Diazapolycyclic Compounds. XXVI. Reactivity of Epoxy- and Dihydroxy Derivatives of Diazaquinone Adducts

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Treatment of epoxy and dihydroxy derivatives of diazaquinone adducts with concentrated sulfuric acid yields the respective oxo derivatives, while the reaction of the epoxides with boron trifluoride etherate affords *trans*-fluorohydrines.

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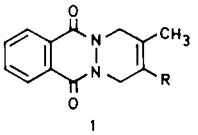
In connection with our investigations on the reactivity of diazapolycyclic systems prepared by Diels-Alder reaction from diazadienophiles, different types of reactions have been performed on the terminal piperidazine ring and a wide variety of compounds have thus been obtained [1,2,3]. Aiming to the preparation of new pyrazolidine and piperidazinone derivatives, we now report the reaction of epoxy- and dihydroxy- derivatives of diazaquinone adducts with acidic reagents.

The starting materials were prepared by epoxidation or hydroxylation at the ethylenic double bond of adducts **1a** and **1b**. Thus, reaction with *m*-chloroperbenzoic acid gave epoxides **2a** and **2b** in good yield [4]. Cleavage of the oxirane ring of these compounds led to diols **3**. Treatment of **3** with isopropenyl acetate afforded the acetylated derivatives **4** in quantitative yield.



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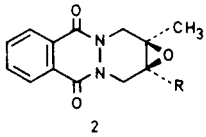
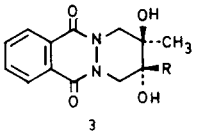


2

a: R=H
b: R=CH_3



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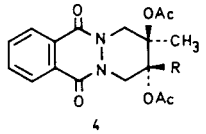

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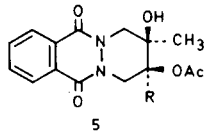
Comparison of the ^{1}H-nmr spectra of compounds **4** (Table 1) with those of the starting diols allowed us to assign a *trans*-diaxial configuration for the hydroxyl groups, in agreement with previously reported results [5]. A deshielding effect of about 1 ppm is observed for the equatorial hydrogens, whereas the axial ones are unaffected. A deshielding of 1.85 ppm is also apparent in the chemical shift of the methynic hydrogen in compound **4a**, which agrees with an equatorial position [6].

X-Ray diffraction results for compound **3b** [7] also agree with the above configurational assignment.

In the hydroxylation of adducts **1** with silver acetate and iodine [8,9], derivatives **5** were the only isolable compounds with quite good yield. Hydrolysis of **5b**, either in acid or basic medium, afforded only mixtures of undetermined nature. On the other hand, hydrolysis of **5a** afforded a small yield of the diol **6a**.



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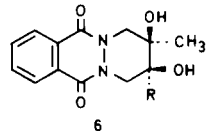
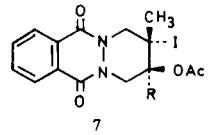


6

a: R=H
b: R=CH_3



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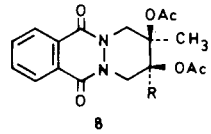
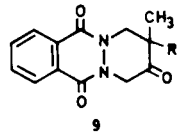


8

The *cis*-configuration for the two new substituents on the terminal piperidazine ring in **5** and **6** was deduced from the isolation of the intermediate *trans*-iodo-acetate **7b** and from its ^{1}H-nmr data, together with those of the diacetates **8** (Table 2).

Structure of compound **5a**, assumed on the basis of literature data [10], was confirmed by the fact that the signal for the methynic hydrogen does not change upon acetylation of the free hydroxyl group. The vicinal coupling constants of 3 and 4 Hz between this hydrogen and the contiguous methylene group, agree with its axial position.

Treatment of **2** and **3** with concentrated sulfuric acid at room temperature afforded compounds **9**, although in low yield. This is probably due to the presence of the carboxamido groups and to the *trans*-diaxial configuration of the hydroxyl groups [11].



