Tetrahedron Vol. 33, pp. 2109 to 2113 Pergamon Press 1977 Printed in Great Britain

DIAZAPOLYCYCLIC COMPOUNDS—XIII

REACTIONS OF DIAZAQUINONE ADDUCTS WITH *N*-BROMOSUCCINIMIDE

F. GÓMEZ CONTRERAS, M. LORA-TAMAYO* and P. NAVARRO
Centro Nacional de Química Orgánica del C.S.I.C. Juan de la Cierva, 3. Madrid, Spain

(*Received in UK 6 January 1977; Accepted for publication 10 February 1977*)

Abstract—The action of *N*-bromosuccinimide on adducts obtained by Diels-Alder reaction of benzo(g)phthalazin-1,4-dione with substituted 1,3-butadienes is reported. Different addition or substitution products are formed depending on the solvent and reaction conditions. The stereochemistry of the most interesting among these compounds has been studied, and a possible mechanism for their formation is proposed.

In recent years we have investigated the possibility of synthesizing diazatetracyclic compounds referable to tetracyclines of known activity. In the course of our work, diazatetracycles with the nitrogen bridge situated either between rings B and C, or C and D, have been prepared,[1] the latter being obtained by Diels–Alder reaction of benzo(g)phthalazin - 1,4 - dione[2] with dienes such as 1,3-butadiene, isoprene and 2,3-dimethylbutadiene to give adducts **1a-c** (Scheme 1), two of which (**1a** and **1b**) have been described previously.[1]

Now, we are interested in the introduction of reactive atoms or groups into ring D of these adducts. The present paper deals with the results obtained by treatment of **1a-c** with *N*-bromosuccinimide (NBS). This reaction has been shown to be very sensitive to the experimental conditions employed, different adduct derivatives resulting depending on the media in which the reaction is carried out. In an aqueous medium or a non-polar solvent, like benzene, only addition to the double bond is observed. However, in a more polar solvent, like the chloroform-ethanol mixture, we assume that the reaction involves an allylic substitution with rearrangement of the double bond in a first step, followed by addition, as can be deduced from the stereochemistry of the compounds obtained.

Results observed in the diverse reaction conditions employed are reported below.

RESULTS AND DISCUSSION

(a) *Acid aqueous medium.* Treatment of the Diels–Alder adducts **1a-c** with *N*-bromosuccinimide in an aqueous suspension containing some drops of sulphuric acid as a catalyst affords, respectively, the bromhydrins **2a-d**, as would be expected (Scheme 2).

In the reaction of compound **1b**, with a double bond unsymmetrically substituted, the two possible isomers (**2b** and **2c**) are obtained, in a ratio of approximately 3/2.

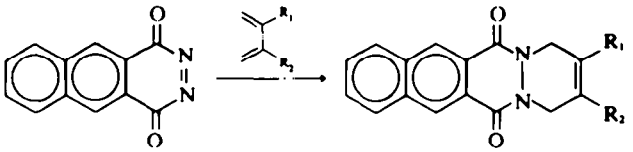
Both isomers are easily differentiated by their ^{1}H NMR spectra, measured in dimethylsulphoxide solution. The methyl group of **2b** is deshielded (δ = 1.92 ppm) with respect to the same group in **2c** (δ = 1.52 ppm), because of the great inductive effect of the neighbouring bromine atom. Moreover, the –OH signal of the **2c** isomer is a singlet (δ = 5.85 ppm), while in **2b** the hydroxy proton gives a doublet (δ = 6.20 ppm) with a coupling constant of $J_{CH\text{-}OH}$ = 4 Hz. The DMSO–OH bonding allows observation of the spin–spin coupling between the –OH and the proton of the methine group adjacent to oxygen, this proton being absent in the **2c** isomer.

(b) *Benzene solution.* The reaction between adducts **1a-c** and *N*-bromosuccinimide in benzene containing catalytical amounts of benzoyl peroxide gives, after 2 h reflux, the brominated derivatives **3a-c** (Scheme 2).

