Norbornadiene-Fused Heterocycles: Synthesis of 5,8-Dihydro-5,8-methanophthalazines and Regioselective Ring Cleavage and Skeletal Rearrangement of 6,7-Epoxy-5,6,7,8-tetrahydro-5,8-methanophthalazine 2-Oxides in Trifluoroacetic Acid

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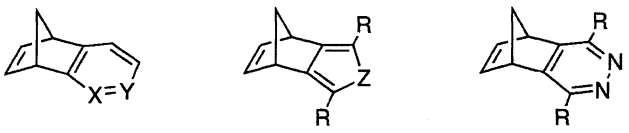
5,8-Dihydro-5,8-methanophthalazine, prepared by the reaction of bicyclo[2.2.1]hepta-2,5-diene-2,3-dicarbaldehyde with hydrazine, reacted with MCPBA to give an *N*-oxide. Further oxidation with MCPBA afforded the corresponding *exo*-6,7-epoxy derivative. Treatments of the epoxide and its diphenyl-substituted derivative with trifluoroacetic acid gave 6,9-bis(trifluoroacetoxy) derivatives by a regioselective ring-opening of the oxirane, accompanied by Wagner–Meerwein rearrangement. The bis(trifluoroacetoxy) derivatives were converted to the corresponding diols for elucidation of their regio- and stereochemistry.

The chemistry of 1,4-dihydro-1,4-methanonaphthalene (benzonorbornene) (**1**) has attracted much attention because benzonorbornene is one of the most suitable models to investigate (i) the effects on chemical and spectral properties due to the fusion of the strained bicyclic skeleton, (ii) the possibility of a through-space and/or through-bond interaction of remote π electrons, and (iii) the behavior of a cationic intermediate formed by an electrophilic attack to the olefinic double bond. Therefore, nitration on the benzene ring,[1] chlorination,[2] and bromination[2—4] of the double bond, the acid-catalyzed ring opening of the epoxide,[5] hydrobromination,[6] cycloaddition reaction with a 3*H*-1,2,4-triazole-3,5(4*H*)-dione,[7] and photochemical[8,9] and thermal[10,11] reactions have been thoroughly studied. In the reactions with electrophiles as well as the acid-induced ring opening of the epoxide of **1**, the resulting cationic intermediates generally undergo a skeletal rearrangement to give 6,9-disubstituted 6,7-dihydrobenzonorbornenes.

On the other hand, chemical properties of heteroaromatic analogues of benzonorbornene are less understood. The syntheses of 5,8-dihydro-5,8-methanoquinoline[12] (**2**) and -methanoisoquinoline[13,14] (**3**) as well as solvolyses of their hydrated products have been reported in detail. The preparation of 1,4-diphenyl-5,8-dihydro-5,8-methanophthalazine (**6**) has been reported, but no spectral and chemical properties were described.[15] Recently, we reported on the syntheses of norbornadiene-fused five-membered heteroaromatics **4** and **5** (Chart 1),[16,17] unusual cycloaddition reactions of **5**,[17] and spectral properties of an imidazole fused with 2-azanorbornene skeleton.[18] However, no electrophilic reaction accompanying a skeletal rearrangement has been reported on these heteroaromatic systems. We present here a novel synthesis of 5,8-dihydro-5,8-methanophthalazine (**7**), oxidation reactions of **7** leading to *exo*-6,7-epoxy-5,6,7,8-tetrahydro-5,8-methanophthalazine 2-oxide (**10**), and its regioselective ring cleavage and a subsequent skeletal rearrangement under acidic conditions, as well as those of the diphenyl-substituted derivative **6**.



1: X = Y = CH
2: X = N, Y = CH
3: X = CH, Y = N

4: R = Ph, Z = NH, O, S
5: R = H, Z = NAr, O

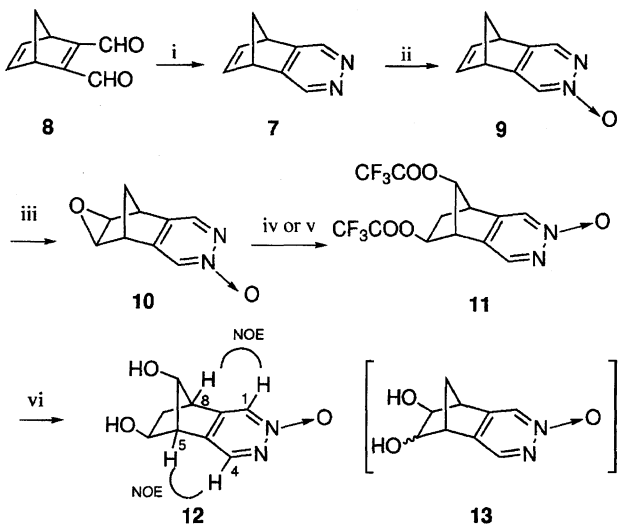
6: R = Ph
7: R = H

Chart 1.

Results and Discussion

The most expedient synthesis of 5,8-dihydro-5,8-methanophthalazine (**7**) appeared to be that from bicyclo[2.2.1]hepta-2,5-diene-2,3-dicarbaldehyde[19] (**8**). The reaction of the dicarbaldehyde **8** with hydrazine monohydrate in a buffer solution with acetic acid, sodium acetate, and ethanol (pH = 5) at 60 °C gave **7** (59%) (Scheme 1). The dihydromethanophthalazine **7** was stable when heated for 20 h in 25% aq sulfuric acid at 100 °C (81% recovery), and gave the stable salts on treatments with hydrogen chloride and methyl iodide.