9

a: R=H
b: R=CH_3

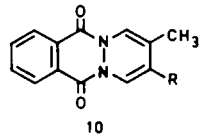


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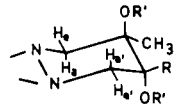
Table 1

^{1}H-NMR Data of Compounds **3** and **4**

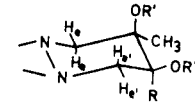


Compound	R	R'	δ H_a	δ H_e	δ $H_{a'}$	δ $H_{e'}$	δ R	δ CH_3	δ R'
3a	H	H	3.60 (d) (J = 13 Hz)	4.26 (d)	3.91 (dd) (J = 13 Hz)	4.37 (dd)	3.65 (m)	1.27 (s)	4.9 (br)
4a	H	Ac	3.75 (d) (J = 14 Hz)	5.22 (d)	3.80 (dd) (J = 14 Hz)	4.85 (dd)	5.52 (m)	1.63 (s)	[b]
3b	CH_3	H	3.55 (d) (J = 14 Hz)	4.45 (d)	3.55 (d) (J = 14 Hz)	4.45 (d)	1.24 (s)		4.7 (br)
4b	CH_3	Ac	3.53 (d) (J = 14 Hz)	5.80 (d)	3.53 (d) (J = 14 Hz)	5.80 (d)	1.72 (s)		2.05 (s)

[a] Spectra of compounds **3** were measured in DMSO-d_6, spectra of compounds **4** in deuteriochloroform. [b] Two singlets at δ 2.05 and 2.12. [c] Aromatic protons of these compounds appear as a multiplet (δ 7.6-8.4).

Table 2

^{1}H-NMR Data of Compounds **5**, **6** and **8**



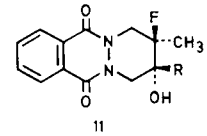
Compound	R	R'	R''	δ H_a	δ H_e	δ $H_{a'}$	δ $H_{e'}$	δ R	δ CH_3	δ R'	δ R''
6a	H	H	H	3.50 (d) (J = 13 Hz)	4.38 (d)	3.3-4.5 (m)			1.28 (s)	4.8 (s)	5.22 (d) (J = 4 Hz)
5a	H	H	Ac	3.68 (d) (J = 14 Hz)	4.62 (d)	4.04 (dd) (J = 9 Hz)	4.54 (dd) (J = 14 Hz) (J = 4 Hz)	5.13 (dd)	1.47 (s)	3.5 (s)	2.17 (s)
8a	H	Ac	Ac	3.94 (d) (J = 14 Hz)	4.21 (d)	4.87 (d) (J = 5 Hz)		5.34 (t) (J = 5 Hz)	1.70 (s)	2.03 (s)	2.13 (s)
5b	CH_3	H	H	4.20 (d) (J = 14 Hz)	5.08 (d)	4.13 (s)		1.73 (s)	1.47 (s)	3.1 (s)	2.10 (s)
8b	CH_3	Ac	Ac	4.45 (d) (J = 14 Hz)	4.84 (d)	4.45 (d) (J = 14 Hz)	4.84 (d)	1.77 (s)		2.08 (s)	

[a] Spectrum of compound **6a** was measured in DMSO-d_6, spectra of compounds **5** and **8** in deuteriochloroform. [b] Aromatic protons of these compounds appear as a multiplet (δ 7.6-8.4).

The presence of an oxo group in **9** was confirmed by a strong band at 1730 cm^{-1} in the ir spectra. As far as their ^{1}H-nmr spectra is concerned, must be pointed out that the expected AB and ABX systems are apparent in **9a**, whereas the two methylene groups appear as singlets in **9b**. This fact reflects the higher conformational mobility for the terminal ring in this compound.

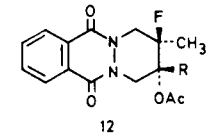
Compounds resulting from a ring contraction were never obtained. However, compound **10b** was isolated from 2,3-dimethylbutadiene derivatives and its formation can be easily explained through an acid-promoted double dehydration of the starting product.

