50% Et_2O–hexane to give a white solid: mp 72–74 °C; ^1H NMR ($CDCl_3$) δ 1.4 (t, 3 H, CH_2CH_3), 1.8 (m, 4 H, CH_2CH_2), 2.0–3.3 (m, 4 H, NCH_2 and $PhCCH_2$), 4.3 (q, 2 H, CH_2CH_3), 4.7 (b s, 1 H, OH), 7.3 (s, 5 H, aromatic).

3-Hydroxy-1-[[(4-nitrophenyl)oxy]carbonyl]-3-phenyl-2-piperidinone (14). A solution of 1.0 g (0.0052 mol) of **12** (n = 1)[11] and 1.1 g (0.0055 mol) p-nitrophenyl chloroformate in 100 mL of toluene was heated at reflux for 18 h. The solvent was removed, the residue triturated with Et_2O, and the mixture filtered to provide 1.1 g (61%) of **14** as a white solid: mp 176–177 °C ($CHCl_3$–hexane); ^1H NMR ($CDCl_3$) δ 1.5–2.8 (m, 4 H, CH_2CH_2), 3.7–4.0 (m, 3 H, CH_2N and OH), 7.2–8.4 (m, 9 H, aromatic); MS (70 eV), m/e 356 (M^+).

Crystallography of 1-Aza-8,9-dioxo-7-oxa-6-phenylbicyclo[4.2.1]nonane (1, n = 2). A crystal of 1 (n = 2) suitable for X-ray diffraction analysis was selected from a sample that had been crystallized by evaporation from an ether–hexane mixture. A 0.08 × 0.12 × 0.58 mm specimen was used for all X-ray measurements. Crystals of 1 (n = 2) are colorless and acicular. The cell constants a = 25.383 (3) Å, b = 6.523 (1) Å, c = 18.945 (2) Å, and β = 133.63 (1)° (d_{calcd} = 1.35 g cm^{-3} for Z = 8) were determined by a least-squares fit to the 2θ values of 15 reflections that had been manually centered on the diffractometer. Systematic absences permit either of two space groups, Cc or $C2/c$; the choice of the centrosymmetric $C2/c$ is confirmed by successful structure solution and refinement.

Intensity data were collected on a Picker FACS-1 diffractometer (Cu Kα radiation, Ni filtered) in the θ–2θ scan mode. Three reference reflections, sampled periodically throughout data collection, varied by no more than 3% from average structure factor values. Intensities were assigned variances according to counting statistics plus an additional term, $(0.02S)^2$, where S is the scan count. Intensities and variances were corrected for Lorentz, polarization, and absorption effects.

Calculations were carried out with the SDP system of programs.[18] Scattering factors and anomalous dispersion corrections were from ref 19. The structure was solved with the aid of the direct-methods program MULTAN 78.[20] All H atoms were located in a difference Fourier map calculated after four cycles of least-squares refinement of the C, N, and O positional and anisotropic temperature parameters. The parameter list in the final cycles of least-squares refinement was augmented by inclusion of an extinction parameter and positional and isotropic thermal parameters for the H atoms. Weights were based on variances of observed intensities. Convergence was achieved in an additional seven cycles; no parameter shift in the final cycle was greater than 0.03 times the corresponding standard deviation. A final difference Fourier map showed no feature greater than 0.1 e/Å^3. For 1823 reflections, GOF = 2.643 and R = 0.050. The molecule is illustrated in Figure 1. Tables of data collection parameters, positional parameters, bond distances and angles, anisotropic thermal parameters, and structural factors are available as supplementary material.

Acknowledgment. Excellent technical assistance was provided by C. Moore and L. Logan. Partial support of this work by a grant from the University of Alabama in Birmingham Graduate School (W.J.B.) is gratefully acknowledged. H. M. Einspahr is the recipient of a Research Career Development Award (DE-00106).

Registry No. 1 (n = 2), 93350-08-4; 1 (n = 3), 93350-09-5; **7** (n = 2), 105-60-2; **7** (n = 3), 673-66-5; **7** (n = 4), 935-30-8; **8** (n = 2), 56987-35-0; **8** (n = 3), 32566-59-9; **8** (n = 4), 32566-63-5; **9**, 93350-10-8; **10** (n = 2), 23996-62-5; **10** (n = 3), 93350-11-9; **11** (n = 2), 37840-08-7; **11** (n = 3), 93350-12-0; **12** (n = 1), 65379-06-8; **12** (n = 2), 51129-01-2; **12** (n = 3), 93350-13-1; **13**, 93350-14-2; **14** (Ar = 4-$NO_2C_6H_4$), 93350-15-3; $ClC(O)O$-p-$C_6H_4NO_2$, 7693-46-1; p-$NO_2C_6H_4OC(O)O$-p-$C_6H_4NO_2$, 5070-13-3; $ClC(O)OEt$, 541-41-3; PhBr, 108-86-1.

Supplementary Material Available: X-ray analytical data (Tables II–VI) for 1 (n = 2) (22 pages). Ordering information is given on any current masthead page.

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Synthesis of Tetrahydrobenzo[*b*]phenazines as Anthracyclinone N-Isosteres

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The anthracycline p-quinone unit has been replaced by a 1,4-di-N-oxide function in the first synthesis of a 7,9-dideoxyanthracyclinone hetero isostere. 4,11-Dimethoxy-9-(methoxycarbonyl)-7,8,9,10-tetrahydrobenzo[*b*]phenazine was synthesized and converted to the 5,12-di-N-oxide, which is isosteric with the 6-deoxycarminomycinone or α-citromycinone types. The heterocyclic C ring of tetrahydrobenzo[*b*]phenazine was formed by coupling 3-methoxy-1,2-benzoquinone as the D-ring moiety with an o-diamine that provided the A,B-ring moiety. The o-diamine was synthesized from 2-carboxy-8-methoxy-1,2,3,4-tetrahydronaphthalene by blocking the 5-position temporarily with a bromo substituent, conducting ortho dinitration in one step at positions 6 and 7, and reducing the nitro groups simultaneously with hydrogenolysis of the Br. A byproduct of the condensation was the regioisomer 1,11-dimethoxy-9-(methoxycarbonyl)-7,8,9,10-tetrahydrobenzo[*b*]phenazine, which was oxidized to the 5-N-oxide.

Introduction

1,4-Di-N-oxide functions (**1**) in nitrogen heterocycles can provide useful isosteric replacement[1] of the p-quinone unit (**2**) that occurs[2-5] in the structure of many antitumor agents. We now report synthesis of the substituted 7,8,9,10-tetrahydrobenzo[*b*]phenazine[6] di-N-oxide **3** and

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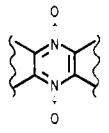
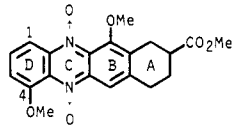
0022-3263/84/1949-5116$01.50/0

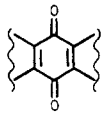
N-oxide **4** as examples of the first successful approach to anthracyclinone isosteres modified at the quinone. In numerous antitumor structures, the *p*-quinone is an important site of biochemical action. Quinone redox properties, the capacity to generate O_2-derived free radicals, or quinone-related alkylating action may contribute importantly to the various biological effects observed with the anthracyclines and the mitomycins—as clinically important examples.[3-5] Structural changes that alter reactivity at the quinone may significantly alter the overall pattern of these biological effects, both therapeutic and toxic. Specific effects cannot be targeted, however, based on current knowledge. For example, circumstantial evidence tends to correlate anthracycline cardiotoxicity with the production of radicals,[7-9] but it is less clear whether O_2 radicals contribute to the antitumor effects—as they appear to do with the mitomycins.[4,5] The statement is made[5] that the quinone unit common to various agents does not confer on them a common mechanism. Isosteric structures can contribute importantly to studies on the origin and possible separation of the various biological effects and mechanisms.



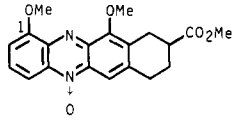
1



3

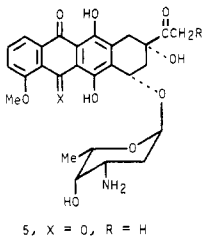


2

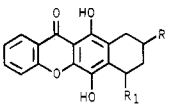


4

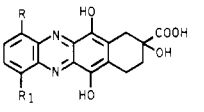
The importance of structural changes at the quinone was seen in the biological evaluation of the 5-imino derivatives[10,11] **7** and **8** of the most important anthracyclines, daunorubicin (**5**) and doxorubicin (**6**). These iminoquinones provide the only type of quinone derivatization in the entire anthracycline series. Quinone redox cycling and radical generation is strongly suppressed in these compounds.[10,11] Rat metabolism studies on **7** showed deletion of the reductive deglycosylation, normally a major pathway, and various tests in vitro and in vivo showed significantly reduced cardiotoxicity.[12] Unlike these derivatives, quinone analogues based on changes in the carbon skeleton of the aglycone require total synthesis, and the only examples so far are the 5-oxa (i.e., xanthone) analogues[13,14] **9** and **10**. The synthetic elaboration and biological testing of these structures, which provide the substitution of a quinone C=O by a hetero atom rather than an isosteric structure, are still being completed. The first approach to isosteric structures was our synthesis[1] of the mixture of 7,8,9,10-tetrahydrobenzo[*b*]phenazine-6,11-diols **11** and **12**. Attempts to convert this intermediate mixture to 5,12-di-*N*-oxides that would be isosteric with the anthracyclinones were unsuccessful because oxidation of the 6,11-diol (or derivatives thereof) gave the 6,11-dione to the exclusion of the desired di-*N*-oxide. Consequently we have redesigned the target N-isosteres to avoid the *p*-dihydroxy substitution that is incompatible with N-oxidation. Recent studies on anthracyclines show that interesting antitumor activity is retained despite alterations in the hydroxylation pattern; apparently only one OH peri to the quinone is sufficient.[15-18] The substitution pattern in **3** will give isosteres of 6-deoxycarminomycinone (the α-citromycinone type) and the 1,11-disubstitution pattern of **4** resembles the 4,6-diol system of 11-deoxycarminomycinone or of aklavinone.[19] Approaches to targets **3** and **4** have required considerable study by us because of the relatively undeveloped state of the art of phenazine synthesis. This is in sharp contrast to the extensive studies in recent years of carbocyclic chemistry for synthesis of anthracyclinones. Continuation of the present studies will lead, e.g., to the fully elaborated isostere **13** of 6-deoxycarminomycin.