Treatment of the dihydromethanophthalazine **7** with an equimolar amount of *m*-chloroperbenzoic acid (MCPBA) gave the *N*-oxide **9** in 78% yield. Further oxidation of **9** with MCPBA resulted in the exclusive formation of the *exo*-6,7-epoxy derivative **10** (90%), whose stereochemistry was



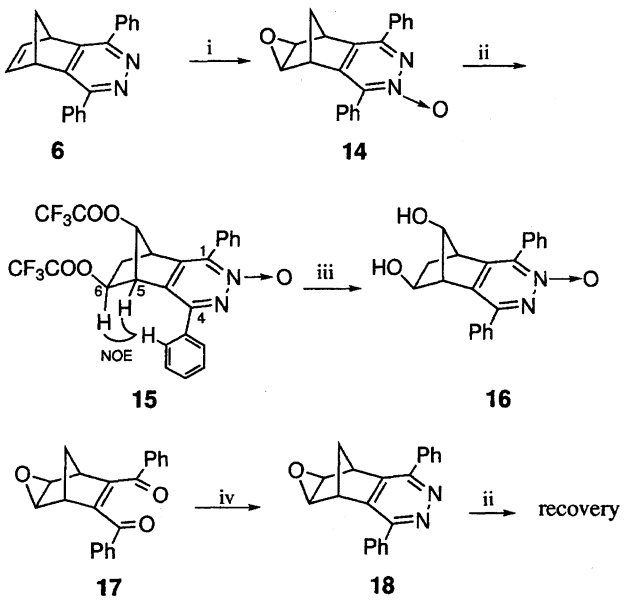
Scheme 1. Reagents an conditions: i, $NH_2NH_2 \cdot H_2O$, AcONa–AcOH, EtOH–H_2O, 60 °C, 30 min, 59%; ii, MCPBA (1.2 molar amount), CH_2Cl_2, room temp, 15 h, 78%; iii, MCPBA, CH_2Cl_2, room temp, 2 d, 90%; iv, CF_3COOH, room temp, 4 d, 55%; v, CF_3COOH–$(CF_3CO)_2O$, room temp, 4 d, 73%; vi, MeOH, 22 h, reflux, 92%.

unequivocally determined from the lack of couplings between 5-H and 6-H, and 7-H and 8-H (almost orthogonal) in the ^{1}H NMR spectrum. The reaction of the epoxide **10** with sulfuric acid, hydrochloric acid, acetic acid, or boron trifluoride–diethyl ether (1/1) resulted in the formation of a complex mixture. However, treatment of the epoxide **10** with trifluoroacetic acid (TFA) at room temperature gave the bis(trifluoroacetoxy) derivative **11** in 55% yield. The yield of **11** was improved to 73% when the reaction was carried out in the presence of trifluoroacetic anhydride (TFAA). Since we could not confirm the regio- and stereochemistry of the two trifluoroacetoxy groups at this stage from the NMR spectra due to overlapping of peaks, we converted the bis(trifluoroacetoxy) derivative **11** to the diol **12** (92%) by heating it in methanol for 22 h. The well-separated ^{1}H NMR spectrum of **12** shows the methylene protons with a relatively large geminal coupling constant (13 Hz) compared with the general values (7—10 Hz) reported for those of the bridge methylene protons of norbornene derivatives.[20] These data as well as the AA′B pattern seen at 7-H_{exo}, 7-H_{endo}, and 6-H eliminate the possibility of structure **13**. The ^{1}H signals for the pyridazine ring were unequivocally assigned to $\delta = 8.26$ for 1-H and $\delta = 8.39$ for 4-H.[21] The NOE's observed between 1-H and 8-H, and 4-H and 5-H clarify the position of the *N*-oxide group. The hydroxy proton at 9-position appears at $\delta = 5.91$ (in DMSO-d_6, d, $J = 5$ Hz) which is rather deshielded relative to those reported for alcohols (e.g. $\delta = 4.35$ for 2-propanol) in DMSO-d_6.[22] No substantial change of the chemical shift for 9-OH was observed when the ^{1}H NMR spectrum was measured at 80 °C or with a diluted sample.[23] Accordingly, the presence of intramolecular hydrogen bond of the hydroxy groups is strongly supported and the configuration of the two hydroxy groups was concluded to be **12**. The H–H and C–H COSY spectra as well as the HMBC measurement also support the structure **12**.