Treatment of **2** with boron trifluoride etherate under similar conditions to those reported in the literature for the preparation of ketones [11,12], gave the *trans*-fluorohydrines **11** as the main reaction products. Only epoxide **2a** afforded a 8% yield of the rearrangement compound **9a**.



11

a: R=H
b: R=CH_3



12

Formation of **11** and its stereochemisty are in good agreement with previous results reported for epoxidated cyclohexanes [12].

Structural assignment for compounds **11** was carried out on the basis of their ^{1}H-nmr data, together with those of the acetylated derivatives **12**.

The methyl groups in compound **11b** appear as doublets (coupling constants H-F: 22 and 1 Hz). A coupling constant of 22 Hz for the doublet due to the methyl group in **11a** indicates a geminal relationship for the methyl group and the fluorine atom. Moreover, if the spectrum of **11a** is registered in DMSO-d_6, the hydroxyl group gives rise to a doublet (J = 5 Hz), due to the coupling with the methynic hydrogen.

Acetylation of **11** originated a deshielding of 1 ppm of one of the hydrogens in the contiguous methylene group, indicating an axial position for the hydroxyl group. On the other hand, the value for the coupling constants between the fluorine atom and the hydrogens of the adjacent methylene group (35 and 12 Hz) also indicates an axial position for the fluorine atom, and this fact allowed us to assign a *trans*-diaxial configuration for **11** and **12**.

EXPERIMENTAL

Melting points are uncorrected. The ir spectra were recorded on a Perkin Elmer 257 spectrophotometer. The ^{1}H-nmr spectra were obtained with a Varian T-60A spectrometer using TMS as internal standard. Compounds **1** and **2** were obtained according to procedures previously described by ourselves [4,13].

r-2,t-3-Dihydroxy-2-methyl-1,2,3,4-tetrahydropyridazino[1,2-*b*]phthalazine-6,11-dione (**3a**).

A solution of 370 mg (1.5 mmoles) of **2a** in 5 ml of water, 5 ml of acetone and 5 drops of sulfuric acid was heated at 50° for 4 hours. The mixture was evaporated under reduced pressure and the residue was washed with water. Recrystallization from water and then from ethyl acetate afforded 320 mg (81% yield) of **3a**, mp 190-192°; ir (potassium bromide): 3420 (O-H), 1625 (C=O), 1090 (C-O) cm^{-1}.

Anal. Calcd. for $C_{13}H_{14}N_2O_4$: C, 59.9; H, 5.4; N, 10.7. Found: C, 59.4; H, 5.2; N, 10.9.

r-2,t-3-Dihydroxy-2,3-dimethyl-1,2,3,4-tetrahydropyridazino[1,2-*b*]phthalazine-6,11-dione (**3b**).

A solution of 650 mg (2.5 mmoles) of **2b** in 5 ml of water, 5 ml of acetone and 5 drops of sulfuric acid was heated at 50° for 2 hours and allowed to cool at room temperature. The resulting precipitate was filtered off and recrystallized from water to give 575 mg (83% yield), of **3b**, mp 231-232°; ir (potassium bromide): 3440 (O-H), 1630 (C=O), 1100 (C-O) cm^{-1}.

Anal. Calcd. for $C_{14}H_{16}N_2O_4$: C, 60.9; H, 5.8; N, 10.1. Found: C, 61.1; H, 5.7; N, 10.1.

r-2-Acetoxy-c-3-hydroxy-3-methyl-1,2,3,4-tetrahydropyridazino[1,2-*b*]-phthalazine-6,11-dione (**5a**).