Since conditions employed are strongly favorable to a free radical mechanism, allylic substitution should take place. Instead, only addition of two bromine atoms to the double bond is observed. It seems that the withdrawing carbonyl groups destabilize the allylic free radical, favoring addition to the double bond. This preference for addition against allylic substitution when withdrawing groups are present in the reacting compound is well known, a characteristic example being that of 3-sulpholene, in which the sulphone group effect causes only addition products to be formed in its reactions with NBS.[3]

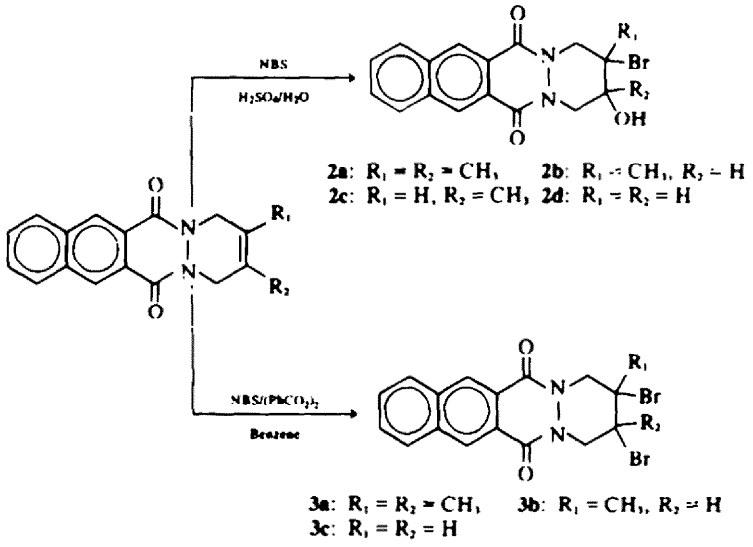
(c) *Chloroform-ethanol solution.* Treatment of the butadiene adduct **1c** with NBS in chloroform containing 1% ethanol and a catalytic amount of benzoyl peroxide affords, after a 2 days reflux, a new compound in a 41% yield.

Unexpectedly, this compound has been shown to have the structure **4** (Scheme 3) in which, for the first time, a substituent is introduced at a carbon atom next to the nitrogen bridge.

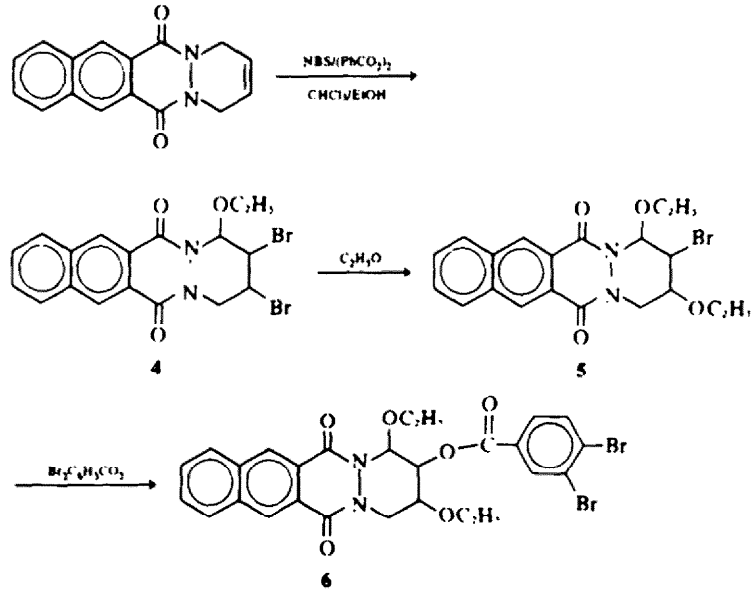


1a: $R_1 = R_2 = CH_3$ **1b**: $R_1 = CH_3$, $R_2 = H$
1c: $R_1 = R_2 = H$

Scheme 1.



Scheme 2.



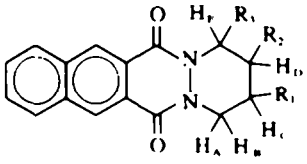
Scheme 3.

The study of the double resonance ^1H NMR spectrum of 4 (Table 1) has shown that the three new substituents are consecutive in the piperidazine ring. The methylenic protons H_A and H_B form the AB signals of an ABX system, resulting in two quartets repectively centred at 5.20 and 4.32 ppm. Irradiation at H_A simplifies the multiplet assigned at H_C to a doublet (δ = 4.50 ppm). The high chemical shift value found for a doublet situated at 6.58 ppm can only be explained by its assignment to an equatorial H_E, vicinal to the nitrogen atom and deshielded both by the electronegative substituent at C-1 and the anisotropic effect of the coplanar carbonyl group, which has been shown to produce a strong deshielding over the protons at C-1 in similar diazaquinone derivatives prepared previously.[4] This effect of the carbonyl group over the neighbouring equatorial proton is also observed when comparing the different chemical shifts of H_A and H_B. Irradiation at the signal assigned to H_E simplifies the multiplet corresponding to H_D to a doublet (α = 4.75 ppm).