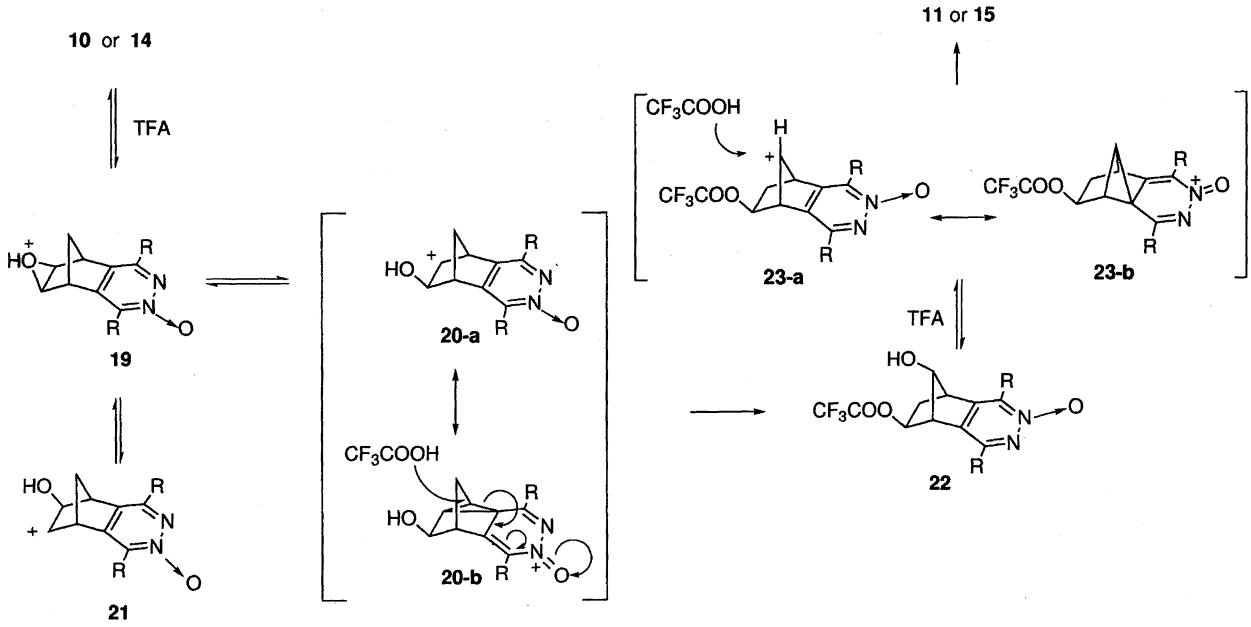
In order to examine the generality of this type of rearrangement, the diphenyl-substituted epoxide **14** was prepared by the MCPBA oxidation of the diphenylmethanophthalazine **6** (Scheme 2). The epoxide **14** was treated with trifluoroacetic acid to give the 6,9-bis(trifluoroacetoxy) derivative **15** in 81% yield as the single product. The AA′B pattern at 6-H and 7-H protons in the ^{1}H NMR spectrum supports the structure of **15**. The regiochemistry of this compound was established by the NOESY measurement: cross peaks were observed between 5,6-H's and *ortho* protons of the 4-phenyl group, which are deshielded in contrast to those of the 1-phenyl group. The *ortho* protons of the 1-phenyl group are shielded by the electronic and/or anisotropic effect of the neighboring *N*-oxide group. The conversion of **15** to the diol **16** (98%) was achieved by the methanolysis of **15** at room temperature. Although this diol **16** is sparingly soluble in various organic solvents, the ^{1}H NMR spectra taken at 80 °C in DMSO-d_6 shows a signal for 9-OH at $\delta = 5.58$: This value supports the presence of intramolecular hydrogen bond.

In order to investigate the effect of the *N*-oxide group for the skeletal rearrangement, we tried to prepare epoxides such as **18** bearing no *N*-oxide group, but attempts to deoxygenate **10** with triphenylphosphine, trialkyl phosphites, and P_2I_4 were unsuccessful. The diphenyl-substituted epoxide **18** was prepared by the reaction of the epoxynorbornene **17** with hydrazine hydrate. Treatment of the epoxide **18** with TFA under the same conditions as those of the TFA-induced reaction of **14** resulted in the recovery of **18**. Thus, the electron donating *N*-oxide group seems to influence not only the selectivity but also the reactivity in the present reaction.

The regio- and stereoselective formation of the bis(trifluo-



Scheme 2. Reagents and conditions: i, MCPBA, CH_2Cl_2, room temp, 4 d, 68%; ii, TFA, room temp, 4 d, 81%; iii, MeOH, room temp, 24 h, 98%; iv $NH_2NH_2 \cdot H_2O$ EtOH, reflux, 3 h, 41%.



Scheme 3. R = H or Ph.

roacetoxy) derivatives **11** and **15** can be explained as shown in Scheme 3. The initial protonation on the oxygen atom of the oxirane ring giving **19** induces a regioselective cleavage of the O–C-6 bond to form a resonance stabilized cation (**20-a**↔**20-b**). Such a stabilization effect cannot be expected for the cation **21** derived from the O–C-7 bond cleavage of **19**. The attack of trifluoroacetic acid results in the formation of the monohydroxy derivative **22**. Displacement of the hydroxy group on the methylene bridge carbon by trifluoroacetoxy group via the cation (**23-a**↔**23-b**) from the *anti*-face to the pyridazine ring,[24] or *O*-trifluoroacetylation of **22** with TFAA should give **11** and **15**.

The MNDO-PM3 calculations[25] were performed on the three protonated 5,8-dihydro-5,8-methanophthalazine 2-oxide isomers (Fig. 1). The calculation with the input-geometry **24** unexpectedly gave the optimized structure **25**, where the atomic distance of C-4a and C-6 is 1.56 Å. On the other hand, the calculation with the input-geometry of **26** afforded an energy minimum corresponding to this structure with a heat of formation which is 16.6 kcal mol^{-1} higher than that of **25**. The results indicate that the cationic intermediate **20** would be significantly stabilized by a contribution of the resonance form **20-b**. Therefore, the regioselectivity in the present reaction would be ascribed to relative stabilities of the cationic intermediates **20** vs. **21** as shown in Scheme 3. Computation on the input-geometry **27** provided the optimized structure **28**, where the C-4a and C-9 atoms are bonded with a distance of 1.56 Å. This outcome is consistent with the presumed existence of delocalization of π electrons between the cationic center on the bridged methylene carbon and the pyridazine *N*-oxide ring, as shown by the resonance structure **23-b**.