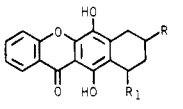
5, X = O, R = H
6, X = O, R = OH
7, X = NH, R = H
8, X = NH, R = OH



9

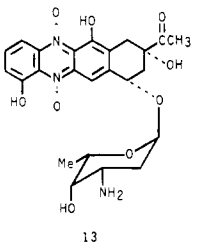


11, R = OMe, R_1 = H
12, R = H, R_1 = OMe



10

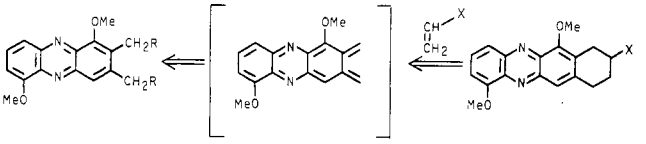
R = H or $COCH_3$
R_1 = H or O-glucosyl



13

Results and Discussion

Initial Approach. Our first plan was to synthesize **3**, and it was designed to give flexibility in building up the A ring by constructing it last. Hence we sought 1,6-dimethoxy-2,3-dimethylphenazine (**14**), which via the 2,3-bis(bromomethyl) derivative **15** might be converted to the intermediate *o*-quinodimethan **16** by 1,4-elimination. Reaction of **16** with a variety of dienophiles might give **17**, by analogy with the Diels–Alder reactions of quinodimethans from benzene[20] or anthraquinone derivatives.[21]



14, R = H
15, R = Br

16

17

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(6) The tetrahydrobenzo[*b*]phenazine system is numbered here by the system commonly adopted for anthracyclinones. Hence the 7,8,9,10-tetrahydro ring is the A ring.
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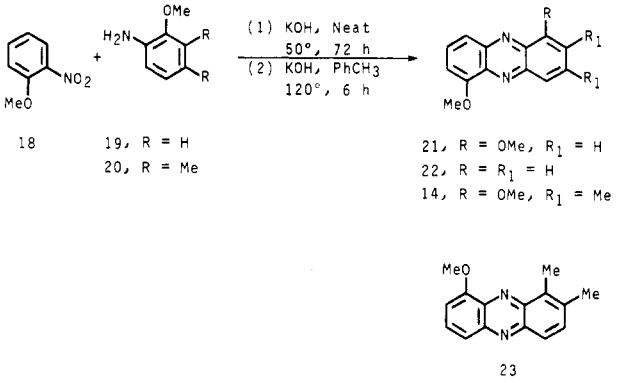
The synthesis of methoxy-substituted phenazines has utilized a variety of methods generally resulting in low yields of the desired product. One of these methods, the Wohl–Aue reaction, has been described as a direct, albeit low yield approach to the synthesis of phenazines and phenazine oxides,[22-24] involving the vigorous heating of anilines and nitrobenzenes in the presence of strong base (Scheme I). Synthesis of 1,6-dimethoxyphenazine **21** in 20% yield from *o*-nitroanisole (**18**) and *o*-anisidine (**19**) has been reported.[25] However, our attempted synthesis of 1,6-dimethoxy-2,3-dimethylphenazine (**14**) from **18** and 2-methoxy-3,4-dimethylaniline (**20**) under various conditions[25,26a] resulted in very low yields of the desired product **14**, along with a second phenazine identified as the 1,2-dimethyl-9-methoxy compound **23**. Wohl–Aue reactions between **18** and **19** gave either **21**[25] or a mixture of **21** (10%) and 1-methoxyphenazine (**22**) (4%), in disagreement with the literature.[26b] Previous examples describing the loss of methoxyl groups in the Wohl–Aue reaction are known[22] but the mechanism for this deletion remains unclear.

In another approach to the phenazine **14** we examined the condensation between 3-methoxy-1,2-benzoquinone (**24**) and an *o*-diamine previously used[1,27] in the synthesis of **11** and **12**. For this synthesis of **14** (Scheme II), *o*-diamine **25** was required as the key intermediate. The expected regioisomer **26**, a byproduct of the reaction would also be of interest to us as a precursor to targets such as **4**.

To produce the 1,2-diamino-3-methoxy substitution pattern with no 6-substituent, **25** had to be prepared indirectly in a series of steps. This was initially attempted (Scheme III) by the mild nitration[28] of the anisidine **20** with NH_4NO_3 and trifluoracetic anhydride (TFAA) in chloroform at room temperature, which proceeded cleanly via intermediate **27** but gave two products, the desired 6-nitro isomer **28** (16%) and the 5-nitro isomer **29** (76%). N-Deacylation of **28** and **29** with methanolic hydrogen chloride yielded the nitro amines **33** and **34** in quantitative yields. The high yield of the undesired 5-nitro amide **29** suggested that suitable blocking of the activated 5-position by an electrophile would probably facilitate synthesis of the *o*-diamine **25**. The use of bromine fitted our purpose, and bromination (Br_2, CCl_4) of the trifluoroacetamide **27** gave the 5-bromo derivative **30** as the sole product in 96% yield. The mild nitration of **30** (NH_4NO_3–TFAA) gave the desired 5-bromo-6-nitro intermediate **31** (85%) and deacylation yielded the nitro amine **32** quantitatively. Simultaneous removal of the 5-bromo blocking substituent and reduction of the nitro group by hydrogenolysis (Pd/C, aqueous EtOH) in the presence of potassium carbonate gave the required *o*-diamine **25** in high yield (67% overall from **20**) identical with a sample prepared by hydrogenation of nitro amine **33**.

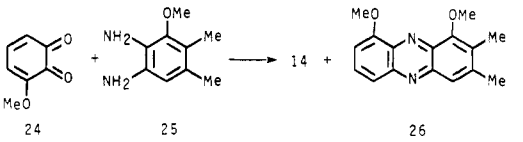
Scheme I



18 19, R = H 20, R = Me 21, R = OMe, R1 = H 22, R = R1 = H 14, R = OMe, R1 = Me

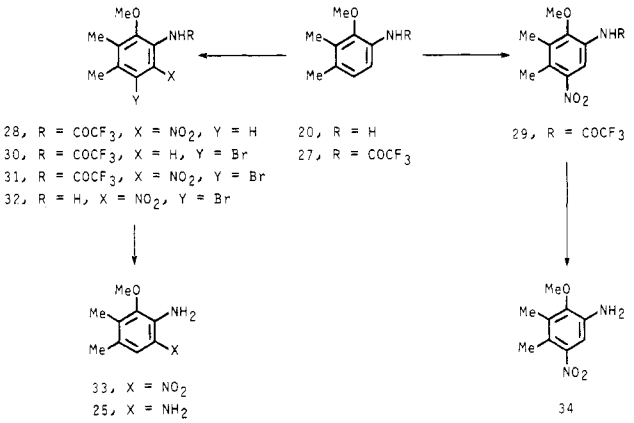
23

Scheme II



24 25 14 26

Scheme III



28, R = $COCF_3$, X = NO_2, Y = H
30, R = $COCF_3$, X = H, Y = Br
31, R = $COCF_3$, X = NO_2, Y = Br
32, R = H, X = NO_2, Y = Br

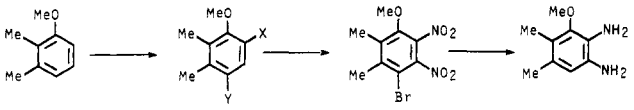
20, R = H
27, R = $COCF_3$

29, R = $COCF_3$

33, X = NO_2
25, X = NH_2

34

Scheme IV



35 36a, X = H, Y = Br 36b, X = Br, Y = H 37 25

While this preparation of the *o*-diamine **25** from commercially available 2,3-dimethylphenol was straightforward, overall, the route was lengthy and included the low yield synthesis of the amine **20**.[29,30] We therefore devised a shorter route (Scheme IV) to **25** based on our success in blocking the position para to the methoxyl group with Br. Bromination (NBS, CH_2Cl_2, 60 °C) of 2,3-dimethylanisole (**35**) gave the 4-bromo derivative **36a** as the sole product in 89% yield. This assignment rather than **36b** was confirmed by observation of a 15% NOE enhancement of the high-field doublet at 6.58 δ on selective irradiation of the OCH_3 resonance. Nitration of **36a** with acetyl nitrate or concentrated nitric acid gave mixtures resulting in part from ipso attack at the 4-bromo position.[31,32] However,

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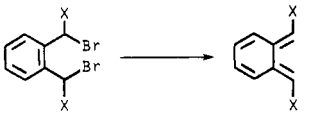
ortho dinitration was effected without ipso attack to yield **37** in 80% yield when **36a** was treated with nitronium tetrafluoroborate in acetonitrile at room temperature. Hydrogenolysis resulted in reduction of both nitro groups and removal of the bromo blocking group to give the required *o*-diamine **25** (63% overall yield from **35**).

Condensation of the *o*-diamine **25** with 3-methoxy-1,2-benzoquinone (**24**) in toluene and acetic acid at room temperature gave (Scheme II) the two isomeric dimethoxy phenazines **14** (25%) and **26** (25%), which were assigned by spectral comparison of **14** with the sample previously isolated from the Wohl–Aue reaction (Scheme I). Free radical bromination of **14** (2.05 mol NBS, Bz_2O_2, CCl_4) gave the 2,3-bis(bromomethyl)-1,6-dimethoxyphenazine (**15**) (73% yield) for intended conversion to the *o*-quinodimethan **16**.



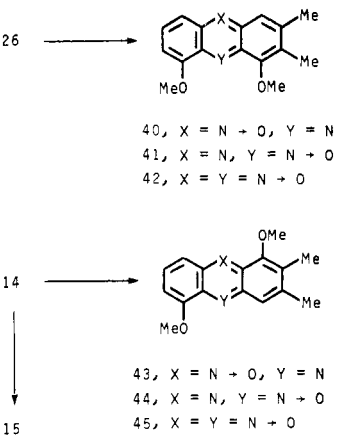
38 39

The generation of an *o*-quinodimethan such as **39** from an *o*-xylene derivative **38** has ample precedent in the literature since its initial discovery by Cava.[33] Recently, substituted derivatives of **38** have found considerable use in the synthesis of anthracyclinones, where the reactive intermediates **39** have been formed by 1,4-elimination[20,34,35] or by 1,4-reduction[21,34,36-38] and have then been trapped by a suitable dienophile.