To a solution of 2.28 g (10 mmoles) of **1a** and 4.18 g (25 mmoles) of silver acetate in 30 ml of acetic acid, 2.54 g (10 mmoles) of powdered iodine were added during 1 hour under stirring. The iodine reacted gradually and after a further hour 0.3 ml of water was added. The mixture was then heated at 70° for 3 hours. The cooled mixture was treated with sodium chloride and the precipitate salts filtered off and washed with acetic acid. The filtrate and washings were concentrated *in vacuo* to give a residue which was taken up in chloroform and washed successively with water, 5% aqueous sodium bicarbonate, 40% aqueous sodium thiosulfate and water. Removal of solvent from the dried solution gave an oil which solidified upon standing in ether. Recrystallization from ethanol afforded 612 mg (20% yield) of **5a**, mp 166-167°; ir (potassium bromide): 3440 (O-H), 1730 (C=O acetate), 1640 (C=O), 1240 (C-O acetate) cm^{-1}.

Anal. Calcd. for $C_{15}H_{16}N_2O_5$: C, 59.2; H, 5.3; N, 9.2. Found: C, 59.5; H, 5.3; N, 9.3.

r-2,c-3-Dihydroxy-2-methyl-1,2,3,4-tetrahydropyridazino[1,2-*b*]phthalazine-6,11-dione (**6a**).

Hydrolysis of the monoacetate **5a** in ethanol with 20% aqueous sodium hydroxide under reflux for 4 hours gave **6a**, which was recrystallized from ethyl acetate, mp 171-172°; ir (potassium bromide): 3600-3200 (O-H), 1660 and 1625 (C=O) cm^{-1}.

Anal. Calcd. for $C_{13}H_{14}N_2O_4$: C, 59.5; H, 5.4; N, 10.7. Found: C, 59.2; H, 5.3; N, 10.4.

r-2-Acetoxy-c-3-hydroxy-2,3-dimethyl-1,2,3,4-tetrahydropyridazino[1,2-*b*]-phthalazine-6,11-dione (**5b**).

This compound was prepared as described above for **5a** from 2.42 g (10 mmoles) of **1b** and the reaction mixture was heated at 100° for 4 hours. The oily residue was chromatographed on silica gel using benzene/ethyl acetate (1:1) as eluent. Chromatography of the major fraction collected using benzene/ethanol (10:1) afforded **5b** (11% yield), mp 156-158°; ir (potassium bromide): 3400 (O-H), 1740 (C=O acetate), 1635 (C=O), 1250 (C-O acetate) cm^{-1}.

Anal. Calcd. for $C_{16}H_{18}H_2O_5$: C, 60.4; H, 5.7; N, 8.8. Found: C, 60.0; H, 5.4; N, 8.5.

r-2-Acetoxy-t-3-iodo-2,3-dimethyl-1,2,3,4-tetrahydropyridazino[1,2-*b*]-phthalazine-6,11-dione (**7b**).

This compound was prepared as described above for **5b**, but the reaction mixture was allowed to stand at room temperature for 64 hours and then was worked up. Chromatography of the residue on silica gel using benzene/ethyl acetate (1:1) gave **7b**, mp 130-131°; ir (potassium bromide): 1750 (C=O acetate), 1660 (C=O), 1230 (C-O acetate) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.9 (s, CH_3-C-OAc, 3H), 2.0 (s, CH_3-C-I, 3H), 2.17 (s, CH_3-COO, 3H), 3.50 (d, H_a[CH_2-C-I], 1H, J = 14 Hz), 3.89 (d, H_a[CH_2-C-OAc], 1H, J = 14 Hz), 4.92 (d, H_e[CH_2-C-I], 1H), 5.69 (d, H_e[CH_2-C-OAc], 1H), 7.5-8.1 (m, aromatic, 4H).

Anal. Calcd. for $C_{16}H_{17}IN_2O_4$: C, 44.9; H, 4.0; N, 6.5. Found: C, 44.9; H, 4.1; N, 6.4.

3-Methyl-3,4-dihydropyridazino[1,2-*b*]phthalazine-2(1*H*)-6,11-trione (**9a**).