In conclusion, we have demonstrated the first example of the Wagner–Meerwein rearrangement of a norbornadiene-fused heteroaromatic system. The present reaction also provides another example of a plausible anchimeric assistance by heteroaromatic analogues of phenonium ion.[12,14,26]

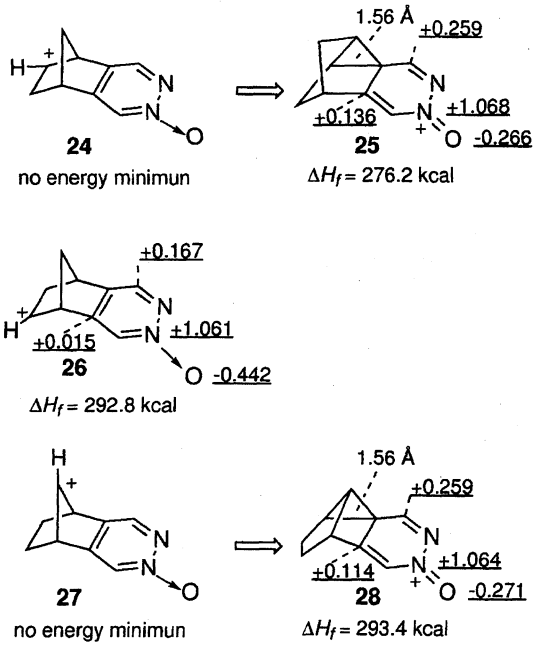


Fig. 1. The PM3-MNDO calculations on the protonated 5, 8-dihydro-5,8-methanophthalazine 2-oxide isomers. Heats of formation, and selected atomic distances (Å) and charges (underlined) are shown.

Experimental

General. All the melting points were determined with a Yanagimoto hot-stage apparatus and are uncorrected. IR spectra were obtained with a Hitachi 345 and JEOL Diamond 20 spectrometers. NMR spectra were recorded respectively with JEOL FX-90Q (^{1}H: 90 MHz; ^{13}C: 22.5 MHz), JEOL JNM-LA300 (^{1}H: 300 MHz; ^{13}C: 75 MHz), JEOL JNM-LA400 (^{1}H: 400 MHz; ^{13}C: 100 MHz), and Bruker DRX500 (^{1}H: 500 MHz; ^{13}C: 125 MHz) spectrometers. Mass spectra were measured with a Shimadzu GCMS-QP1000EX spectrometer operating in the electron impact mode (70 eV). UV

spectra were recorded with a Shimadzu UV-260 spectrophotometer. Elemental analyses were performed with a Perkin–Elmer Model 240 apparatus.

Bicyclo[2.2.1]hepta-2,5-diene-2,3-dicarbaldehyde (8):[19] A solution of 1,1,4,4-tetraethoxy-2-butyne (25.0 g, 109 mmol) in formic acid (95 cm^3) was stirred at room temperature for 1.5 h. Dichloromethane (150 cm^3) was added to the solution and the mixture was cooled to 0 °C. A cooled solution of cyclopentadiene (8.5 g, 129 mmol) in dichloromethane (150 cm^3) was added and the mixture was left for 1.5 h at room temperature. The solution was washed with water (50 cm^3), aq sodium hydrogencarbonate and water, and the organic phase was dried over Na_2SO_4. After removal of the solvent, the residue was distilled under vacuum to give the dicarbaldehyde **8** (11.7 g, 73%) as yellow liquid: Bp 90—93 °C (3 Torr, 1 Torr = 133.322 Pa); IR (neat) 2990, 2860, 1715 (CO), 1660, 1585, 1330, 1285 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 2.18 (1H, d, J = 7 Hz, 7-H), 2.24 (1H, d, J = 7 Hz, 9-H), 4.17 (2H, m, 1- and 4-H), 6.64 (2H, t, J = 2 Hz, 5- and 6-H), 10.50 (2H, s, CHO); ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ = 49.6 (d, C-1 and C-4), 72.2 (t, C-7), 142.3 (d, C-5 and C-6), 164.8 (s, C-2 and C-3), 185.2 (d, CHO); MS *m/z* (rel intensity) 138 (M^+;7), 119 (M−CHO; 30), 91 (norbornadienyl; 100), 66 (cyclopentadiene; 78).

5,8-Dihydro-5,8-methanophthalazine (7): To a solution of the dicarbaldehyde **8** (8.9 g, 60 mmol) in a mixture of acetic acid–sodium acetate buffer solution (240 cm^3, pH = 5) and ethanol (400 cm^3) was added an 85% aq solution of hydrazine hydrate (3.9 g, 66 mmol). The mixture was stirred at 60 °C for 30 min. The solution was saturated with sodium chloride and the product was extracted with dichloromethane. The organic phase was dried over Na_2SO_4 and concentrated. The resulting solid was recrystallized from hexane to give the methanophtalazine **7** (5.13 g, 59%) as colorless needles: Mp 105—106 °C; IR (KBr) 2990, 1450, 1300, 1235, 1220, 1025, 730 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 2.31 (1H, dt, J = 8 and 2 Hz, 9-H), 2.44 (1H, dt, J = 8 and 2 Hz, 9-H), 4.04 (2H, m, 5- and 8-H), 6.84 (2H, t, J = 2.0 Hz, 6- and 7-H), 9.15 (2H, s, 1- and 4-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 48.4 (dm, J = 153 Hz, C-5 and C-8), 72.0 (t, J = 137 Hz, C-9), 142.7 (dm, J = 178 Hz, C-6 and C-7), 145.4 (d, J = 182 Hz, C-1 and C-4), 152.8 (s, C-4a and C-8a); MS *m/z* (rel intensity) 144 (M^+; 100), 114 (M−N_2H; 32), 66 (C_5H_6; 55); UV (EtOH) λ_{max} (log ϵ) 249 (3.32), 314 (2.65) nm; UV (CH_2Cl_2) λ_{max} (log ϵ) 248 (3.17), 327 (2.70) nm. Found: C, 75.17; H, 5.65; N, 19.63%. Calcd for $C_9H_8N_2$: C, 74.98; H, 5.59; N, 19.43%.