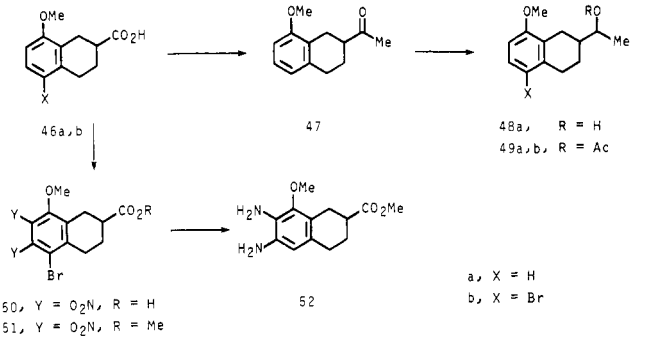
We attempted to form the reactive intermediate, 2,3-dihydro-1,6-dimethoxy-2,3-bis(methylene)phenazine (**16**) from **15** in the presence of a dienophile under a variety of conditions by using NaI in DMF or DMA, with *N*-phenylmaleimide, or activated Zn in DMF with maleic anhydride. These experiments resulted in decomposition of the starting material and no evidence for incorporation of the dienophile into the molecule. The use of ultrasound[39] to accelerate the reaction between **15** and zinc in dioxane at room temperature proved ineffective and merely led to the recovery of starting materials. Further investigation of this approach was discontinued in favor of synthesizing the target 7,8,9,10-tetrahydrobenzo[*b*]-phenazines by the condensation of an *o*-diamine containing the relevant AB moiety and an appropriately substituted 1,2-benzoquinone as in Scheme VII.

At this point, model experiments on the N-oxidation of phenazines **14** and **26** were undertaken (Scheme V) to see if the oxidation conditions were compatible, as assumed, with 1,6- and 1,9-dimethoxy substitution. This was important because of the difficulties we encountered[1] in attempted N-oxidation of the di-*O*-methyl derivatives of **11** and **12**. Treatment of phenazine **26** with *m*-chloroperbenzoic acid (mCPBA) in dichloromethane gave the 5-oxide **40** in 81% yield. Further treatment of **40** with mCPBA or pertrifluoroacetic acid in dichloromethane gave none of the desired 5,10-dioxide **42**, and prolonged exposure to the oxidant resulted in destruction of the phenazine nucleus. Attempted formation of the 10-oxide **41** from **26** by the use of Caro's acid[40] also led to decomposition of the starting material. Oxidation of phenazine **14** with mCPBA gave a 1:1 mixture of the 5- and 10-oxides **44** and **43** (78%) and the desired 5,10-dioxide **45** (10%, yields based on recovered **14**) as expected.[41] Evidently there is sufficient hindrance with the 1,9-disubstitution in **26** to permit only mono N-oxidation. The position of N-oxidation in the phenazines—i.e., at 5 or 10 or 5 and 10—was confirmed by ^1H NMR. The presence of an N→O function in the molecule results in a downfield shift of 0.2–0.5 ppm for the aromatic protons in the peri position.[1]

Scheme V



Scheme VI



Completion of the Synthesis of Targets 3 and 4. Our approach to the synthesis of 6,7-diamino-1,2,3,4-tetrahydro-8-methoxynaphthalene intermediates, e.g., **53** (required for Scheme VII), used the methodology previously outlined in Scheme IV and included a side chain in the 2-position suitable for easy conversion to the methyl ketone desired.

The starting material, 2-carboxylic acid **46a**, was conveniently synthesized in three steps from 1,6-dihydroxynaphthalene by the method of Mander[42] in 50% overall yield. Treatment with methyllithium in tetrahydrofuran (THF) with the chlorotrimethylsilane quenching procedure of Rubottom[43] then gave the desired 2-methyl ketone **47**

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(32) For a review on ipso attack in aromatic nitration, see: Moodie, R. B.; Schofield, K. *Acc. Chem. Res.* **1976**, *9*, 287.
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(37) Cf. Elix, J. A.; Sargent, M. V.; Sondheimer, F. *J. Am. Chem. Soc.* **1970**, *92*, 962.
(38) The reaction is analogous to the 1,4-reduction of 1,4-dibromo-2-butene to butadiene with zinc in ethanol. See: Thiel, J. *Liebigs Ann. Chem.* **1899**, *308*, 339.
(39) Han, B. H.; Boudjouk, P. *J. Org. Chem.* **1982**, *47*, 751.
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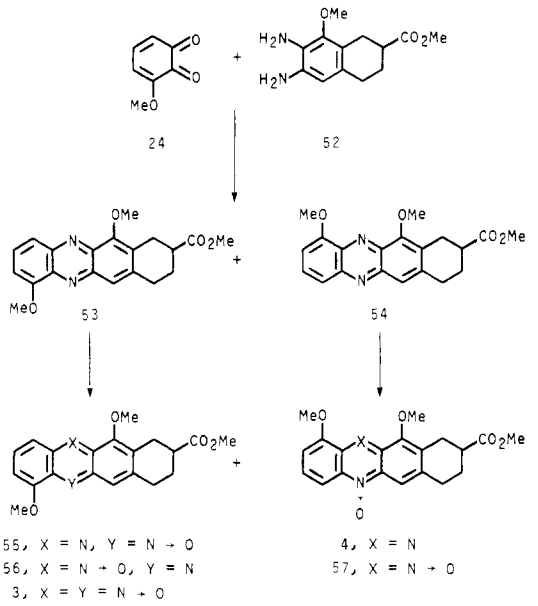
(43) Rubottom, G. M.; Kim, C. *J. Org. Chem.* **1983**, *48*, 1550.
(44) Tsunoda, T.; Suzuki, M.; Noyori, R. *Tetrahedron Lett.* **1980**, 1357.

Scheme VII



(95%), free from any unwanted tertiary alcohol. Reduction of **47** with $NaBH_4$ gave the secondary alcohol **48a** as a mixture of diastereomers (84%) that were not separated. Acetylation and bromination (NBS) then gave the 5-bromo derivative **49b** as the sole product in 76% yield. Assignment of the structure as **49b** was confirmed by an NOE experiment similar to that carried out on 4-bromo-2,3-dimethylanisole (**36a**). Attempted ortho dinitration of the ester **49b** with NO_2BF_4 in acetonitrile led to side chain decomposition, while nitration with acetyl nitrate gave product mixtures resulting from mono- and dinitration involving ipso attack on the bromo position.[31]

Our attention thus reverted to the underivatized starting 2-carboxylic acid **46a**. Bromination (NBS) gave the 5-bromo acid **46b** as the sole product in excellent yield (92%). Ortho dinitration (NO_2BF_4) proceeded as planned and gave the desired 6,7-dinitro acid **50** (69%) which was esterified (CH_2N_2) to give the methyl ester **51** quantitatively. Hydrogenolysis gave the *o*-diamine **52** in excellent yield (94%). Condensation with 3-methoxy-1,2-benzoquinone (**24**) (Scheme VII) then gave the two desired 7,8,9,10-tetrahydrobenzo[*b*]phenazine regioisomers **53** (20%) and **54** (21%). These two compounds could be separated by chromatography and comparison of their ^1H NMR spectra with those obtained for the phenazine regioisomers **14** and **26** led to the structural assignment.

Completion of the prospective total synthesis (e.g., **13** from **53**) of the phenazine *N*-oxide analogues of daunorubicin (**5**) requires oxidation to the 5,12-di-*N*-oxide as one of the final steps, along with functionalization at positions 7 and 9 and glycosidation. Consequently, at this stage we wanted to demonstrate that the methoxy substitution patterns present in **53** and **54** would allow N-oxidation similar to that shown for the simple phenazines **14** and **26**. N-Oxidation of the hindered **54** (mCPBA, CH_2Cl_2) proceeded very cleanly in 1 h and gave the yellow 5-oxide **4** in good yield (64%), but attempted conversion to the 5,12-dioxide **57** failed and resulted in decomposition of the starting material. Assignment of the structure as the 5-rather than the 12-oxide was made by ^1H NMR spectral comparision with phenazine **40**. On the other hand, oxidation of **53** to the desired di-*N*-oxide **3** could be demonstrated. Under the same conditions as for **54**, **53** gave a 2:1 mixture of the 5- and 12-oxides **55** and **56** (85%). Retreatment of this isolated mixture yielded the red 5,12-dioxide **3** (29%, yield based on recovered starting material), along with unreacted **55** and **56**. Although the yields were low in the experiments so far, the successful formation of **3** demonstrates that the 1,6-dimethoxy substitution pattern is compatible with oxidation of both nitrogens, as required in target **13**. Hence, its successful synthesis from intermediate **59** can be anticipated by known methods for anthracycline synthesis. This report therefore constitutes the first successful synthetic approach to isosteric modification in the C ring of an anthracyclinone derivative.

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Experimental Section

General Methods. Solutions in organic solvents were dried over anhydrous $MgSO_4$ and filtered. Evaporations were carried out in vacuo. mCPBA was 80–85% technical grade. Anhydrous THF and toluene were distilled from sodium and benzophenone. CCl_4, $CDCl_3$, and MeCN were dried over activated molecular sieves. Column chromatography was carried out on E. Merck silica gel 60, 70–230 mesh or 230–400 mesh, when no medium is stated and on Woelm alumina N activity III. Preparative LC was performed on a Waters Associates Prep LC/System 500 instrument by using a PrepPak-500/silica cartridge column and a refractive index detector. Melting points were uncorrected.

Spectral Methods. IR spectra were determined with a Perkin-Elmer 1310 spectrophotometer. ^1H NMR spectra were recorded on a JEOL FX90Q FT spectrometer ($CDCl_3$ solution). Low-resolution mass spectra were determined on an LKB 9000 GC–MS at 12 eV interfaced with a PDP 12 computer and high-resolution mass spectra were determined with an AEI-MS 12. UV–vis spectra were obtained on a Perkin-Elmer Model 575 recording spectrometer.