Analysis of the mass spectrum of 4 led us to assume that the ethoxy group was located at C-1. All the fragmentation series of significant abundance involved expulsion of the $CHOC_2H_5$ fragment, preceded or followed by loss of bromine or hydrogen bromide, as can be seen in Scheme 4. This is consistent with the position assigned to the ethoxy group, since the carbon lost by ring contraction must be close to nitrogen, according to the behaviour showed by similar heterocycles[5] and on the basis of the easy cleavage of the C–N bond. Mechanisms for the formation of fragments shown in Scheme 4 from the molecular ion of 4 have been widely studied by us.[6]

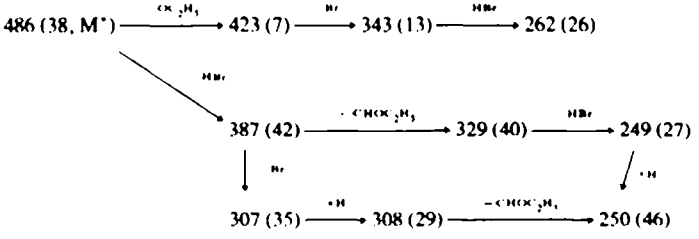
The stereochemistry of the new substituents in 4 was established from the vicinal coupling constant values (Table 1). In the ABX system formed by the methylenic protons H_A and H_B at C-4 and the methinic H_C at C-3, the coupling constant between the methylenic axial H_B and H_C is 11 Hz. This result is evidence for an axial orientation of H_C. Coupling between axial H_C and H_D is 3 Hz,

Table 1. ^{1}H NMR data of compounds obtained in chloroform-ethanol solution



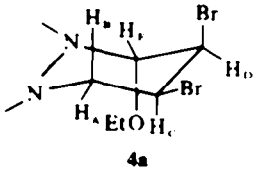
4: $R_1 = R_2 = Br$, $R_3 = OEt$
5: $R_1 = OEt$, $R_2 = Br$, $R_3 = OEt$
6: $R_1 = OEt$, $R_2 = BzOBr_2$, $R_3 = OEt$

Compound	4	5	6
Chemical shifts (δ) ($CDCl_3$)	$H_A = 5.20$ (c) $H_B = 4.32$ (c) $H_C = 4.50$ (m) $H_D = 4.75$ (m) $H_E = 6.58$ (d)	$H_A = 5.28$ (c) $H_B = 4.50$ (c) $H_C = 4.15$ (m) $H_D = 3.2$–3.9 $H_E = 6.58$ (d)	$H_A = 5.26$ (c) H_B, H_C, $H_D = 3.6$–5.0 $H_E = 6.38$ (d)
Coupling constants (Hz)	$J_{H_AH_B} = 12$ $J_{H_AH_C} = 4$ $J_{H_BH_C} = 11$ $J_{H_CH_D} = 3$ $J_{H_DH_E} = 2$	$J_{H_AH_B} = 18$ $J_{H_AH_C} = 2$ $J_{H_BH_C} = 1.5$ $J_{H_CH_D} = 6$ $J_{H_DH_E} = 3.5$	$J_{H_AH_B} = 14$ $J_{H_AH_C} = 5$ $J_{H_DH_E} = 3$

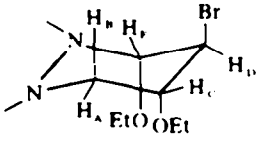


Scheme 4.

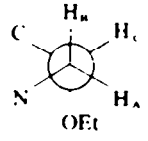
clearly corresponding to an equatorial position for H_D. The small value of $J_{H_DH_E}$ (2 Hz) is in good agreement with the equatorial character assigned to H_E on the basis of the strong deshielding effect of the carbonyl group over this proton. Therefore, we propose for the piperidazine ring of **4** a conformation in which the ethoxyl group and adjacent bromine are in an axial–axial relationship, whereas the second bromine is equatorially oriented (form **4a**).