5,8-Dihydro-5,8-methanophthalazine Hydrochloride: Colorless needles (from ethyl acetate–ethanol); mp 188—190 °C; ^{1}H NMR ($CDCl_3$, 90 MHz) δ = 2.67 (2H, s, 9-H), 4.49 (2H, s, 5- and 8-H), 7.03 (2H, s, 6- and 7-H), 9.57 (2H, s, 1- and 4-H), 10.65 (1H, br s, NH); ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ = 49.9 (d, J = 158 Hz, C-5 and C-8), 74.1 (t, J = 139 Hz, C-9); 143.1 (d, C-1, C-4, C-6, and C-7), 162.8 (s, C-4a and C-8a). Found: C, 59.73; H, 4.93; N, 15.80%. Calcd for $C_9H_9N_2Cl$: C, 59.84; H, 5.02; N, 15.51%.

5,8-Dihydro-2-methyl-5,8-methanophthalazinium Iodide: Mp 104—106 °C; ^{1}H NMR ($CDCl_3$, 90 MHz) δ = 2.71 (2H, t, J = 1.4 Hz, 9-H), 4.61 (2H, t, J = 1.4 Hz, 5- and 8-H), 4.71 (3H, s, CH_3), 7.08 (2H, m, 6- and 7-H), 9.58 (1H, s, 4-H), 10.39 (1H, s, 1-H); ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ = 49.3 (d, C-5 or C-8), 49.4 (d, C-8 or C-5), 52.1 (q, J = 147 Hz, CH_3), 73.3 (t, J = 139 Hz, C-9), 141.6 (d, C-4), 142.7 (d, C-6 and C-7), 145.8 (d, J = 194 Hz, C-1), 163.3 (s, C-4a or C-8a), 164.3 (C-8a or C-4a). Found: C, 42.07; H, 3.50; N, 9.51%. Calcd for $C_{10}H_{11}N_2I$: C, 41.98; H, 3.88; N, 9.79%.

5,8-Dihydro-5,8-methanophthalazine 2-Oxide (9): A solution of the 5,8-dihydro-5,8-methanophthalazine (**7**) (1.73 g, 12 mmol) and *m*-chloroperbenzoic acid (85%, 2.68 g, 13.2 mmol) in dichloromethane (20 cm^3) was stirred at room temperature for 15 h. The mixture was washed with 5% aq sodium hydrogensulfite and aq sodium hydrogencarbonate, and dried over Na_2SO_4. The solution was concentrated and the resulting solid was collected by filtration to give the 2-oxide **9** (1.55 g, 78%): Colorless needles (from ethyl acetate); mp 153—155 °C; IR (KBr) 2990, 1605, 1375, 1280, 1060, 725 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 2.31 (1H, dt, J = 8.1, 1.5 Hz, 9-H), 2.43 (1H, dt, J = 8.1, 1.5 Hz, 9-H), 4.02 (1H, m, 5- or 8-H), 4.42 (1H, m, 8- or 5-H), 6.75 (1H, dd, J = 5, 3 Hz, 6- or 7-H), 6.85 (1H, dd, J = 5, 3 Hz, 7- or 6-H), 8.17 (1H, s, 1-H), 8.20 (1H, s, 4-H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 47.4 (d, J = 154 Hz, C-5 or C-8), 48.7 (d, J = 154 Hz, C-8 or C-5), 68.6 (t, J = 137 Hz, C-9), 130.4 (d, J = 192, C-1), 140.4 (d, J = 184 Hz, C-4), 140.8 (d, J = 177 Hz, C-6 or C-7), 141.4 (s, C-4a), 143.1 (d, J = 177 Hz, C-7 or C-6), 160.8 (s, C-8a); MS *m/z* (rel intensity) 160 (M^+; 95), 130 (phthalazine; 20), 77 (M−C_5H_7; 100); UV (EtOH) λ_{max} (log ϵ) 216 (3.85), 259 (3.85), 276 (3.85), 313 (3.61) nm. Found: C, 67.47; H, 5.01; N, 17.73%. Calcd for $C_9H_8ON_2$: C, 67.49; H, 5.03; N, 17.49%.

***exo*-6,7-Epoxy-5,6,7,8-tetrahydro-5,8-methanophthalazine 2-Oxide (10):** A solution of the 2-oxide **9** (160 mg, 1 mmol) and *m*-chloroperbenzoic acid (80%, 650 mg, 3.8 mmol) in dichloromethane (15 cm^3) was stirred at room temperature for 2 d. The mixture was washed with 20% aq sodium hydrogensufite and aq sodium hydrogencarbonate, and dried over Na_2SO_4. The solvent was removed and the resulting solid was collected by filtration to give the epoxide **10** (159 mg, 90%): Colorless needles (from ethyl acetate); mp 161—163 °C; IR (KBr) 3025, 1605, 1380, 1275, 1065, 840 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 1.64 (1H, d, J = 10 Hz, 9-H_s), 2.08 (1H, d, J = 10 Hz, 9-H_a), 3.51 (2H, s, 6- and 7-H), 3.59 (2H, br s, 5- and 8-H), 8.16 (1H, s, 1-H), 8.25 (1H, s, 4-H); ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ = 38.2 (t, J = 143 Hz, C-9), 41.7 (d, C-8 or C-5), 43.1 (d, C-5 or C-8), 53.8 (d, C-7 or C-6), 54.2 (d, C-6 or C-7), 130.9 (d, J = 193 Hz, C-1), 137.4 (s, C-4a), 142.1 (d, J = 186 Hz, C-4), 156.5 (s, C-8a); MS *m/z* (rel intensity) 176 (M^+; 88), 147 (M−CHO; 74), 117 (M−$C_2H_2O_2$; 100); UV (EtOH) λ_{max} (log ϵ) 234 (3.44), 273 (3.73), 313 (3.30) nm. Found: C, 61.66; H, 4.54; N, 16.19%. Calcd for $C_9H_8O_2N_2$: C, 61.36; H, 4.58; N, 15.90%.