9-Methoxy-1,2-dimethylphenazine (23) and 1,6-Dimethoxy-2,3-dimethylphenazine (14). 3,4-Dimethyl-*o*-anisidine (**20**)[29] (2.0 g, 13 mmol), *o*-nitroanisole (**18**) (5.0 g, 33 mmol), and powdered KOH (5.0 g, 89 mmol) in anhydrous toluene (25 mL) were stirred mechanically at 120 °C under argon for 6 h. The mixture was allowed to cool to 50 °C, the supernatant was poured into water and the residue dissolved in more water. The two-phase mixture was neutralized with 1 N HCl and extracted with $CHCl_3$. The organic phase was concentrated, stirred with activated Woelm alumina (40 g) for 0.5 h, and then filtered off. The residual alumina was washed with $CHCl_3$ until the filtrate was almost colorless. The filtrates were dried and evaporated. Chromatography of the residue, elution with CH_2Cl_2, gave a slow-moving, bright yellow fraction containing the phenazine mixture. Preparative layer chromatography on silica gel, elution with 100% $CHCl_3$ (run three times), gave two main bands. The front fraction (R_f 0.44) gave **23** (25 mg, 1 %), recrystallized from toluene:hexane as yellow crystals: mp 165–168 °C; IR ($CHCl_3$) 2990–2840 (CH), 1625, 1605, 1560, 1525, 1125, (COC); ^1H NMR δ 8.14 (1 H, d, H-4, $J_{4,3}$ = 9 Hz), 7.86 (1 H, dd, H-6, $J_{6,7}$ = 9 Hz, $J_{6,8}$ = 1.6 Hz), 7.68 (1 H, dd, H-7, $J_{7,6}$ = 9 Hz, $J_{7,8}$ = 7.1 Hz), 7.63 (1 H, d, H-3, $J_{3,4}$ = 9 Hz), 7.02 (1 H, dd, H-8, $J_{8,7}$ = 7.1 Hz, $J_{8,6}$ = 1.6 Hz), 4.16 (3 H, s, OCH_3), 2.86 (3 H, s, 1-CH_3), 2.58 (3 H, s, 2-CH_3); MS, *m/e* 238 (M^+), 237 $(M - H)^+$; high-resolution MS, *m/e* calcd for $C_{15}H_{14}N_2O$ 238.1106, found 238.1105.

The rear fraction (R_f 0.18) gave **14** (30 mg, 1%) recrystallized from toluene as yellow needles: mp 185–187 °C; IR ($CHCl_3$) 3000–2840 (CH), 1630, 1555, 1515, 1480, 1152 (COC), 1115 (COC); ^1H NMR δ 7.97 (1 H, uq, H-4), 7.91 (1 H, dd, H-9, $J_{9,8}$ = 9 Hz, $J_{9,7}$ = 1.4 Hz), 7.68 (1 H, dd, H-8, $J_{8,7}$ = 7.4 Hz, $J_{8,9}$ = 9 Hz), 7.03 (1 H, dd, H-7, $J_{7,8}$ = 7.4 Hz, $J_{7,9}$ = 1.4 Hz), 4.18 (3 H, s, OCH_3), 4.16 (3 H, s, OCH_3), 2.55 (3 H, d, 3-CH_3, $J_{CH_3,4}$ = 1.1 Hz), 2.48 (3 H, s, 2-CH_3); MS, *m/e* 268 (M^+), 253 $(M - CH_3)^+$; UV (EtOH) λ_{max} (log ϵ) 268.6 (4.97), 374.5 (3.97). Anal. Calcd for $C_{16}H_{16}N_2O_2$: C, 71.62; H, 6.01; N, 10.44. Found: C, 71.68; H, 5.93; N, 10.49.

1,6-Dimethoxyphenazine (21) and 1-Methoxyphenazine (22). Prepared by Wohl–Aue condensation of *o*-anisidine (**19**) (3.0 g, 24.4 mmol) and *o*-nitroanisole (**18**) (7.0 g, 45.8 mmol) by the same method as **14** and **23**. Chromatography of the residue, elution with CH_2Cl_2, gave **22** (0.19 g, 4%) recrystallized from

toluene as bright yellow needles, mp 166 °C (lit.[46] mp 167–169 °C), and **21** (0.61 g, 10%) also recrystallized from toluene as bright yellow needles, mp 260–262 °C (lit.[25b] mp 260 °C).

1-(Trifluoroacetamido)-2-methoxy-3,4-dimethyl-5-nitrobenzene (29) and 1-(Trifluoroacetamido)-2-methoxy-3,4-dimethyl-6-nitrobenzene (28). To a suspension of amine **20**[29] (0.30 g, 2 mmol) and NH_4NO_3 (0.17 g, 2.1 mmol) in $CHCl_3$ (2 mL) at 0 °C was added trifluoroacetic anhydride (1 mL, 7.1 mmol). The mixture was allowed to warm up to room temperature, stirred for 6 h, poured into water, and extracted with $CHCl_3$. The organic phase was then washed with aqueous $NaHCO_3$ and water, dried, and evaporated. Chromatography of the residue, elution with $CHCl_3$, gave two fractions. The front fraction (R_f 0.58) was recrystallized from hexane and gave **29** (0.44 g, 76%) as colorless needles: mp 84 °C; IR (KBr) 3400 (NH), 1725 (C=O), 1345 (NO_2); ^1H NMR δ 8.63 (1 H, s, H-6), 8.52 (1 H, s, NH), 3.82 (3 H, s, OCH_3) 2.38 (3 H, s, CH_3), 2.32 (3 H, s, CH_3); MS, *m/e* 292 (M^+), 275 (M − OH)$^+$. Anal. Calcd for $C_{11}H_{11}F_3N_2O_4$: C, 45.21; H, 3.79; N, 9.59. Found: C, 44.92; H, 3.63; N, 9.32.

The rear fraction (R_f 0.38) was recrystallized from ether:hexane (3:1) and gave **28** (90 mg, 16%) as pale yellow crystals: mp 167 °C; IR (KBr) 3240 (NH), 1720 (C=O), 1345 (NO_2); ^1H NMR δ 8.62 (1 H, bs, NH), 7.70 (1 H, s, H-5), 3.75 (3 H, s, OCH_3), 2.37 (3 H, s, CH_3), 2.32 (3 H, s, CH_3); MS, *m/e* 292 (M^+), 246 (M − NO_2)$^+$. Anal. Calcd for $C_{11}H_{11}F_3N_2O_4$: C, 45.21; H, 3.79; N, 9.59. Found: C, 45.08; H, 3.50; N, 9.40.

General Procedure for the Removal of the *N*-Trifluoroacetyl Group: Preparation of 1-Amino-2-methoxy-3,4-dimethyl-6-nitrobenzene (33). The trifluoroacetamide **28** (0.15 g, 0.51 mmol) was dissolved in MeOH (15 mL) and the solution saturated with HCl at 0 °C. After allowing the mixture to warm up to room temperature it was stirred for 18 h and carefully evaporated. The pale yellow residue was dissolved in $CHCl_3$ and extracted with aqueous $NaHCO_3$. The aqueous phase was back-extracted with $CHCl_3$, the organic phases were combined, washed with water, and dried, and the solvent was removed in vacuo. Recrystallization of the residue from hexane gave **33** (90 mg, 89%) as orange needles: mp 84 °C (lit.[47] mp 85–86 °C); ^1H NMR δ 7.71 (1 H, uq, H-5), 6.19 (2 H, bs, NH_2), 3.74 (3 H, s, OCH_3), 2.22 (3 H, s, 2-CH_3), 2.19 (3 H, d, 3-CH_3, $J_{CH_3,4}$ = 0.9 Hz).

1-Amino-2-methoxy-3,4-dimethyl-5-nitrobenzene (34). Prepared from trifluoroacetamide **29** (0.30 g, 1.03 mmol) by the same method as **33**. Recrystallization from hexane gave **34** (0.19 g, 94%) as orange needles: mp 91 °C; IR ($CHCl_3$) 3490 (NH_2), 3400 (NH_2), 3005–2840 (CH), 1625, 1600, 1525, 1350 (NO_2); ^1H NMR δ 7.07 (1 H, s, H-6), 3.84 (2 H, bs, NH_2), 3.77 (3 H, s, OCH_3), 2.30 (3 H, s, CH_3), 2.27 (3 H, s, CH_3); MS, *m/e* 196 (M^+), 179 (M − OH)$^+$. Anal. Calcd for $C_9H_{12}N_2O_3$: C, 55.09; H, 6.17; N, 14.28. Found: C, 55.02; H, 6.03; N, 13.86.

1-(Trifluoroacetamido)-2-methoxy-3,4-dimethylbenzene (27). To a solution of amine **20** (1.51 g, 10 mmol) in CH_2Cl_2 (10 mL) at 0 °C was added dropwise trifluoroacetic anhydride (4.2 mL, 30 mmol). The solution was stirred for 10 min then allowed to warm up to room temperature and evaporated. Recrystallization of the residue from hexane gave **27** (2.36 g, 96%) as white needles: mp 87–88 °C; IR (KBr) 3300 (NH), 1713 (C=O), 1535; ^1H NMR δ 8.50 (1 H, bs, NH), 8.00 (1 H, d, H-6, $J_{6,5}$ = 9 Hz), 6.95 (1 H, d, H-5, $J_{5,6}$ = 9 Hz), 3.80 (3 H, s, OCH_3), 2.28 (3 H, s, CH_3), 2.25 (3 H, s, CH_3); MS, *m/e* 247 (M^+). Anal. Calcd for $C_{11}H_{12}F_3NO_2$: C, 53.44; H, 4.89; N, 5.67. Found: C, 53.61; H, 4.92; N, 5.64.

5-Bromo-1-(trifluoroacetamido)-2-methoxy-3,4-dimethylbenzene (30). A solution of trifluoroacetamide **27** (2.47 g, 10 mmol) and iodine (3 crystals) in CCl_4 (40 mL) at room temperature was treated dropwise with bromine (0.56 mL, 11 mmol) and the mixture stirred for 18 h. More bromine (0.18 mL, 3.5 mmol) was then added and the stirring continued for another 12 h. The solution was then washed with 10% aqueous $Na_2S_2O_3$, aqueous $NaHCO_3$, water and dried, and the solvent removed in vacuo. Recrystallization of the residue from hexane gave **30** (3.13 g, 96%) as white crystals: mp 101–103 °C; IR ($CHCl_3$) 3400 (NH), 1730 (C=O), 1600, 1525; ^1H NMR δ 8.38 (2 H, bs, H-6 and NH), 3.74 (3 H, s, OCH_3), 2.35 (3 H, s, CH_3), 2.28 (3 H, s, CH_3); MS, *m/e* 327 (M + 2)$^+$, 325 (M^+), 312 (M + 2 − CH_3)$^+$, 310 (M − CH_3)$^+$. Anal. Calcd for $C_{11}H_{11}BrF_3NO_2$: C, 40.51; H, 3.40; N, 4.30. Found: C, 40.43; H, 3.39; N, 4.19.