4a



5a



View along C3–C4 bond of **5a**

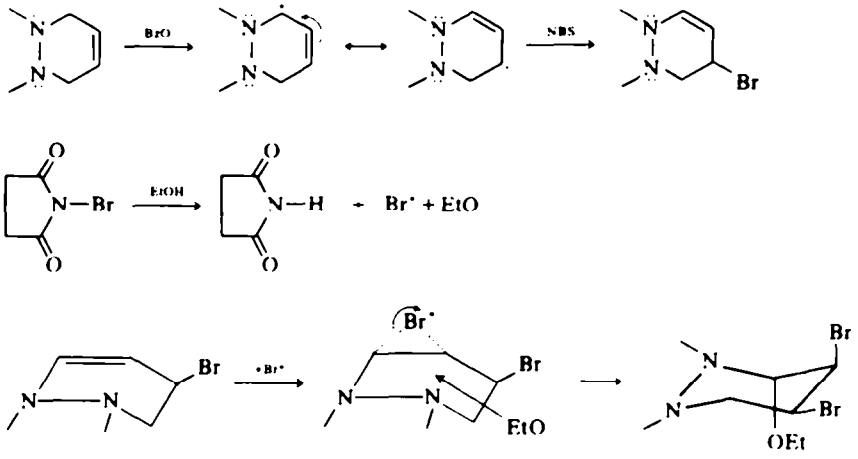
The stereochemistry found for these three substituents led us to suggest the following mechanism for the formation of **4**. In a first step an allylic bromination takes place, with rearrangement of the allylic radical intermediate to a more stable one, owing to conjugation established with the lone pair of the adjacent nitrogen atom; after that, trans-diaxial addition of bromine and ethoxyl to the new double bond formed occurs. This mechanism is shown in Scheme 5. Similar rearrangements are frequently found in substitution reactions of *N*-bromosuccinimide.[7]

Repetition of the reaction for a longer period (7 days reflux) affords, after a laborious chromatographic separation, three different compounds. One of them, obtained as the major product in 32% yield, is identified as **4**. Structures **5** and **6** have been assigned to the other two compounds, obtained in 20 and 5% yields respectively (Scheme 3). It seems that both of these are formed from **4** by successive substitutions of the two bromine atoms by a second ethoxyl group and dibromobenzoate produced in the bromination with *N*-bromosuccinimide of the benzoyl peroxide employed as catalyst. The bromination of an aromatic ring with NBS is not unusual.[8]

The consecutive location of the substituents in the piperidazine ring of **5** and **6** has been established in the same way as previously described for **4**. NMR spectra of both compounds present a doublet at very low field (Table 1) corresponding to the isolated proton at C-1, and the two quadruplets of the ABX system referable to the methylenic protons.

Study of the spectrum of **5** confirms that the ethoxy group and bromine atom at C-1 and C-2 have the same *trans*-diaxial orientation shown in **4**. However, the new ethoxy at C-3 has an axial situation (form **5a**) in opposition with that equatorial of the bromine atom in **4**. Comparison of the coupling constants between H_C and the axial methylenic H_B in both compounds (11 Hz and 1.5 Hz) establishes the equatorial orientation of H_C in **5**.

On the other hand, axial-equatorial coupling between



Scheme 5.

H_B and H_C is lower than the equatorial-equatorial between H_A and H_C, contrary to what would be expected from the Karplus relationship. However, this result is completely reasonable: H_B and H_C are both *trans*-coplanar with electronegative substituents (H_B/OEt, H_C/N), while H_A is not so oriented (see Fig.) and this fact is held responsible for the lower values found in $J_{H_BH_C}$. The influence of an electronegative substituent upon J vic is greatest when it is *trans*-coplanar to a coupling proton, according to studies performed by Booth *et al.*[9] Other apparently anomalous differences between coupling constants observed in **4** and **5** (for example, values of $J_{H_CH_D}$ in both compounds) are easily explained on the same basis.

The different orientation of substituents at C-3 in both **4** and **5** is consistent with the formation of **5** by S_N1 reaction of the bromine atom in **4**, with configurational inversion at C-3. Such a phenomenon would be favoured by the small stability of the carbonium ion formed as intermediate.

Stereochemistry at the piperidazine ring of compound **6** has not yet been resolved, owing to the great complexity of the NMR spectrum obtained in this case. Location of the two bromine atoms in the benzoate ring has been made possible by calculating the theoretical chemical shifts of the aromatic protons, and comparing them with the experimental values obtained.

Finally, we note that all the reactions between Diels–Alder adducts and *N*-bromosuccinimide described in this work have been shown to be stereospecific, only one stereoisomer being obtained in each case. Stereochemistry of the piperidazine ring in compounds **2** and **3** will be discussed in a further paper.

EXPERIMENTAL

M.ps are uncorrected, and were determined in capillary tubes. IR spectra were recorded on a Perkin–Elmer 257 spectrophotometer. ^{1}H NMR spectra were obtained with Perkin–Elmer R-12 and Varian XL-100 spectrophotometers, using TMS as internal standard. Chemical shifts are given in ppm (δ scale). Direct inlet MS were determined on a Varian MAT spectrometer. Thin layer chromatography plates were prepared with silica gel G (Merck). The term "solvent was removed" means by rotary evaporation, unless otherwise stated.