The Reaction of the Epoxide 10 with Trifluoroacetic Acid. A solution of the epoxide **10** (352 mg, 2 mmol) in trifluoroacetic acid (2 cm^3) was stirred at room temperature for 4 d. The mixture was concentrated and dichloromethane was added to the residue. The organic phase was washed with aq. sodium hydrogencarbonate and dried over Na_2SO_4. After concentration, the product was collected and washed with hexane to give the bis(trifluoroacetoxy) derivative **11** (428 mg, 55%) as white powder: Mp 170—172 °C (from benzene), IR (KBr) 1770 (C=O), 1615, 1400, 1220, 1165 cm^{-1}; ^{1}H NMR (acetone-d_6, 90 MHz) δ = 2.38—2.58 (2H, m, 7-H), 3.80 (1H, br s, 8-H), 4.07 (1H, s, 5-H), 5.06 (2H, m, 6- and 9-H), 8.15 (1H, s 1-H), 8.43 (1H, s, 4-H); ^{13}C NMR (acetone-d_6, 22.5 MHz) δ = 32.6 (t, C-7), 45.2 (d, C-8), 48.4 (d, C-5), 78.4 (d, C-6), 85.3 (d, C-9), 115.3 (q, $^1J_{C-F}$ = 286 Hz), 115.4 (q, $^1J_{C-F}$ = 286 Hz), 127.2 (s, C-4a), 130.7 (d, C-1), 145.8 (d, C-4), 152.0 (s, C-8a), 157.2 (q, $^2J_{C-F}$ = 44 Hz), 157.3 (q, $^2J_{C-F}$ = 44 Hz); MS *m/z* (rel intensity) 386 (M^+; 56), 272 (M−$C_2F_3O_2H$; 84), 175 ($C_9H_7O_2N_2$; 53), 159 (75), 149 (88), 69 (CF_3; 100). Found: C, 40.13; H, 2.14; N, 7.51%. Calcd for $C_{13}H_8N_2O_5F_6$: C, 40.43; H, 2.09; N, 7.25%.

A similar reaction of the epoxide **10** (1.41 g, 8 mmol) with trifluoroacetic acid (10 cm^3) in the presence of trifluoroacetic anhydride

(2 cm^3) gave the bis(trifluoroacetoxy) derivative **11** (2.24 g, 73%).

6-*exo*,9-*anti*-Dihydroxy-5,6,7,8-tetrahydro-5,8-methanophthalazine 2-Oxide (12): A solution of the bis(trifluoroacetoxy) derivative **11** (193 mg, 0.5 mmol) in methanol (10 cm^3) was refluxed for 22 h. The solution was concentrated and benzene was added to the residue. The resulting solid was collected to give the diol **12** (89 mg, 92%) as light tan needles: Mp 171—173 °C (from benzene); IR (KBr) 3400, 3200, 1600, 1380, 1240, 1085, 1050 cm^{-1}; ^{1}H NMR (DMSO-d_6, 500 MHz) δ = 1.94 (1H, dd, J = 13 and 6 Hz, 7-H$_{endo}$), 2.24 (1H, dt, J = 13 and 4 Hz, 7-H$_{exo}$), 3.36 (1H, br s, 5-H), 3.39 (1H, d, J = 4 Hz, 8-H), 3.79 (1H, dt, J = 6 and 4 Hz, 6-H), 3.99 (1H, br s, 9-H), 4.51 (1H, br d, J = 4 Hz, 6-OH), 5.69 (1H, br d, J = 5 Hz, 9-OH), 8.06 (1H,s, 1-H), 8.25 (1H, s, 4-H); ^{13}C NMR (DMSO-d_6, 125 MHz) δ = 34.1 (C-7), 46.3 (C-5), 50.8 (C-8), 72.2 (C-6), 84.0 (C-9), 129.1 (C-1), 130.8 (C-4a), 143.5 (C-4), 153.5 (C-8a); Observed cross peaks by NOESY: 1-H and 8-H; 4-H and 5-H. Observed cross peaks by HMBC: 4-H and C-8a, C-4a; 1-H and C-4a; 8-H and C-8, C-4a, C-8a, C-6; 5-H and C-7, C-6, C-4a, C-4; 7-H$_{exo}$ and C-8, C-6, C-8a; 7-H$_{endo}$ and C-8, C-9. MS *m/z* (rel intensity) 194 (M^+; 19), 176 (M−H_2O; 100), 148 (67), 147 (65), 134 (96), 91 (62), 65 (62). Found: C, 55.40; H, 5.13; N, 14.66%. Calcd for $C_9H_8N_2O_3$: C, 55.67; H, 5.19; N, 14.43%.