5-Bromo-1-(trifluoroacetamido)-2-methoxy-3,4-dimethyl-6-nitrobenzene (31). A suspension of trifluoroacetamide **30** (3.26 g, 10 mmol) and NH_4NO_3 (0.88 g, 11 mmol) in $CHCl_3$ (20 mL) at room temperature was treated with trifluoroacetic anhydride (5.4 mL, 38 mmol). The mixture was stirred for 18 h, poured into water, and extracted with $CHCl_3$. The organic phase was then washed with aqueous $NaHCO_3$ and water, dried, and evaporated. Recrystallization of the residue from ether:hexane (1:1) gave **31** (3.15 g, 85%) as white crystals: mp 173 °C; IR ($CHCl_3$), 3400 (NH), 1750 (C=O), 1540 (NO_2), 1360 (NO_2); ^1H NMR δ 7.92 (1 H, bs, NH), 3.77 (3 H, s, OCH_3), 2.48 (3 H, s, CH_3), 2.37 (3 H, s, CH_3); MS, *m/e* 372 (M + 2)$^+$, 370 (M^+), 326 (M + 2 − NO_2)$^+$, 324 (M − NO_2)$^+$, 311 (M + 2 − NO_2 − CH_3)$^+$, 309 (M − NO_2 − CH_3)$^+$. Anal. Calcd for $C_{11}H_{10}BrF_3N_2O_4$: C, 35.60; H, 2.72; N, 7.55. Found: C, 35.71; H, 2.65; N, 7.46.

1-Amino-5-bromo-2-methoxy-3,4-dimethyl-6-nitrobenzene (32). Prepared from trifluoroacetamide **31** (3.71 g, 10 mmol) by the same method as **33**. Recrystallization from hexane gave **32** (2.53 g, 92%) as orange needles: mp 114 °C; IR ($CHCl_3$) 3500 (NH_2), 3400 (NH_2), 1610, 1510 (NO_2), 1350 (NO_2); ^1H NMR δ 4.73 (2 H, bs, NH_2), 3.73 (3 H, s, OCH_3), 2.33 (3 H, s, CH_3), 2.27 (3 H, s, CH_3); MS, *m/e* 276 (M + 2)$^+$, 274 (M^+), 261 (M + 2 − CH_3)$^+$ 259 (M − CH_3)$^+$. Anal. Calcd for $C_9H_{11}BrN_2O_3$: C, 39.29; H, 4.03; N, 10.18. Found: C, 39.23; H, 3.95; N, 10.06.

4-Bromo-1-methoxy-2,3-dimethylbenzene (36a). 2,3-Dimethylanisole (**35**) (4.08 g, 30 mmol) and NBS (6.14 g, 34.5 mmol) were dissolved in CH_2Cl_2 (75 mL) and the solution was refluxed for 18 h. The solvent was removed in vacuo, and the residue dissolved in $CHCl_3$ and filtered. The filtrate was washed with warm water, dried, and evaporated. Distillation of the residue gave **36a** (5.74 g, 89%) as a colorless oil: bp 140–143 °C (18 mm) (lit.[48] bp 139–140 °C (17 mm)); ^1H NMR δ 7.34 (1 H, d, H-5, $J_{5,6}$ = 9 Hz), 6.58 (1 H, d, H-6, $J_{6,5}$ = 9 Hz), 3.79 (3 H, s, OCH_3), 2.36 (3 H, s, 3-CH_3), 2.20 (3 H, s, 2-CH_3).

6-Bromo-3-methoxy-4,5-dimethyl-1,2-dinitrobenzene (37). A stirred solution of bromide **36a** (0.22 g, 1 mmol) in anhydrous MeCN (5 mL) at room temperature under argon was treated with nitronium tetrafluoroborate (0.53 g, 4 mmol). After 0.5 h, a further portion of nitronium tetrafluoroborate (0.27 g, 2 mmol) was added and the stirring continued for 2.5 h. The yellow solution was then poured slowly into ice–water (50 mL), and the pale yellow precipitate removed by filtration, washed with water, and dried. Recrystallization from EtOH gave **37** (0.25 g, 80%) as cream crystals: mp 137–138 °C; IR ($CHCl_3$) 2950 (CH), 1550 (NO_2), 1350 (NO_2); ^1H NMR δ 3.90 (3 H, s, OCH_3), 2.52 (3 H, s, 5-CH_3), 2.39 (3 H, s, 4-CH_3); MS, *m/e* 306 (M+2)$^+$, 304 (M^+). Anal. Calcd for $C_9H_9BrN_2O_5$: C, 35.43; H, 2.97; N, 9.18. Found: C, 35.64; H, 3.12; H, 9.13.

1,2-Diamino-3-methoxy-4,5-dimethylbenzene (25). (a) Preparation from 32. A slurry of *o*-nitroamine **32** (2.75 g, 10 mmol), powdered K_2CO_3 (1.38 g, 10 mmol), and 5% palladium on activated carbon (0.35 g) in aqueous EtOH (80 mL) was hydrogenated on a Parr apparatus (2 atm) at room temperature for 6 h. The mixture was filtered through Celite and the residue washed thoroughly. The solvent was removed in vacuo, the residue was dissolved in CH_2Cl_2, filtered, and evaporated, and the residue chromatographed, elution with 5% EtOH:95% CH_2Cl_2, giving **25** (1.54 g, 93%) (R_f 0.52) as a pale pink oil which crystallized on standing. No further purification was carried out on the material to be used in the next step but sublimation (25 °C (0.1 mm)) of a small quantity produced a sample for analysis, mp 125–135 °C.

(b) Preparation from 37. Preparation by the same method as described above from *o*-dinitrobromide **37** (3.05 g, 10 mmol) gave **25** (1.46 g, 88%).

(c) Preparation from 33. A slurry of *o*-nitroamine **33** (0.20 g, 1 mmol) and 5% palladium on activated carbon (40 mg) in aqueous EtOH (20 mL) was hydrogenated on a Parr apparatus (2 atm) at room temperature for 8 h. Workup of the residue as

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(47) Nijenhuis, B. te; Mulder, A. C.; Berends, W. *Recl. Trav. Chim. Pays-Bas* **1980**, *99*, 115.

(48) Short, W. F.; Stromberg, H.; Wyes, A. E. *J. Chem. Soc.* **1936**, 319.

described above gave **25** (0.16 g, 94%): IR ($CHCl_3$) 3430 (NH_2), 3360 (NH_2), 3010–2840 (CH), 1625, 1595, 1500; ^1H NMR δ 6.35 (1 H, s, H-6), 3.71 (3 H, s, OCH_3), 3.05 (4 H, bs, 1- and 2-NH_2), 2.11 (6 H, bs, 4- and 5-CH_3); MS, *m/e* 166 (M^+), 151 $(M - 15)^+$, 123. Anal. Calcd for $C_9H_{14}N_2O$: C, 65.03; H, 8.49; N, 16.85. Found: C, 65.10; H, 8.42; N, 16.84.

1,6-Dimethoxy-2,3-dimethylphenazine (14) and 1,9-Dimethoxy-2,3-dimethylphenazine (26). A stirred solution of 3-methoxy-1,2-benzoquinone (**24**)[1] (5.52 g, 40 mmol) in toluene (700 mL) at room temperature was treated quickly with *o*-diamine **25** (6.64 g, 40 mmol) in toluene (150 mL) and glacial acetic acid (110 mL). The mixture was stirred for 18 h and the black suspension formed then filtered off. The filtrate was washed with 5% aqueous NaOH and water, dried, and evaporated. The dark residue was dissolved in CH_2Cl_2 (250 mL), stirred with activated Woelm alumina (200 g) for 0.5 h, and then filtered off. The residual alumina was washed with CH_2Cl_2 until the yellow eluant turned pale red. The solvent was removed in vacuo and the residue was then chromatographed by HPLC on silica gel, elution with 5% ethyl acetate:95% CH_2Cl_2, giving **14** (R_{fCHCl_3} 0.34) (2.43 g), **26** (R_{fCHCl_3} 0.22) (1.65 g), and a mixture of the two phenazines (1.60 g). The mixture was rechromatographed on Woelm alumina, elution with toluene, giving **26** (1.02 g) and **14** (0.26 g). (The order of elution of the phenazines on alumina compared to silica gel was reversed). **14** (2.69 g, 25%) was recrystallized from toluene as yellow needles, mp 184–186 °C.

26 (2.67 g, 25%) was also recrystallized from toluene as bright yellow needles: mp 183–184 °C; IR ($CHCl_3$) 3000–2840 (CH), 1630, 1605, 1560, 1480, 1155 (COC), 1115 (COC); ^1H NMR δ 7.80–7.58 (3 H, m, H-4, 6 and 7), 7.05–6.96 (1 H, m, H-8), 4.25 (3 H, s, OCH_3), 4.13 (3 H, s, OCH_3), 2.56 (3 H, d, 3-CH_3, $J_{CH_3,4}$ = 1.2 Hz), 2.55 (3 H, s, 2-CH_3); MS, *m/e* 268 (M^+), 253 $(M - CH_3)^+$; UV (EtOH) λ_{max} (log ϵ) 269 (4.94), 373 (3.95). Anal. Calcd for $C_{16}H_{16}N_2O_2$: C, 71.62; H, 6.01; N, 10.44. Found: C, 71.53; H, 6.11; N, 10.49.

2,3-Bis(bromomethyl)-1,6-dimethoxyphenazine (15). Phenazine **14** (2.68 g, 10 mmol), recrystallized NBS (3.65 g, 20.5 mmol), and benzoyl peroxide (50 mg) were dissolved in anhydrous CCl_4 (300 mL) and the solution was refluxed for 18 h. The mixture was cooled and the white precipitate filtered off. The filtrate was then washed with warm water, dried, and evaporated. Chromatography of the residue, elution with $CHCl_3$, gave **15** (3.11 g, 73%), which was recrystallized from toluene as bright yellow needles: mp 212 °C; IR ($CHCl_3$) 3000–2845 (CH), 1630, 1520, 1480, 1162 (COC), 1120 (COC); ^1H NMR δ 8.21 (1 H, s, H-4), 7.96–7.66 (2 H, m, H-8 and 9), 7.14–7.04 (1 H, m, H-7), 5.06 (2 H, s, CH_2), 4.88 (2 H, s, CH_2), 4.44 (3 H, s, OCH_3), 4.17 (3 H, s, OCH_3); MS, *m/e* 428 $(M + 4)^+$, 426 $(M + 2)^+$, 424 (M^+), 347 $(M + 2 - Br)^+$, 345 $(M - Br)^+$, 266 $(M - 2Br)^+$. Anal. Calcd for $C_{16}H_{14}Br_2N_2O_2$: C, 45.10; H, 3.31; N, 6.57. Found: C, 45.41; H, 3.39; N, 6.59.

