Tetrahedron Vol 33, pp 1345 to 1348 Pergamon Press 1977 Printed in Great Britain

REACTION OF BICYCLIC DIENES WITH 4-SUBSTITUTED-1,2,4-TRIAZOLINE-3,5-DIONES

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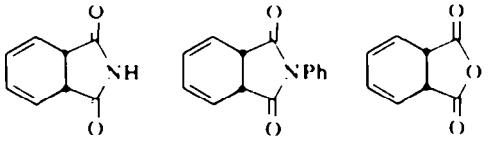
(*Received in the UK 27 September 1976; Accepted for publication 16 November 1976*)

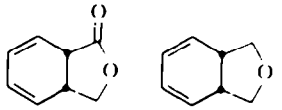
Abstract—Reaction of 1,2-dihydrophthalic anhydride and several of its imide derivatives, 1,2-dihydrophthalide and 1,2-dihydrophthalan with N-methyl- and N-phenyl-1,2,4-triazoline-3,5-dione affords two configurational families of adducts through attack from both possible directions. Major attack in the first three cases occurs mainly *syn*- to the hetero-ring but in the two latter cases *anti*- to it. These results may be explained by invoking stabilization of the transition state in the former cases through secondary orbital overlap and by simple steric effects in the latter.

For several years we have been investigating the reasons for the great selectivity in the attack of various propellanes containing cyclohexadiene rings by dienophiles in general[1] and by 4-phenyl-1,2,4-triazoline-3,5-dione in particular.[1,2] These investigations have not yet led to an incontrovertible interpretation and are still in progress. In this connection we wished to determine whether similar bicyclic systems in which one of the propellane rings is absent and its place is marked by two *cis*-hydrogen atoms, also exert analogous control of the direction of approach by this very reactive dienophile.

Thus, compounds **1–4** were available[3] and **5** was prepared, albeit impure[4] for purposes of comparison.



1 **2** **3**



4 **5**

In the propellane series we had examples of imides analogous to **1** and to **2** in that the third, 6-membered, ring which formally replaces the bridgehead hydrogens in these compounds was either a cyclohexadiene, a cyclohexene or a cyclohexane ring. Most of our experience, however, was with the N-methylimide.[1,2] In the case of **3** analogous propellanes with the added cyclohexadiene ring or cyclohexane ring were studied.[1] In all of these cases we had attack exclusively on the side which is *syn*- with respect to the CO-containing ring. It is these findings which caused us to propose the thesis of secondary orbital overlap (kindly sorted out by Prof. R. Gleiter of T. H. Darmstadt) between π^* orbitals of the CO groups and an n unsymmetric combination of the lone pair orbitals of the dienophiles, causing stabilization of this particular transition state as compared to that which would obtain, if attack occurred from the side *anti*- to the carbonyl-containing ring.[5] Thus, *a priori*, on the basis of this thesis we should expect, at the least, more *syn*-attack (with respect to the carbonyl-containing ring, i.e. more *anti*-attack with respect to the bridgehead hydrogens) in compounds **1–3** as compared to **4** and **5**. The table shows that this expectation was indeed fulfilled although the relative yield of *syn*- and *anti*- adducts for the various substrates **1–3** varies. In the case of **5**, albeit hampered by impure starting material, only one adduct was isolated and though it is possible that the other isomer formed as well we are certain that the latter would have been isolated had it been formed in significant (>2–3%) yield.

In the attack of **1**, **2** and **3** by either the N-methyl or the N-phenyl dienophile, more *syn*-attack occurs (with respect to the heterocyclic ring). In the attack of **4** and **5** more *anti*-attack occurs, i.e. attack occurs overwhelmingly from the side *syn*- to the bridged hydrogens.

For **1–3** we should expect relatively little, if any, steric hindrance to attack from the side *syn*- to the heterocyclic ring or, in fact, from the side *anti*- to it. The bridgehead hydrogens too should exert very little, if any, hindrance to attack from the side *syn*- to themselves. For this reason we do indeed get relatively to the propellanes we have studied, a great deal of attack on the side *anti*- to the heterocyclic ring (i.e. *syn* to the bridgehead hydrogens).

For **4** and **5** the same steric situation holds for attack *syn*- to the bridgehead hydrogens but for attack *syn*- to the lactone or ether ring, not only is there less or no possibility for secondary orbital overlap between attacker and attacked but we must add to this the steric hindrance,

Table 1. Relative % yields of products of bicyclic dienes and 4-substituted-1,2,4-triazoline-3,5-diones

1	94	6	90	10
2	67	33	66	33
3	4	96	52	48
4	12	88	5	95
5		[illegible]		100

opposing the attacker, which is exerted by the hydrogen (in **4**), hydrogens (in **5**) in the CH_2 group(s) within the hetero-ring. Both of these effects, the absence of stabilization through overlap from the CO groups and the totality of steric interactions cause attack to occur overwhelmingly from the side *anti*- to the hetero-ring. In fact we have adducts of **5** which belong only to the *anti*-family.

The reaction scheme shows the interrelations between the various mono-adducts in both configurational families. Thus, in the *syn*-series which preponderates in the cases **1–3** for both the N-methyl and N-phenyl dienophiles, alcoholysis followed by bromination leads to a dibromo-acid-ester and it is the formation of a bromo-lactone-ester from **11b** rather than from **10a** or **10b** which proves the relative configurations of the anhydrides **10** and **11**. Clearly then, **6b**, **8a**, **8b** and **12a** and **b** are of the same configurational family as **10a** and **b**. The logic imposed, dually, by symmetry and by chemistry, requires that **13a** and **b**, **14a** and **b** and **11a** and **b** be members of the same configurational family.