Adducts **1a** and **1b** were obtained by methods previously described.[1] The starting hydrazide has been prepared according to Drew and Garwood.[10]

4a,12a - Diaza - 1,4,4a,5,12,12a - hexahydronaphthacen - 5,12 - dione **1c**. To a cooled (10°) methylene chloride suspension of the cyclic hydrazide of 2,3 - naphthalenedicarboxilic acid (2.1 g or 10 mmole in 150 ml), 2 ml of glacial acetic acid were added whilst stirring, and a vivacious stream of pure 1,3-butadiene was passed through until the suspension was saturated. After that, 4.5 g (10 mmole) of lead tetraacetate were added over a period of 45 min, and the reaction mixture stirred at 0° for 2 h. The white precipitate formed was filtered off (lead acetate), and the filtrate washed successively with aqueous 5% sodium bicarbonate and water, and dried over magnesium sulphate. Solvent was removed and crude **1c** recrystallised from ethanol to give the pure compound as yellow needles—(1.5 g, 56% yield), m.p. 236–7°. By stirring for 24 h at room temperature, the yield of **1c** rises up to 72%. IR (KBr) ν_{max} 765, 920, 1130, 1220, 1260, 1360, 1385, 1460, 1625 (C=C), 1650 (C=O), cm^{-1}; NMR (CCl_3D) δ 4.65 (s, 4, CH_2) 6.05 (s, 2, CH=) 7.70 (m, 2, aromat. ring A) 8.05 (m, 2, aromat. ring A) 8.80 (s, 2, aromat. ring B) ppm. (Found: C, 72.78; H, 4.79; N, 10.83. $C_{16}H_{12}N_2O_2$ requires: c, 72.62; H, 4.54; N, 10.66%).

2 - Bromo - 3 - hydroxy - 2,3 - dimethyl - 4a,12a - diaza - 1,2,3,4,4a,5,12,12a - octahydronaphthacen - 5,12 - dione **2a**. To an aqueous suspension of **1a** (0.5 g or 2 mmole in 20 ml), 0.45 g (2.4 mmole) of *N*-bromosuccinimide and 5 drops of concentrated sulphuric acid were added. The mixture was stirred for 4 h at 50–60°, and 48 h more at room temp. Filtration of the suspension afforded an orange precipitate which was purified by thin layer chromatography, developed in 10:1 mixture of benzene and ethanol. After recrystallisation from water, 0.17 g (28%) of **2a** were obtained. M.p. 218°. IR (KBr) ν_{max} 765, 915, 1065 (C–O), 1280, 1360, 1385, 1460, 1625 (C=C), 1645 (C=O), 3030, 3400 (–OH) cm^{-1}; NMR (DMSO-d_6) δ 1.48 (s, 3, HO–C–CH_3) 1.88 (s, 3, Br–C–CH_3) 3.85 (d, 1, CH–C–OH axial) 3.95 (d, 1, CH–C–Br axial) 3.60–4.40 (broad m, 1, OH) 4.62 (d, 1, CH–C–OH equatorial) 4.85 (d, 1, CH–C–Br equatorial) 7.83 (m, 2, aromat. ring A) 8.35 (m, 2, aromat. ring A) 8.88 (s, 2, aromat. ring B) ppm. (Found: C, 55.66; H, 4.51; N, 7.30; Br, 20.40. $C_{18}H_{17}N_2O_3Br$ requires: C, 55.53; H, 4.37; N, 7.19; Br, 20.56%).

2 - Bromo - 2 - methyl - 3 - hydroxy - 4a,12a - diaza - 1,2,3,4,4a,5,12,12a - octahydronaphthacen - 5,12 - dione **2b**. This compound was prepared as described above for **2a** from 0.8 g (2.2 mmole) of **1b** and 0.5 g (2.6 mmole) of *N*-bromosuccinimide, to give a solid which by TLC developed in 50:1 mixture of benzene and ethanol was shown to be a mixture of **2b** and **2c** in a 3/2 ratio. Yield of **2b** was 24%. M.p. 167–9°. IR (KBr) ν_{max} 760, 915, 1035 (C–O), 1280, 1360, 1385, 1460, 1625 (C=C), 1645 (C=O), 3400 (–OH) cm^{-1}; NMR (DMSO-d_6) δ 1.90 (s, 3, CH_3) 3.80–4.80 (m, 5, protons ring D) 6.20 (d, 1, OH) 7.82 (m, 2, aromat. ring A) 8.30 (m, 2, aromat. ring A) 8.82 (s, 2, aromat. ring B) ppm. (Found: C, 54.30; H, 4.16; N, 7.71; Br, 20.98. $C_{17}H_{15}N_2O_3Br$ requires: C, 54.40; H, 4.00; N, 7.47; Br, 21.32%).