A solution of 1.0 g (4 mmoles) of **2a** in 5 ml of sulfuric acid was stirred at room temperature for 15 hours. The mixture was poured over *ca.* 20 g of crushed ice and filtered. The filtrate was extracted with methylene chloride and the organic layer was washed successively with 5% aqueous sodium bicarbonate and water. Removal of the solvent from the dried solution gave an oil which was chromatographed on silica gel using benzene/ethyl acetate (1:1) as eluent to give a white solid. Recrystallization from ethanol afforded 93 mg (19% yield) of **9a**, mp 142-143°; ir (potassium bromide): 1730 (C=O), 1640 (C=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.26 (d, CH_3, 3H, J = 7 Hz), 2.9 (m, CH, 1H), 3.76 (dd, H_a[CH_2-CH], 1H, J = 14 Hz, J = 11 Hz), 4.35 (d, H_a[CH_2-CO], 1H, J = 18 Hz), 4.93 (dd, H_e[CH_2-CH], 1H, J = 14 Hz, J = 5 Hz), 5.27 (d, H_e[CH_2-CO], 1H), 7.4-8.2 (m, aromatic, 4H).

Anal. Calcd. for $C_{13}H_{12}N_2O_3$: C, 63.9; H, 5.0; N, 11.5. Found: C, 63.7; H, 5.0; N, 11.6.

2,3-Dimethylpyridazino[1,2-*b*]phthalazine-6,11-dione (**10b**).

Compound **2b** (500 mg, 2 mmoles) in 5 ml of sulfuric acid was stirred at room temperature for 15 hours. The mixture was poured over *ca.* 20 g of crushed ice and the precipitate was filtered off and washed repeatedly with water to free it from acid. Recrystallization from ethanol furnished

156 mg (36% yield) of **10b** as orange needles, mp 176-178°; ir (potassium bromide): 1630 (C=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 2.0 (s, CH_3, 6H), 7.8-8.4 (m, ethylenic and aromatic, 6H).

Anal. Calcd. for $C_{14}H_{12}N_2O_2$: C, 70.0; H, 5.0; N, 11.7. Found: C, 69.8; H, 5.1; N, 11.4.

3,3-Dimethyl-3,4-dihydropyridazino[1,2-*b*]phthalazine-2(1*H*)-6,11-trione (**9b**).

The filtrate obtained from the previous reaction was extracted with methylene chloride and the extract was worked up to give 99 mg (20% yield) of **9b**, which recrystallized from ethanol, mp 148-150°; ir (potassium bromide): 1730 (C=O), 1640 (C=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.2 (s, CH_3, 6H), 4.37 (s, CH_2-C, 2H), 4.90 (s, CH_2-CO, 2H), 7.7-8.2 (m, aromatic, 4H).

Anal. Calcd. for $C_{14}H_{14}N_2O_3$: C, 65.1; H, 5.5; N, 10.8. Found; C, 64.8; H, 5.4; N, 10.5.

t-3-Fluoro-r-2-hydroxy-3-methyl-1,2,3,4-tetrahydropyridazino[1,2-*b*]-phthalazine-6,11-dione (**11a**).

To a solution of 1.16 g (4.7 mmoles) of **2a** in 50 ml of dry benzene, 0.8 ml of boron trifluoride-etherate was added. The reaction mixture was stirred at room temprature for 5 hours, diluted with chloroform and washed with 5% aqueous sodium bicarbonate and water. The organic layer was dried over magnesium sulfate and evaporated. Chromatography of the residue using benzene/ethyl acetate (2:1) led to the isolation of two products. The less retained one was identified as **9a**, and only 97 mg (8% yield) was obtained. The more retained compound recrystallized from ethanol affording 300 mg (24% yield) of **11a**, mp 178-180°; ir (potassium bromide): 3440 (O-H), 1640 (C=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.60 (d, CH_3, 3H, $J_{H,F}$ = 22 Hz), 3.3-5.3 (m, CH_2, CH and OH, 6H), 7.6-8.4 (m, aromatic, 4H); ^{1}H-nmr (hexadeuteriodimethyl sulfoxide): δ 1.46 (d, CH_3, 3H, $J_{H,F}$ = 22 Hz), 3.2-4.8 (m, CH_2 and CH, 5H), 5.78 (d, OH, 1H, J = 5 Hz), 7.5-8.0 (m, aromatic, 4H).