1,9-Dimethoxy-2,3-dimethylphenazine 5-Oxide (40). Phenazine **26** (0.27 g, 1 mmol) and mCPBA (1.08 g, 5 mmol) dissolved in CH_2Cl_2 (20 mL) were stirred at room temperature for 1.5 h. The solution was then washed with 10% aqueous $NaHSO_3$, aqueous $NaHCO_3$, and water, dried (Na_2SO_4), and evaporated. Chromatography of the residue on Woelm alumina, elution with CH_2Cl_2, gave **40** (0.23 g, 81%) which was recrystallized from toluene:hexane (2.5:1) as yellow needles: mp 214–216 °C; IR ($CHCl_3$) 3000–2840 (CH), 1620, 1603, 1480, 1340 (NO), 1095 (COC), 1075 (COC); ^1H NMR δ 8.24 (1 H, uq, H-4), 8.22 (1 H, dd, H-6, $J_{6,7}$ = 9 Hz, $J_{6,8}$ = 1.2 Hz), 7.62 (1 H, dd, H-7, $J_{7,6}$ = 9 Hz, $J_{7,8}$ = 7.9 Hz), 7.03 (1 H, dd, H-8, $J_{8,7}$ = 7.9 Hz, $J_{8,6}$ = 1.2 Hz), 4.24 (3 H, s, OCH_3), 4.12 (3 H, s, OCH_3), 2.55 (3 H, d, 3-CH_3, $J_{CH_3,4}$ = 1 Hz), 2.44 (3 H, s, 2-CH_3); MS, *m/e* 284 (M^+), 269 $(M - CH_3)^+$; UV (EtOH) λ_{max} (log ϵ) 279 (5.13), 368 (3.67), 389 (3.91), 451 (3.80). Anal. Calcd for $C_{16}H_{16}N_2O_3$: C, 67.59; H, 5.67; N, 9.85. Found: C, 67.71; H, 5.81; N, 9.67.

mCPBA Oxidation of 1,6-Dimethoxy-2,3-dimethylphenazine (14). Phenazine **14** (0.27 g, 1 mmol) and mCPBA (1.08 g, 5 mmol) dissolved in CH_2Cl_2 (20 mL) were stirred at room temperature for 18 h. Workup as described for **40** gave recovered starting material **14** (54 mg, 20%) (R_f 0.68), a 1:1 mixture of the two yellow **1,6-dimethoxy-2,3-dimethylphenazine 10-oxide (43)** and **1,6-dimethoxy-2,3-dimethylphenazine 5-oxide (44)** (178 mg, 78%) (R_f 0.37), which were not separated, and the red **1,6-dimethoxy-2,3-dimethylphenazine 5,10-dioxide (45)** (23 mg, 10%, yields of oxides based on recovered starting material) (R_f 0.10). Recrystallization from toluene:hexane gave **45** as red crystals: IR ($CHCl_3$) 3010–2850 (CH), 1610, 1545, 1472, 1342 (NO), 1105 (COC), 1065 (COC); ^1H NMR δ 8.35 (1 H, uq, H-4), 8.33 (1 H, dd, H-9, $J_{9,8}$ = 9 Hz, $J_{9,7}$ = 1.2 Hz), 7.61 (1 H, dd, H-8, $J_{8,7}$ = 8 Hz, $J_{8,9}$ = 9 Hz), 7.06 (1 H, dd, H-7, $J_{7,8}$ = 8 Hz, $J_{7,9}$ = 1.2 Hz), 4.13 (3 H, s, OCH_3), 3.99 (3 H, s, OCH_3), 2.51 (3 H, d, 3-CH_3, $J_{CH_3,4}$ = 0.8 Hz), 2.42 (3 H, s, 2-CH_3); MS, *m/e* 300 (M^+), 284 $(M - O)^+$; UV (EtOH) λ_{max} (log ϵ) 261 (4.30), 281.8 (4.39), 291.4 (4.26). Anal. Calcd for $C_{16}H_{16}N_2O_4$: C, 63.99; H, 5.37; N, 9.33. Found: C, 63.95; H, 5.40; N, 9.37.

^1H NMR **43** and **44**, 1:1 mixture: δ 8.24 (1 H_{43}, dd, H-9, $J_{9,8}$ = 9.2 Hz, $J_{9,7}$ = 1.1 Hz), 8.23 (1 H_{44}, uq, H-4), 7.95 (1 H_{43}, uq, H-4), 7.86 (1 H_{44}, dd, H-9, $J_{9,8}$ = 8.8 Hz, $J_{9,7}$ = 1.4 Hz), 7.60 (1 H_{43}, 1 H_{44}, 2 dd, H-8), 7.03 (1 H, dd, H-7), 6.95 (1 H, dd, H-7), 4.16–3.98 (6 H_{43}, 6 H_{44}, 4 s, 4 × OCH_3), 2.52 (3 H, d, 3-CH_3, $J_{CH_3,4}$ = 1 Hz), 2.49 (3 H, d, 3-CH_3, $J_{CH_3,4}$ = 1 Hz), 2.43 (3 H_{43}, 3 H_{44}, 2 s, 2 × 2-CH_3).

2-Acetyl-8-methoxy-1,2,3,4-tetrahydronaphthalene (47). To a stirred solution of 2-carboxy-8-methoxy-1,2,3,4-tetrahydronaphthalene (**46a**)[42] (4.12 g, 20 mol) in anhydrous THF (150 mL) at 0 °C was added rapidly methyllithium in ether (57 mL, 1.4 M, 80 mol). After 2 h at 0 °C, freshly distilled chlorotrimethylsilane (50 mL, 0.4 mol) was added and the reaction allowed to warm up to room temperature. 1 N HCl was then added and the two-phase mixture stirred for a further 0.5 h. The mixture was extracted with ether, and the organic phase washed with aqueous $NaHCO_3$ and water, dried, and evaporated. Chromatography of the residue, elution with 20% hexane:80% CH_2Cl_2 gave **47** (3.88 g, 95%) as a colorless oil: IR (neat) 3000–2840 (CH), 1708 (C=O); ^1H NMR δ 7.10 (1 H, t, H-6, $J_{6,5}$ = $J_{6,7}$ = 7.8 Hz), 6.74–6.62 (2 H, m, H-5 and 7), 3.81 (3 H, s, OCH_3), 3.14–1.54 (7 H, m), 2.25 (3 H, s, $COCH_3$); MS, *m/e* 204 (M^+), 189 $(M - CH_3)^+$, 161 $(M - CH_3CO)^+$; UV (EtOH) λ_{max} (log ϵ) 271.5 (3.17), 278.5 (3.20). Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44, H, 7.90. Found: C, 76.26, H, 8.08.

2-(1-Hydroxyethyl)-8-methoxy-1,2,3,4-tetrahydronaphthalene (48a). A solution of ketone **47** (0.20 g, 1 mmol) in EtOH (5 mL) at 0 °C was treated with sodium borohydride (20 mg, 0.5 mmol) and the mixture stirred for 1 h, then allowed to warm up to room temperature over the next 1 h. The solution was poured into saturated NH_4Cl, stirred for 0.5 h, and extracted with CH_2Cl_2. The organic phase was washed with water, dried, and evaporated. Chromatography of the residue, elution with CH_2Cl_2, gave **48a** (0.17 g, 84%) as a mixture of diastereomers which were recrystallized from hexane as white crystals: mp 108–131 °C; IR ($CHCl_3$) 3620 (OH), 3015–2845 (CH), 1585, 1468, 1440; ^1H NMR δ 7.17 (1 H, t, H-6, $J_{6,5}$ = $J_{6,7}$ = 7.8 Hz), 6.74–6.60 (2 H, m, H-5 and 7), 3.81 (3 H, s, OCH_3), 3.74 (1 H, dq, H-1′, $J_{1',2}$ = 12.6 Hz, J_{1',CH_3} = 6.3 Hz), 3.12–2.75 (3 H, m), 2.42–1.20 (4 H, m), 1.52 (1 H, s, OH), 1.30 and 1.28 (1 H, 2 d, 2′-CH_3, $J_{CH_3,1'}$ = 6.3 Hz, indicates presence of diastereomers); MS, *m/e* 206 (M^+), 188 $(M - H_2O)^+$, 173 $(M - H_2O - CH_3)^+$. Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.61; H, 8.82.

2-(1-Acetoxyethyl)-8-methoxy-1,2,3,4-tetrahydronaphthalene (49a). A solution of alcohol **48a** (0.20 g, 1 mmol) in acetic anhydride (1.5 mL, 16 mmol) and triethylamine (2 mL) at 0 °C was treated with 4-(dimethylamino)pyridine (25 mg, 0.2 mmol) and the mixture stirred for 10 min, allowed to warm up to room temperature, and stirred for a further 2.5 h. The solution was then slowly poured into cold 2 N HCl and extracted with ether. The organic phase was combined, washed with more HCl, aqueous $NaHCO_3$, and water, dried, and evaporated. Chromatography of the residue, elution with CH_2Cl_2, gave **49a** (0.20 g, 83%) as a colorless oil: IR (neat) 2990–2845 (CH), 1730 (C=O), 1587, 1250 (CC=O—O); ^1H NMR δ 7.08 (1 H, t, H-6, $J_{6,5}$ = $J_{6,7}$ = 7.8 Hz), 6.74–6.60 (2 H, m, H-5 and 7), 4.93 (1 H, dq, H-1′, $J_{1',2}$ 12.6 Hz, J_{1',CH_3} = 6.3 Hz), 3.81 (3 H, s, OCH_3), 3.08–2.74 (3 H, m), 2.44–1.25 (4 H, m), 2.06 (3 H, 2s, $COCH_3$, indicates presence of diastereomers), 1.30 (3 H, d, 2′-CH_3, $J_{CH_3,1'}$ = 6.3 Hz); MS, *m/e* 248 (M^+), 188 $(M - CH_3CO_2H)^+$; UV (EtOH) λ_{max} (log ϵ) 271 (3.25), 278.5 (3.27). Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.38; H, 7.98.