1,4-Diphenyl-5,8-dihydro-5,8-methanophthalazine (6):[15] A solution of 2,3-dibenzoylnorbornadiene (7.99 g, 27 mmol) and hydrazine hydrate (80%, 2.11 g, 34 mmol) in a mixture of acetic acid (250 cm^3) and water (150 cm^3) was refluxed for 1.5 h. Water (500 cm^3) was added and the resulting solid was collected by suction and recrystallized from ethanol to give the diphenyldihydromethanophthalazine **6** (6.54 g, 83%) as colorless needles: Mp 210—211 °C (lit,[15] 202 °C; IR (KBr) 3070, 3050, 3010, 1560, 1485, 1425, 1370, 1300, 1210 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 2.27 (1H, d, J = 8 Hz, 9-H$_s$), 2.38 (1H, d, J = 8 Hz, 9-H$_a$), 4.34 (2H, t, J = 2 Hz, 5- and 8-H), 7.07 (2H, t, J = 2 Hz, 6- and 7-H), 7.59 (6H, m, Ph), 7.88 (4H, m, Ph); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 49.4 ($^1J_{C-H}$ = 154 Hz, C-5 and C-6), 70.9 ($^1J_{C-H}$ = 137 Hz, C-9), 128.5 ($^1J_{C-H}$ = 160 Hz), 128.7 ($^1J_{C-H}$ = 160 Hz), 129.0 ($^1J_{C-H}$ = 160 Hz), 136.7 ($^2J_{C-H}$ = 7 Hz), 143.0 ($^1J_{C-H}$ = 177 Hz, C-6 and C-7), 150.9 (C-4a and C-8a), 153.4 (t, $^3J_{C-H}$ = 4 Hz, C-1 and C-4); MS *m/z* (rel intensity) 296 (M^+; 29), 202 (M−C_5H_6−N_2; 100). Found: C, 85.38; H, 5.23; N, 9.25%. Calcd for $C_{21}H_{16}N_2$: C, 85.11; H, 5.44; N, 9.45%.

***exo*- 6, 7- Epoxy- 1, 4- diphenyl- 5, 6, 7, 8- tetrahydro- 5, 8-methanophthalazine 2-Oxide (14):** A solution of the diphenyldihydromethanophthalazine **6** (2.11 g, 7.1 mmol) and MCPBA (80%, 3.36 g, 15.5 mmol) in dichloromethane (200 cm^3) was stirred at room temperature for 4 d. The mixture was washed with aq sodium sulfite, aq sodium hydrogencarbonate, and aq saturated NaCl solution, and dried over Na_2SO_4. After removal of the solvent, the resulting solid was collected and recrystallized from ehtanol to give the epoxide **14** (1.60 g, 68%): Colorless needles (from ethanol), mp 212—213 °C (decomp); IR (KBr) 3020, 1600, 1555, 1485, 1450, 1375, 1270, 1245, 1190, 1065, 1025, 1015 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ = 1.67 (1H, d, J = 10 Hz, 9-H$_s$), 1.99 (1H, d, J = 10 Hz, 9-H$_a$), 3.47 (1H, s, 8-H), 3.62 (1H, d, J = 3 Hz, 7-H), 3.81 (1H, d, J = 3 Hz, 6-H), 3.84 (1H, s, 5-H), 7.55 (8H, m, Ph), 7.74 (2H, m, *ortho* protons of 4-phenyl); ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 38.5 (C-9), 43.5 (C-5), 44.3 (C-8), 54.7 (C-7), 54.8 (C-6), 128.3 (Ph), 128.7 (Ph), 128.9 (Ph), 129.4 (C-1), 129.5 (Ph), 130.0 (Ph), 130.1 (Ph), 133.8 (C), 135.3 (s, C-4a), 140.7 (C), 152.3 (C-4), 156.2 (C-8a); Observed cross peaks by COLOC: C-8a and 9-H$_a$, C-4a and 9-H$_a$; Observed cross peaks by NOESY: δ = 7.74 and 6-H; MS *m/z* (rel intensity) 328 (M^+; 100), 327 (57), 299 (M−CHO; 52), 281 (34), 269 (M−$C_2H_3O_2$; 53). Found: C, 76.90; H, 4.93; N, 8.37%. Calcd for $C_{21}H_{16}N_2O_2$: C, 76.81; ;H, 4.91; N, 8.53%.

The Reaction of the Diphenyl Epoxide 14 with Trifluoroacetic Acid. A solution of the diphenyl epoxide **14** (260 mg, 0.8 mmol) in trifluoroacetic acid (5 cm^3) was stirred at room temperature for 4 d. The mixture was concentrated and dichloromethane was added to the residue. The organic phase was washed with aq sodium hydrogencarbonate and dried over Na_2SO_4. After concentration, the product was collected to give the bis(trifluoroacetoxy derivative **15** (345 mg, 81%): Colorless needles from benzene–hexane (1/1); mp decomp ca. 213 °C; IR (KBr) 1783 (CO), 1562, 1496, 1380, 1222 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 2.53 (1H, dd, J = 14 and 7 Hz, 7-H$_{endo}$), 2.57 (1H, dt, J = 14 and 4 Hz, 7-H$_{exo}$), 3.66 (1H, dd, J = 4 and 2 Hz, 8-H), 4.22 (1H, s, 5-H), 5.00 (1H, br s, 9-H), 5.37 (1H, dd, J = 7 and 4 Hz, 6-H), 7.54 (8H, m), 7.88 (2H, m, *ortho* protons of 4-phenyl); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 32.2, (C-7), 44.9 (C-8), 49.2 (C-5), 76.7 (C-6), 83.8 (C-9), 114.1 (q, $^1J_{C-F}$ = 286 Hz, CF_3), 114.3 (q, $^1J_{C-F}$ = 286 Hz, CF_3), 123.4 (C-1), 128.5 (quaternary Ph), 128.6 (Ph), 128.9 (Ph), 129.3 (Ph), 129.5 (Ph), 130.5 (Ph), 130.9 (Ph), 132.7 (quaternary Ph), 138.9 (C-4a), 149.8 (C-8a), 154.1 (C-4), 156.5 (q, $^4J_{C-F}$ = 42 Hz), 157.4 (q, $^4J_{C-F}$ = 42 Hz); Observed cross peaks by COLOC: C-8a and 7-H, 9-H; C-1 and 5-H, 8-H; Observed cross peaks by NOESY: δ = 7.88 and 5-H, 6-H; MS *m/z* (rel intensity) 538 (M^+; 44), 327 (M−$(CF_3CO)_2O$; 100). Found: C, 56.08; H, 2.90; N, 4.90%. Calcd for $C_{25}H_{16}N_2O_5F_6$: C, 55.77; H, 3.00; N, 5.20%.