2 - Hydroxy - 2 - methyl - 3 - bromo - 4a,12a - diaza - 1,2,3,4,4a,5,12,12a - octahydronaphthacen - 5,12 - dione **2c**. This compound was obtained in the same reaction as **2b**, from the thin

layer chromatography described above. Yield at **2c** 16%, IR (KBr) ν_{max} 760, 1065 (C–O), 1280, 1360, 1385, 1460, 1625 (C=C), 1645 (C=O), 3100–3650 (associated OH) cm $^{-1}$; NMR (DMSO-d_6) δ 1.50 (s, 3, CH_3) 3.80–4.80 (m, 5, ring D) 5.85 (s, 1, OH) 7.82 (m, 2, aromat. ring A) 8.30 (m, 2, aromat. ring A) 8.82 (s, 2, aromat. ring B).

2 - *Bromo* - 3 - *hydroxy* - 4*a*,12*a* - *diaza* - 1,2,3,4,4*a*,5,12,12*a* - *octahydronaphthacen* - 5,12 - *dione* **2d**. This compound was prepared as described for **2a**, from 0.4 g (1.1 mmole) of **1c** and 0.3 g (1.6 mmole) of NBS, to give a creamy solid which by preparative TLC developed in 10:1 mixture of benzene and ethanol afforded 0.5 g of a white solid, which was recrystallised from water and identified as the title compound. Yield was 91%, m.p. 227° IR (KBr) ν_{max} 725, 765, 920, 1040 (C–O), 1310, 1465, 1625 (C=C), 1660 (C=O), 3060, 3400 (OH) cm $^{-1}$; NMR (DMSO-d_6) δ 4.05 (d, 1, CH–C–OH axial) 4.05 (m, 1, CH–OH) 4.35 (m, 1, OH) 4.38 (m, 1, CH–Br) 4.42 (d, 1, CH–C–OH equatorial) 4.55 (d, 1, CH–C–Br equatorial) 7.80 (m, 2, aromat. ring A) 8.28 (m, 2, aromat. ring A) 8.76 (s, 2, aromat. ring B) ppm. (Found: C, 53.47; H, 3.82; N, 7.73; Br, 21.86. $C_{16}H_{13}N_2O_3Br$ requires: C, 53.18; H, 3.60; N, 7.75; Br, 22.16%).

2,3 - *Dibromo* - 2,3 - *dimethyl* - 4*a*,12*a* - *diaza* - 1,2,3,4,4*a*,5,12,12*a* - *octahydronaphthacen*- 5,12 - *dione* **3a**. To a solution of **1a** (0.7 g, 2.4 mmole) in 60 ml of "dry" benzene, 0.9 g (5.0 mmole) of *N*-bromosuccinimide were added. The solution was refluxed for 2 h. After cooling at room temp., a brown solid precipitated. The mixture was filtered off and the filtrate washed with water and dried over magnesium sulphate. Solvent was removed, and the residual red-yellow oil treated with several drops of acetone, to give a yellow solid which recrystallised from ethyl acetate. 0.5 g (46% yield) of **3a** were obtained, m.p. 177°. IR (KBr) ν_{max} 760, 915, 1215, 1275, 1360, 1385, 1630 (C=C), 1665 (C=O), 3050 cm $^{-1}$; NMR (CF_3–COOH) δ 2.22 (s, 6, CH_3) 4.33 (d, 2, CH axial) 5.38 (d, 2, CH equatorial) 7.88 (m, 2, aromat. ring A) 8.12 (M, 2, aromat. ring A) 8.85 (s, 2, aromat. ring B) ppm. (Found: C, 47.87; H, 3.71; N, 6.21; Br, 35.68. $C_{18}H_{16}N_2O_2Br_2$ requires: C, 47.79; H, 3.54; N, 6.19; Br, 35.40%).