2-(1-Acetoxyethyl)-5-bromo-8-methoxy-1,2,3,4-tetrahydronaphthalene (49b). Ester **49a** (0.50 g, 2 mmol), NBS (0.37 g, 2.1 mmol), and hydroquinone (5 mg) were dissolved in CH_2Cl_2 (25 mL) and refluxed with stirring for 18 h. The solvent was

removed in vacuo, and the residue dissolved in $CHCl_3$ and filtered. The filtrate was washed with warm water, dried, and evaporated. Chromatography of the residue, elution with $CHCl_3$, gave **49b** (0.60 g, 91%) as a colorless oil, which crystallized on standing. Recrystallization from hexane gave **49b** as white crystals: mp 108–110 °C; IR ($CHCl_3$) 2980–2840 (CH), 1730 (C=O), 1570, 1460, 1240 (CC=O—O); ^1H NMR δ 7.34 (1 H, d, H-6, $J_{7,6}$ = 8.7 Hz), 6.56 (1 H, d, H-7, $J_{6,7}$ = 8.7 Hz), 4.93 (1 H, dq, H-1′, $J_{1',2}$ = 12.6 Hz, J_{1',CH_3} = 6.3 Hz), 3.80 (3 H, s, OCH_3), 3.12–1.28 (7 H, m), 2.07 and 2.06 (3 H, 2 s, $COCH_3$, indicates presence of diastereomers), 1.30 (3 H, d, 2′-CH_3, $J_{CH_3,1'}$ = 6.3 Hz); MS, *m/e* 328 $(M + 2)^+$, 326 (M^+), 268 $(M + 2 - CH_3CO_2H)^+$, 266 $(M - CH_3CO_2H)^+$. Anal. Calcd for $C_{15}H_{19}BrO_3$: C, 55.06; H, 5.85. Found: C, 55.11; H, 5.90.

5-Bromo-2-carboxy-8-methoxy-1,2,3,4-tetrahydronaphthalene (46b). Acid **46a**[42] (2.06 g, 10 mmol), NBS (1.87 g, 10.5 mmol), and hydroquinone (20 mg) were dissolved in CH_2Cl_2 (80 mL) and refluxed with stirring for 18 h. The solvent was removed in vacuo, and the residue dissolved in $CHCl_3$, washed with warm water, and extracted with 10% aqueous K_2CO_3. Acidification of the aqueous extract with 2 N HCl gave a white precipitate that was removed by filtration, washed with water, and dried. Recrystallization from MeOH:water (5:1) gave **46b** (2.62 g, 92%) as white needles: mp 180 °C; IR ($CHCl_3$) 3400–2400 (OH), 3010–2840 (CH), 1710 (C=O), 1575, 1460, 1440; ^1H NMR δ 7.36 (1 H, d, H-6, $J_{6,7}$ = 8.7 Hz), 6.58 (1 H, d, H-7, $J_{7,6}$ = 8.7 Hz), 3.80 (3 H, s, OCH_3), 3.30–1.60 (7 H, m); MS, *m/e* 286 $(M + 2)^+$, 284 (M^+), 240 $(M + 2 - HCO_2H)^+$, 238 $(M - HCO_2H)^+$. Anal. Calcd for $C_{12}H_{13}BrO_3$: C, 50.55; H, 4.60. Found: C, 50.60; H, 4.70.

5-Bromo-2-carboxy-8-methoxy-6,7-dinitro-1,2,3,4-tetrahydronaphthalene (50). A slurry of acid **46b** (2.85 g, 10 mmol) in anhydrous MeCN (175 mL) at room temperature under argon was treated with nitronium tetrafluoroborate (5.31 g, 40 mmol). After 0.5 h a further portion of nitronium tetrafluoroborate (2.66 g, 20 mmol) was added and the stirring continued for 0.5 h. The solution was then poured into ice–water (400 mL), and the oil that separated was left to crystallize. The yellow precipitate was filtered off, washed with water, dried, and recrystallized from aqueous EtOH giving **50** (2.60 g, 69%) as pale yellow crystals: mp 202–207 °C; IR (Nujol) 3300–2300 (OH), 1710 (C=O) 1550; ^1H NMR (CD_3OD) δ 3.95 (3 H, s, OCH_3), 3.16–1.85 (7 H, m); MS, *m/e* 376 $(M + 2)^+$, 374 (M^+), 358 $(M + 2 - H_2O)^+$, 356 $(M - H_2O)^+$. Anal. Calcd for $C_{12}H_{11}BrN_2O_7$: C, 38.42; H, 2.96; N, 7.47. Found: C, 38.20; H, 2.95; N, 7.46.

5-Bromo-8-methoxy-2-(methoxycarbonyl)-6,7-dinitro-1,2,3,4-tetrahydronaphthalene (51). To a stirred solution of acid **50** (3.75 g, 10 mmol) in ethyl acetate (200 mL) at 0 °C was added an ethereal solution of diazomethane (~0.50 g, 12 mmol), prepared from *N*-methyl-*N*-nitrosourea (1.78 g),[49] until a permanent bright yellow color was obtained. Glacial acetic acid (2 mL) was then added and the solution evaporated in vacuo. Recrystallization of the residue from MeOH gave **51** (3.70 g, 95%) as pale yellow crystals: mp 136–138 °C; IR ($CHCl_3$) 3040–2900 (CH), 1740 (C=O), 1553, 1355; ^1H NMR δ 3.94 (3 H, s, 8-OCH_3), 3.76 (3 H, s, CO_2CH_3), 3.14–1.75 (7 H, m); MS, *m/e* 390 $(M + 2)^+$, 388 (M^+), 372 $(M + 2 - H_2O)^+$, 370 $(M - H_2O)^+$. Anal. Calcd for $C_{13}H_{13}BrN_2O_7$: C, 40.12; H, 3.37; N, 7.20. Found: C, 40.20; H, 3.40; N, 7.25.

6,7-Diamino-8-methoxy-2-(methoxycarbonyl)-1,2,3,4-tetrahydronaphthalene (52). Prepared from *o*-dinitro bromo ester **51** (3.89, 10 mmol) by the same method as **25** from **37**. Chromatography of the residue, elution with EtOH:CH_2Cl_2 (5:95), gave **52** (2.35 g, 94%) as a pale pink oil that crystallized on standing. No further purification was carried out on this material, which decomposed rapidly on exposure to atmospheric conditions and was thus used immediately in the next step of the sequence: ^1H NMR (CD_3OD) δ 6.24 (1 H, s, H-5), 3.71 (6 H, bs, OCH_3 and CO_2CH_3), 3.13–1.50 (7 H, m).

4,11-Dimethoxy-9-(methoxycarbonyl)-7,8,9,10-tetrahydrobenzo[*b*]phenazine (53) and 1,11-Dimethoxy-9-(methoxycarbonyl)-7,8,9,10-tetrahydrobenzo[*n*]phenazine (54). Prepared from 3-methoxy-1,2-benzoquinone (**24**)[1] (1.38 g, 10 mmol) and *o*-diamine **52** (2.50 g, 10 mmol) by the same method as **14** and **26**. Chromatography of the orange residue, elution with ethyl acetate:$CHCl_3$ (15:85), gave **53** (0.40 g) (R_f 0.38), **54** (0.35 g) (R_f 0.31), and a mixture of the two phenazines (0.80 g). The mixture was then rechromatographed on Woelm alumina, elution with toluene, giving **54** (0.38 g) and **53** (0.32 g). (The order of elution of the phenazines on alumina compared to silica gel was again reversed as in the case of **14** and **26**.) **53** (0.72 g, 20%) was recrystallized from toluene as bright yellow needles: mp 204–205 °C; IR ($CHCl_3$) 3010–2840 (CH), 1735 (C=O), 1630, 1518, 1480, 1155 (COC), 1120 (COC); ^1H NMR δ 7.94 (1 H, s, H-6), 7.89 (1 H, dd, H-1, $J_{1,2}$ = 9 Hz, $J_{1,3}$ = 1.4 Hz), 7.68 (1 H, dd, H-2, $J_{2,1}$ = 9 Hz, $J_{2,3}$ = 7.4 Hz), 7.03 (1 H, dd, H-3, $J_{3,2}$ = 7.4 Hz, $J_{3,1}$ = 1.4 Hz), 4.25 (3 H, s, OCH_3), 4.16 (3 H, s, OCH_3), 3.78 (3 H, s, CO_2CH_3), 3.70–1.80 (7 H, m); MS, *m/e* 352 (M^+) 327 $(M - CH_3)^+$; UV (EtOH) λ_{max} (log ϵ) 270.5 (4.96), 376 (3.97). Anal. Calcd for $C_{20}H_{20}N_2O_4$: C, 68.17; H, 5.72; N, 7.95. Found: C, 68.13; H, 5.88; N, 7.78.

54 (0.73 g, 21%) was also recrystallized from toluene as bright yellow needles: mp 186 °C; IR ($CHCl_3$) 3010–2840 (CH), 1735 (C=O), 1630, 1605, 1558, 1480, 1150 (COC), 1118 (COC); ^1H NMR δ 7.80–7.58 (3 H, m, H-3, 4 and 6), 7.04–6.95 (1 H, m, H-2), 4.33 (3 H, s, OCH_3), 4.13 (3 H, s, OCH_3), 3.77 (3 H, s, CO_2CH_3), 3.68–1.75 (7 H, m); MS, *m/e* 352 (M^+), 337 $(M - CH_3)^+$; UV (EtOH) λ_{max} (log ϵ) 271.4 (4.96), 374.5 (3.97). Anal. Calcd for $C_{20}H_{20}N_2O_4$: C, 68.17; H, 5.72; N, 7.95. Found: C, 67.95; H, 5.81; N, 7.78.