Anal. Calcd. for $C_{13}H_{13}FN_2O_3$: C, 59.1; H, 5.0; N, 10.6. Found: C, 58.8; H, 4.9; N, 10.6.

t-3-Fluoro-r-2-hydroxy-2,3-dimethyl-1,2,3,4-tetrahydropyridazino[1,2-*b*]-phthalazine-6,11-dione (**11b**).

This compound was prepared as described above for **11a** from 1.25 g (4 mmoles) of **2b**, using a reaction time of 21 hours. Chromatography of the oily residue using benzene/ethyl acetate (4:1) afforded a white solid. Recrystallization from ethanol gave 222 mg (20% yield) of **11b**,mp 185-187°; ir (potassium bromide): 3410 (O-H), 1630 (C=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.39 (d, CH_3-C-OH, 3H, $J_{H,F}$ = 1 Hz), 1.52 (d, CH_3-C-F, 3H, $J_{H,F}$ = 22 Hz), 3.48 (dd, H_a[CH_2-C-OH], 1H, $J_{H,H}$ = 14 Hz, $J_{H,F}$ = 3 Hz), 3.66 (dd, H_a[CH_2-C-F], 1H, $J_{H,H}$ = 14 Hz, $J_{H,F}$ = 35 Hz), 3.8-4.0 (broad, OH, 1H), 4.67 (dd, H_e[CH_2-C-OH], 1H, $J_{H,F}$ = 2 Hz), 4.75 (dd, H_e[CH_2-C-F], $J_{H,F}$ = 12 Hz), 7.4-8.1 (m, aromatic, 4H).

Anal. Calcd. for $C_{14}H_{15}FN_2O_3$: C, 60.4; H, 5.4; N, 10.1. Found: C, 60.1; H, 5.3; N, 10.1.

Acetylation. General Procedure.

To a solution of 1 mmole of starting compound in 15 ml of freshly distilled isopropenyl acetate, 50 mg of *p*-toluenesulfonic acid was added. The reaction mixture was refluxed for 3 hours, cooled to room temperature and successively washed with 5% aqueous sodium bicarbonate and water. The organic layer was dried over magnesium sulfate and the excess of isopropenyl acetate was evaporated under reduced pressure. Recrystallization of the residue from ethanol afforded the desired compound.

r-2,t-3-Diacetoxy-2-methyl-1,2,3,4-tetrahydropyridazino[1,2-*b*]phthalazine-6,11-dione (**4a**).

From 96 mg (0.36 mmoles) of **3a**, 90 mg (70% yield) of **4a** was obtained, mp 138-139°; ir (potassium bromide): 1755 (C=O acetate), 1640 (C=O), 1235 (C-O acetate) cm^{-1}.

Anal. Calcd. for $C_{17}H_{16}N_2O_6$: C, 59.0; H, 5.2; N, 8.1. Found: C, 58.8; H, 5.0; N, 8.0.

r-2,t-3-Diacetoxy-2,3-dimethyl-1,2,3,4-tetrahydropyridazino[1,2-*b*]phthalazine-6,11-dione (**4b**).

From 110 mg (0.4 mmoles) of **3b**, 116 mg (80% yield) of **4b** was obtained. It separated *in situ*, mp 252-254°; ir (potassium bromide): 1735 (C=O acetate), 1640 (C=O), 1240 (C-O acetate) cm^{-1}.

Anal. Calcd. for $C_{18}H_{20}N_2O_6$: C, 60.0; H, 5.6; N, 7.8. Found: C, 59.7; H, 5.7; N, 7.5.

r-2,c-3-Diacetoxy-2-methyl-1,2,3,4-tetrahydropyridazino[1,2-*b*]phthalazine-6,11-dione (**8a**).