2,3 - *Dibromo* - 2 - *methyl* - 4*a*,12*a* - *diaza* - 1,2,3,4,4*a*,5,12,12*a* - *octahydronaphthacen* - 5,12 - *dione* **3b**. This compound was prepared as described for **3a**, from 0.5 g (1.8 mmole) of **1b** and 0.6 g (3.4 mmole) of *N*-bromosuccinimide, to give a yellow solid. Recrystallization from ethanol afforded 0.5 g (62% yield) of pure **3b**, m.p. 189–90°. IR (KBr) ν_{max} 770, 920, 1275, 1365, 1390, 1405, 1635 (C=C), 1670 (C=O) cm $^{-1}$; NMR (CF_3–COOH) δ 2.20 (s, 3, CH_3) 4.22 (d, 1, CH–C–CH_3 axial) 4.78 (c, 1, CH–C–Br axial) 4.80 (m, 1, CH–Br) 5.22 (c, 1, CH–C–CH_3 equatorial) 5.32 (c, 1, CH–C–Br equatorial) 7.85 (m, 2, aromat. ring A) 8.16 (m, 2, aromat. ring A) 8.90 (s, 2, aromat. ring B) ppm. (Found: 46.21; H, 3.14; N, 5.98; Br, 36.82. $C_{17}H_{14}N_2O_2Br_2$ requires: C, 46.57; H, 3.20; N, 6.19; Br, 36.53%).

2,3 - *Dibromo* - 4*a*,12*a* - *diaza* - 1,2,3,4,4*a*,5,12,12*a* - *octahydronaphthacen* - 5,12 - *dione* **3c**. This compound was prepared as described for **3a**, from 0.5 g (2.0 mmole) of **1c** and 0.8 g (4.5 mmole) of *N* - bromosuccinimide, to give a red oil. Preparative TLC developed in the mixture petroleum ether : ether : chloroform in 5:15:1 proportions afforded 0.32 g of a white solid, identified as the title compound. Yield was 40%, m.p. 227–8°. IR (KBr) ν_{max} 715, 765, 895, 935, 1200, 1285, 1345, 1465, 1625 (C=C), 1655 (C=O), 3040 cm $^{-1}$; NMR (CF_3–COOH) δ 4.60–5.50 (broad multiplet, 6, protons of ring D) 7.95 (m, 2, aromat. ring A) 8.25 (m, 2, aromat. ring A) 9.00 (s, 2, aromat. ring B) ppm. (Found: C, 45.51; H, 2.94; N, 6.54; Br, 38.23. $C_{16}H_{12}N_2O_2Br_2$ requires: C, 45.28; H, 2.83; N, 6.60; Br, 37.83%).

1 - *Ethoxy* - 2,3 - *dibromo* - 4*a*,12*a* - *diaza* - 1,2,3,4,4*a*,5,12,12*a* - *octahydronaphthacen* - 5,12 - *dione* **4**. To a solution of 0.5 g (2.0 mmole) **1c** and 0.6 g (3.4 mmole) *N*-bromosuccinimide in 30 ml of commercial chloroform, 0.05 g benzoyl peroxide were added. The mixture was heated under reflux for 48 h, and stirred at room temp. for 4 days more. Solvent was removed to give a yellow oil which was taken up in acetone and allowed to crystallize. The solid obtained was purified by preparative thin layer chromatography developed in 12:1 mixture of benzene and ethanol, affording a yellow solid which recrystallised from methanol to yield 0.38 g (41%) of pure **4**, m.p. 143°. IR (KBr) ν_{max} 695, 725, 740, 755, 1065 (C–O), 1210, 1285, 1325, 1385, 1415, 1630 (C=C), 1665 (C=O), 2980 cm $^{-1}$; NMR ($CDCl_3$) δ 1.28 (t, 3, CH_3) 3.75 (c, 2, OCH_2) 4.32 (c, 1, H_A) 4.50 (m, 1, H_D) 4.75 (m, 1, H_B) 5.22 (C, 1, H_A) 6.58 (d, 1, H_E) 7.80 (m, 2, aromat. ring A) 8.15 (m, 2, aromat. ring A) 8.85 (s, 2, aromat. ring B) ppm; MS *m/e* (% rel. abund.) 470(20) 469(8) 468 (38, M^+) 466(20) 423(7) 389(42) 388(13) 387(42) 343(13) 331(40) 329(40) 308(19) 307(35) 279(12) 264(14) 263(39) 262(26) 251(33) 250(46) 249(27) 236(20) 225(40) 210(19) 180(46) 155(26) 154(59) 127(33) 126(100) 82(25) 80(25) 46(58). (Found: C, 46.11; H, 3.68; N, 5.86; Br, 33.98. $C_{18}H_{16}N_2O_3Br_2$ requires: C, 46.15; H, 3.42; N, 5.98; Br, 34.18%).

