N, 9.85. Found: C, 71.61; H, 7.14; N, 9.54.

1,4-Diphenyl-6,13-dioxo-1,2,3,4,6,8,9,10,11,13-decahydrobenzo[*g*]pyridazine[1,2-*b*]phthalazine (**7d**).

This compound was prepared as described in the general procedure

from 0.5 g (1.2 mmoles) of adduct **1d** (60 psi, 72 hours). After usual work-up, the residue was crystallised from cyclohexane to give 0.19 g (38% yield) of **7d**, mp 193-195°; ir (nujol): ν max 3040, 1640 (C=O), 1610, 1270, 950, 765, 740, 705 cm^{-1}; ms: m/e (% relative abundance) 422 (23, M^+), 305 (35), 96 (100).

Anal. Calcd. for $C_{28}H_{26}N_2O_2$: C, 79.59; H, 16.20; N, 6.62. Found: C, 79.37; H, 6.41; N, 6.62.

1,4-Diphenyl-8-methoxy-6,13-dioxo-1,2,3,4,6,13-hexahydrobenzo[*g*]pyridazine[1,2-*b*]phthalazine (**8**).

This compound was prepared according to the general procedure described above from 0.4 g (0.89 mmoles) of adduct **2d** (45 psi, 4 hours). After usual work-up, the residue was analyzed by tlc with benzene/ethyl acetate/chloroform (2/1/1) as eluent, showing to be a mixture of two compounds with Rf = 0.62 and 0.83. Preparative tlc on silica gel with the same eluent composition as above afforded 0.3 g of the fraction with Rf = 0.62, as a solid which crystallized from ethyl acetate (30% yield) and was identified as the tetracyclic hydrogenation product **8**, mp 230-232° ir (potassium bromide): ν max 3070, 3040, 2940, 1645 (C=O), 1620, 1450, 1270, 925, 750, 705 cm^{-1}; ms: m/e (% relative abundance) 448 (83, M^+), 332 (100), 156 (42), 91 (67).

Anal. Calcd. for $C_{29}H_{24}N_2O_3$: C, 77.65; H, 5.39; N, 6.24. Found: C, 77.54; H, 5.50; N, 6.36.

The fraction with Rf = 0.83 resulted to be formed by a mixture of isomers **9a** and **9b** which crystallized together from benzene/cyclohexane to give 0.19 g (35% whole yield), mp 152-153°; ir (chloroform): ν max, 3500-2500 (N-H), 3070, 3010, 2950, 1640 (C=O), 1615, 1580, 1460, 1270, 925, 705 cm^{-1}; ms: m/e (% relative abundance) 450 (21, M^+), 331 (43), 242 (57), 91 (100).

Anal. Calcd. for $C_{29}H_{26}N_2O_3$: C, 77.31; H, 5.81; N, 6.21. Found: C, 77.32; H, 5.87; N, 6.09.

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