1,11-Dimethoxy-9-(methoxycarbonyl)-7,8,9,10-tetrahydrobenzo[*b*]phenazine 5-Oxide (4). Prepared from **54** (0.18 g, 0.5 mmol) by the same method as **40** and worked up after 0.75 h. Chromatography of the residue, elution with ethyl acetate:$CHCl_3$ (5:95), gave **4** (0.12 g, 64%) which was recrystallized from toluene:hexane (3:1) as yellow crystals: mp 221–222 °C; IR ($CHCl_3$) 3010–2850 (CH), 1735 (C=O), 1620, 1480, 1350 (NO), 1072 (COC); ^1H NMR δ 8.20 (1 H, s, H-6), 8.20 (1 H, dd, H-4, $J_{4,3}$ = 9 Hz, $J_{4,2}$ = 1.1 Hz), 7.62 (1 H, dd, H-3, $J_{3,2}$ = 7.7 Hz, $J_{3,4}$ = 9 Hz), 7.02 (1 H, dd, H-2, $J_{2,3}$ = 7.7 Hz, $J_{2,4}$ = 1.1 Hz), 4.32 (3 H, s, OCH_3), 4.12 (3 H, s, OCH_3), 3.76 (3 H, s, CO_2CH_3), 3.53–1.75 (7 H, m); MS, *m/e* 368 (M^+), 353 $(M - CH_3)^+$; UV (EtOH) λ_{max} (log ϵ) 281 (5.11), 392 (3.90), 460 (3.76). Anal. Calcd for $C_{20}H_{20}N_2O_5$: C, 65.21; H, 5.47; N, 7.61. Found: C, 65.27; H, 5.52; N, 7.51.

4,11-Dimethoxy-9-(methoxycarbonyl)-7,8,9,10-tetrahydrobenzo[*b*]phenazine 5-Oxide (55) and 12-Oxide (56). Prepared from **53** (0.35 g, 1 mmol) by the same method as **43** and **44** and worked up after 4 h. Chromatography on Woelm alumina, elution with CH_2Cl_2, gave recovered starting material **53** (0.17 g, 49%) and a 2:1 mixture of the two possible yellow mono *N*-oxides **55** and **56** (0.16 g, 85%, based on recovered starting material) which were used in the next step without further purification. ^1H NMR, **55** and **56**, 2:1 mixture: δ 8.21 (1 H_{56}, dd, H-1, $J_{1,2}$ = 8.7, $J_{1,3}$ = 1.2 Hz), 8.18 (1 H_{55}, s, H-6), 7.90 (1 H_{56}, s, H-6), 7.82 (1 H_{55}, dd, H-1, $J_{1,2}$ = 8.7, $J_{1,3}$ = 1.4 Hz), 7.58 (1 H_{55}, 1 H_{56}, 2 dd, H-2, $J_{2,1}$ = 8.7 Hz, $J_{2,3}$ = 7.7 Hz), 7.03 (1 H_{56}, dd, H-3, $J_{3,2}$ = 7.7 Hz, $J_{3,1}$ = 1.2 Hz), 6.94 (1 H_{55}, dd, H-3, $J_{3,2}$ = 7.7 Hz, $J_{3,1}$ = 1.4 Hz), 4.22–4.02 (6 H_{55}, 6 H_{56}, 4 s, 4 × OCH_3), 3.77 (3 H_{55}, 3 H_{56}, 2 s, 2 × CO_2CH_3), 3.60–1.80 (7 H_{55}, 7 H_{56}, m).

4,11-Dimethoxy-9-(methoxycarbonyl)-7,8,9,10-tetrahydrobenzo[*b*]phenazine 5,12-Dioxide (3). A mixture of the two benzo[*b*]phenazine *N*-oxides **55** and **56** (0.10 g, 0.27 mmol) and mCPBA (0.30 g, 1.4 mmol) dissolved in CH_2Cl_2 (5 mL) was stirred at room temperature for 12 h. The crude reaction mixture was chromatographed on Woelm alumina initial elution with CH_2Cl_2 to yield recovered starting material **55** and **56** (50 mg 50%) and then elution with chloroform yielded the red-orange 5,12-dioxide **3** (15 mg, 29%, based on recovered starting material): IR ($CHCl_3$) 3010–2850 (CH), 1735 (C=O), 1620, 1515, 1480, 1350 (NO), 1105 (COC), 1065 (COC); ^1H NMR 8.31 (1 H, dd, H-1, $J_{1,2}$ = 9 Hz, $J_{1,3}$ = 1.1 Hz), 8.31 (1 H, s, H-6), 7.60 (1 H, dd, H-2, $J_{2,1}$ = 9 Hz, $J_{2,3}$ = 8 Hz), 7.05 (1 H, dd, H-3, $J_{3,2}$ = 8 Hz, $J_{3,1}$ = 1.1 Hz), 4.08 (3 H, s, OCH_3), 4.04 (3 H, s, OCH_3), 3.76 (3 H, s, CO_2CH_3), 3.60–1.75 (7 H, m); MS, *m/e* 384 (M^+), 368 $(M - O)^+$; high-resolution MS, *m/e* calcd for $C_{20}H_{20}N_2O_6$ 384.1322, found 384.1321.

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Institute, DHHS. We thank John G. Johansson for resynthesis of intermediate **46a**.

Registry No. **3**, 93349-61-2; **4**, 93349-62-3; **14**, 93349-63-4; **15**, 93349-64-5; **18**, 91-23-6; **19**, 90-04-0; **20**, 67291-62-7; **21**, 13398-79-3; **22**, 2876-17-7; **23**, 93349-65-6; **24**, 60855-15-4; **25**, 93349-66-7; **26**, 93349-67-8; **27**, 93349-68-9; **28**, 93383-20-1; **29**, 93349-69-0; **30**, 93349-70-3; **31**, 93349-71-4; **32**, 93349-72-5; **33**, 74783-59-8; **34**, 93349-73-6; **35**, 2944-49-2; **36a**, 50638-48-7; **37**, 93349-74-7; **40**, 93349-76-9; **43**, 93349-77-0; **44**, 93349-78-1; **45**, 93349-79-2; **46a**, 32178-63-5; **46b**, 93349-90-7; **47**, 93349-80-5; **48a**, 93349-81-6; **49a**, 93349-82-7; **49b**, 93349-75-8; **50**, 93349-83-8; **51**, 93349-84-9; **52**, 93349-85-0; **53**, 93349-86-1; **54**, 93349-87-2; **55**, 93349-88-3; **56**, 93349-89-4.

Solution and Flash Vacuum Pyrolyses of β-(3,5-Disubstituted-phenyl)ethanesulfonyl Azides. Sultam, Pyrindine, and Azepine Formation

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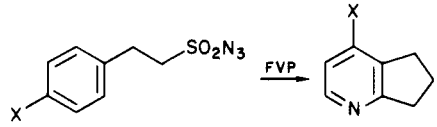
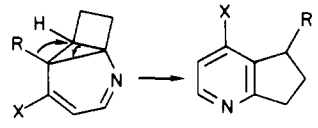
The solution and flash vacuum pyrolyses of β-(3,5-disubstituted-phenyl)ethanesulfonyl azides are reported. When R = Me, FVP results suggest that the substituents stabilize the intermediate leading to the 3,4-dihydro-2,1-benzothiazepine 2,2-dioxide (**6a**). A new product, 2-cyclopropyl-3,5-dimethylpyridine (**10**) is observed, and a modification is proposed in the mechanism proposed earlier[3] to account for the FVP of β-arylethanesulfonyl azides. No dihydropyrindine, which would have required a methyl migration, is observed. When R = Cl, Cl migration does occur and a mixture of 5*H*- and 7*H*-1-pyrindines is obtained, together with other products. When R = OCH_3, some methoxy migration occurs on FVP to give 6,7-dihydro-3,5-dimethoxy-5*H*-1-pyrindine. Monodemethoxylation to give 6-methoxy-3,4-dihydro-2,1-benzothiazine 2,2-dioxide (**14**) also takes place and a possible mechanism is proposed. When R = CF_3 the main product on FVP at 300 °C is the fused azepine **19** in respectable yield. This is the first example of the isolation of an *N*-sulfonylazepine from the intramolecular reaction of a sulfonylnitrene and from a FVP.

The flash vacuum pyrolysis (FVP) of β-phenylethanesulfonyl azides (**1**) has been studied.[3] One of the most interesting products, formed in good yields at the higher column temperatures, is the dihydropyrindine ring system (**2**). A mechanism was proposed to explain this trans-



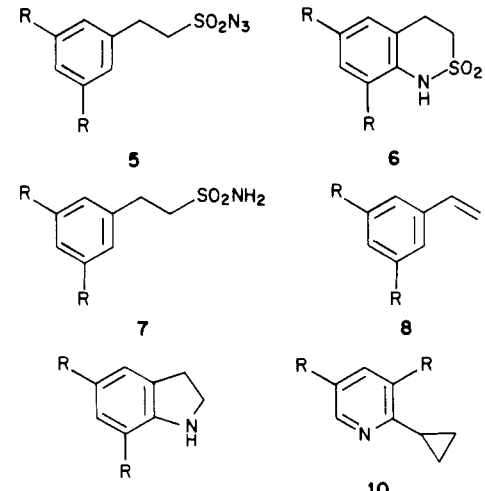
1 **2**

formation which, in its final stage, involved a 1,2-hydrogen shift accompanied by ring opening: **3** → **4** (R = H). The obvious question we asked ourselves was the following: assuming such a mechanism to be correct, what would happen when R ≠ H? It is this question we now address by studying the FVP of a series of β-(3,5-disubstituted-phenyl)ethanesulfonyl azides (R = Me, Cl, OMe, CF_3). The results obtained suggest a slight modification in the mechanism proposed[3] for the transformation **1** → **2**.



3 **4**

The sulfonyl azides **5** (R = Me, Cl, OMe, CF_3) were synthesized by standard methods (see Experimental Section).



a, R = Me; **b**, R = Cl; **c**, R = OMe; **d**, R = CF_3

Thermolysis of **5a** in Freon 113 at 135 °C gave the expected sultam 6,8-dimethyl-3,4-dihydro-2,1-benzothiazepine 2,2-dioxide (**6a**), together with the hydrogen abstraction product, β-(3,5-dimethylphenyl)ethanesulfonamide (**7a**) (7%). FVP of **5a** at 400 °C gave **6a** (46–61.5%), 3,5-dimethylstyrene (**8a**) (3.8%), and 5,7-dimethylindoline (**9a**) (trace). On the other hand FVP at 650 °C led to a decreased yield (20.5%) of **6a**, a much larger amount (14.8%) of **9a**, and a novel product for such reactions,

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(2) Work done at the University of Alabama.
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