From 116 mg (0.38 mmoles) of **5a**, 85 mg (65% yield) of **8a** was obtained, mp 150-152°; ir (potassium bromide): 1740 (C=O acetate), 1650 (C=O), 1250 and 1230 (C-O acetate) cm^{-1}.

Anal. Calcd. for $C_{17}H_{18}N_2O_6$: C, 59.0; H, 5.2; N, 8.1. Found: C, 58.7; H, 5.3; N, 8.1.

r-2,c-3-Diacetoxy-2,3-dimethyl-1,2,3,4-tetrahydropyridazino[1,2-*b*]phthalazine-6,11-dione (**8b**).

From 98 mg (0.3 mmoles) of **5b**, 92 mg (85% yield) of **8b** was obtained, mp 182-184°; ir (potassium bromide): 1740 (C=O acetate), 1640 (C=O), 1250 and 1240 (C-O acetate) cm^{-1}.

Anal. Calcd. for $C_{18}H_{20}N_2O_6$: C, 60.0; H, 5.6; N, 7.8. Found: C, 59.8; H, 5.6; N, 7.7.

r-2-Acetoxy-t-3-fluoro-3-methyl-1,2,3,4-tetrahydropyridazino[1,2-*b*]phthalazine-6,11-dione (**12a**).

From 265 mg (1 mmole) of **11a**, 192 mg (62% yield) of **12a** was obtained, mp 128-130°; ir (potassium bromide): 1750 (C=O acetate), 1655 (C=O), 1230 (C-O acetate) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.55 (d, CH_3, 3H, $J_{H,F}$ = 22 Hz), 2.15 (s, CH_3-COO, 3H), 3.66 (dd, H_a[CH_2-C-F], 1H, $J_{H,H}$ = 15 Hz, $J_{H,F}$ = 32 Hz), 3.88 (dd, H_a[CH_2-C-OAc], 1H, $J_{H,H}$ = 15 Hz, $J_{H,F}$ = 3 Hz), 4.6-5.4 (m, H_e[CH_2-C-F], H_e[CH_2-C-OAc], CH, 3H), 7.6-8.4 (m, aromatic, 4H).

Anal. Calcd. for $C_{15}H_{15}FN_2O_4$: C, 58.8; H, 4.9; N, 9.2. Found: C, 59.0; H, 5.2; N, 9.2.

r-2-Acetoxy-t-3-fluoro-2,3-dimethyl-1,2,3,4-tetrahydropyridazino[1,2-*b*]-phthalazine-6,11-dione (**12b**).

From 250 mg (0.9 mmoles) of **11b**, 208 mg (72% yield) of **12b** was obtained, mp 140-141°; ir (potassium bromide): 1750 (C=O acetate), 1670 and 1650 (C=O), 1230 (C-O acetate) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.55 (d, CH_3-C-F, 3H, $J_{H,F}$ = 20 Hz), 1.75 (s, CH_3-C-OAc, 3H), 2.03 (s, CH_3-COO, 6H), 3.58 (dd, H_a[CH_2-C-OAc], 1H, $J_{H,H}$ = 14 Hz, $J_{H,F}$ = 4 Hz), 3.61 (dd, H_a[CH_2-C-F], 1H, $J_{H,H}$ = 15 Hz, $J_{H,F}$ = 35 Hz), 4.96 (dd, H_e[CH_2-C-F], 1H, $J_{H,F}$ = 11 Hz), 5.80 (dd, H_e[CH_2-C-OAc], 1H, $J_{H,F}$ = 2 Hz), 7.7-8.4 (m, aromatic, 4H).

Anal. Calcd. for $C_{16}H_{17}FN_2O_4$: C, 60.0; H, 5.4; N, 8.8. Found: C, 60.3; H, 5.6; N, 8.9.

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