6-*exo*,9-*anti*-Dihydroxy-1,4-diphenyl-5,6,7,8-tetrahydro-5,8-methanophthalazine (16): A solution of the bis(trifluoroacetoxy) derivative **15** (538 mg, 1 mmol) in anhydrous methanol (40 cm^3) was stirred at room temperature for 24 h. The resulting precipitates was collected by filtration to give the diphenyl diol **16** (338 mg, 98%): Colorless needles (from acetonitrile); mp decomp ca. 245 °C; IR (KBr) 3399 (OH), 3181, 1442, 1400, 1369, 1358, 1228, 1176, 1112, 1093 cm^{-1}; ^{1}H NMR (DMSO-d_6, 80 °C, 400 MHz) δ = 2.10 (2H, br s, 7-H), 3.04 (1H, br s, 8-H), 3.37 (1H, s, 5-H), 4.10 (1H, s, 9-H) 4.14 (1H, br s, 6-H), 4.84 (1H, br s, 6-OH), 5.58 (1H, br s, 9-OH), 7.54 (8H, m, Ph), 7.77 (2H, m, *ortho* protons of 4-phenyl); ^{13}C NMR (DMSO-d_6, 80 °C; 100 MHz) δ = 33.8 (C-7), 47.2 (C-8), 52.2 (C-5), 72.0 (C-6), 83.1 (C-9), 127.7 (Ph), 127.8 (Ph), 127.9 (C-1), 128.4 (Ph), 128.9 (Ph), 129.2 (Ph), 129.5 (Ph), 129.8 (quaternary Ph), 133.8 (quaternary Ph), 137.6 (C-4a), 151.4 (C-4), 152.4 (C-8a); Observed cross peaks by COLOC: C-8a and 7-H, 5-H; C-1 and 8-H; Observed cross peaks by NOESY: δ = 7.77 and 5-H, 6-H; MS *m/z* (rel intensity) 346 (M^+; 4), 328 (M−H_2O; 58), 299 (M−H_2O−HCO; 100). Found: C, 73.04; H, 5.33; N, 8.32 %. Calcd for $C_{21}H_{18}N_2O_3$: C, 72.82; H, 5.24; N, 8.09%.

2,3-Dibenzoyl-*exo*-5,6-epoxybicyclo[2.2.1]hept-2-ene (17): A solution of 2,3-dibenzoylbicyclo[2.2.1]hepta-2,5-diene (427 mg, 1.4 mmol) and MCPBA (80%, 307 mg, 1.4 mmol) in dichloromethane (20 cm^3) was stirred at room temperature for 4 d. The organic phase was washed with aq sodium sulfite and aq sodium hydrogencarbonate, and dried over Na_2SO_4. After removal of the solvent, hexane was added to the residue and the resulting solid was collected by suction to give the epoxynorbornene **17** (1.449 g, 91%): Colorless rods (from DMF); mp decomp 162 °C; IR (KBr) 1649 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 1.89 (1H, d, J = 9 Hz, 7-H), 1.99 (1H, d, J = 9 Hz, 7-H), 3.63 (2H, br s, 1- and 4-H), 3.89 (2H, br s, 5- and 6-H), 7.17 (6H, m), 7.36 (4H, m); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 39.4 (C-7), 48.7 (C-1 and C-4), 58.1 (C-5 and C-6), 128.3, 128.4, 133.1, 137.4, 155.6 (C-2 and C-3), 193.6 (CO); MS *m/z* (rel intensity) 316 (M^+; 100), 287 (M−CHO; 5), 105 (PhCO; 100). Found: C, 79.92; H, 5.04%. Calcd for $C_{21}H_{16}O_3$: C,

79.73; H, 5.10%.

***exo*- 6, 7- Epoxy- 1, 4- diphenyl- 5, 6, 7, 8- tetrahydro- 5, 8- methanophthalazine (18):** A solution of the epoxynorbornene **17** (189 mg, 0.6 mmol) and hydrazine monohydrate (80%, 63 mg, 1.0 mmol) in ethanol (15 cm^3) was refluxed for 30 min. The solution was concentrated and dichloromethane (30 cm^3) was added to the residue. The organic phase was washed with water and dried over Na_2SO_4. After removal of the solvent, the resulting solid was collected and washed with ethanol to give the epoxytetrahydromethanophthalazine **18** (77 mg, 41%) as white powder: Mp decomp ca. 245 °C (from ethanol); IR (KBr) 2997, 1448, 1369, 1242 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) $\delta = 1.64$ (1H, d, $J = 10$ Hz, 7-H), 2.05 (1H, d, $J = 10$ Hz, 7-H), 3.74 (2H, br s, 6- and 7-H), 3.86 (2H, br s, 5- and 8-H), 7.57 (6H, m), 7.88 (4H, m); ^{13}C NMR ($CDCl_3$, 100 MHz) $\delta = 40.1$ (C-9), 43.8 (C-5 and C-8), 55.9 (C-6 and C-7), 128.5, 128.9, 129.5, 136.0 (C), 147.2 (C), 154.7 (C); MS *m/z* (rel intensity) 312 (M^+; 100), 283 (M−CHO; 68), 77 (Ph; 61). Found: C, 80.71; H, 5.19; N, 9.13%. Calcd for $C_{21}H_{16}N_2O$: C, 80.75; H, 5.16; N, 8.97%.

A solution of the epoxytetrahydromethanophthalazine **18** (98 mg, 0.3 mmol) in trifluoroacetic acid (2 cm^3) was stirred at room temperature for 4 d. After the usual work-up, **18** (71 mg, 72%) was recovered.

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