1,3 - *Diethoxy* - 2 - *bromo* - 4*a*,12*a* - *diaza* - 1,2,3,4,4*a*,5,12,12*a* - *octahydronaphthacen* - 5,12 - *dione* **5**. A solution of 1 g (4.0 mmole) **1b** and 1.5 g (8.5 mmole) *N*-bromosuccinimide in 50 ml commercial chloroform containing 0.1 g of benzoyl peroxide, was heated under reflux for 7 days. The solvent was then removed to give a red oil. Preparative TLC developed in 5:1 mixture of benzene and ethanol led to the isolation of a more retained yellow solid and a less polar red oil. The solid was rechromatographed in benzene: ethanol mixture in 15:1 proportions as eluent, affording two different products, the less retained of which was identified as **4** (0.6 g, 32% yield), the other being a white solid which recrystallised from methanol to give 0.34 g (20% yield) of pure **5**, m.p. 139–41°. IR (KBr) ν_{max} 765, 915, 1070 (C–O), 1205, 1335, 1375, 1390, 1620 (C=C), 1655 (C=O), 2970 cm $^{-1}$; NMR (CCl_4,D) δ 1.08 (t, 3, CH_3) 1.30 (t, 3, CH_3) 3.2–3.9 (m, 5, OCH_2, and H_D) 4.15 (m, 1, H_C) 4.50 (c, 1, H_A) 5.28 (c, 1, H_B) 6.58 (d, 1, H_E) 7.78 (m, 2, aromat. ring A) 8.17 (m, 2, aromat. ring A) 8.93 (s, 2, aromat. ring B) ppm. (Found: C, 55.53; H, 4.84; N, 6.62; Br 18.86. $C_{20}H_{21}N_2O_4Br$ requires: C, 55.43; H, 4.85; N, 6.47; Br, 18.46%).

2 - (1,3 - *Diethoxy* - 4*a*,12*a* - *diaza* - 1,2,3,4,4*a*,5,12,12*a* - *octahydro* - 5,12 - *dione*) - *naphthacenyl* 3,4 - *dibromobenzoate* **6**. This compound was obtained as a byproduct in the synthesis of **5** described above. The red oil isolated by preparative TLC in that reaction was rechromatographed using benzene:ethanol (25:1) to give 0.1 g (5% yield) of a white solid identified as **6**, m.p. 103–4°. IR (KBr) ν_{max} 750, 905, 1020, 1080, 1275, 1375, 1385, 1400, 1620 (C=C), 1660 (C=O amide), 1700 (C=O benzoate), 2970 cm $^{-1}$; NMR ($CDCl_3$) δ 0.9–1.6 (m, 6,CH_3))3.3–4.0 (m, 3, OCH_2 and 1H ring D) 4.1–5.0 (m, 4, OCH_2 and 2H ring D) 5.26 (c, 1, H_B) 6.38 (d, 1, H_E) 7.65 (m, 3, aromat. ring A and H-C5' benzoate) 7.92 (m, 1, H-C6' benzoate ring) 8.10 (m, 2, aromat. ring A) 8.28 (d, 1, H-C2' benzoate) 8.85 (s, 2, aromat. ring B) ppm. (Found: C, 51.61; H, 3.68; N, 4.63; Br, 25.09. $C_{27}H_{24}N_2O_6Br_2$ requires: C, 51.27; H, 3.79; N, 4.43; Br, 25.31%).

REFERENCES

[1]B. López, M. Lora-Tamayo, P. Navarro and J. L. Soto, *Heterocycles* **2**, 649 (1974).

[2]E. H. White, E. G. Nash, D. R. Roberts and O. C. Zafiriou, *J. Am. Chem. Soc.* **90**, 5932 (1968).

[3]H. J. Backer, W. Stevens and N. Dost, *Rec. Trav. Chim. Pays-Bas* **67**, 451 (1948); J. M. Landsberg and M. Siegel, *J. Org. Chem.* **35**, 1674 (1970).

[4]M. F. Braña, M. Lora-Tamayo, P. Navarro and J. L. Soto, *An. Quim.* **68**, 523 (1972).

[5]J. Seibl, Massenspektrometrie, Akademische Verlaggesellschaft, Frankfurt-am-Main (1970).

[6]F. Gómez Contreras, Thesis (Dr.), Universidad Complutense, Madrid (1976).

[7]L. Bateman and J. I. Cuneen, *J. Chem. Soc.* 941 (1950).

[8]J. S. Pizey, *Synthetic Reagents*, Vol. 2. Wiley, New York (1974).

[9]H. Booth, *Tetrahedron Letters* 411 (1965).

[10]H. D. K. Drew and R. F. Garwood, *J. Chem. Soc.* **836** (1939).