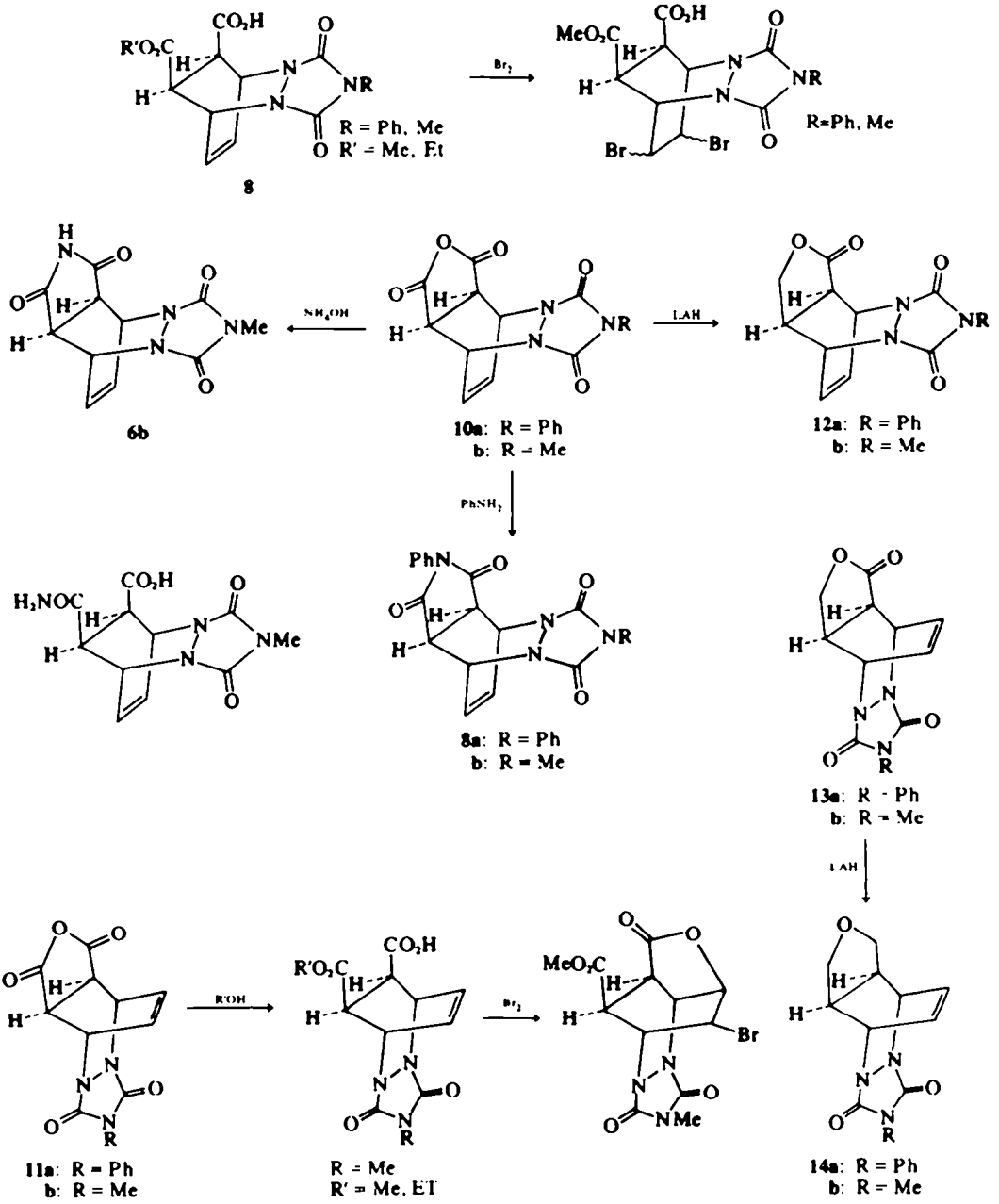
We must therefore conclude that the thesis deduced from the use of propellanes as stereochemical models appears to be applicable also to the simpler bicyclic cases described herein.

EXPERIMENTAL

IR spectra were measured on a Perkin Elmer model 257 grating spectrophotometer. NMR spectra were measured on a Varian T-60 spectrometer. Mass spectra were measured on a Varian 711 spectrometer using the heated inlet system at 200°. The electron energy was maintained at 100 eV. Only the major fragments are listed. All m.ps are uncorrected.

Reaction of dienes with 4-phenyl-1,2,4-triazoline-3,5-dione

(a) A soln of the dienophile (49 mg) in CH_2Cl_2 (5 ml) was added to a soln of **1** (42 mg) in CH_2Cl_2 (5 ml) at room temp. The reaction,



as evidenced by immediate discharge of the red color is instantaneous. The products (87 mg; 95%) precipitated from soln and were removed by filtration and fractional crystallization was conducted in acetone.

The adduct **6a** was obtained as the product insoluble in hot acetone (41 mg; 47%), m.p. 339–340°. (Found: M.W. 324.0850. $C_{16}H_{12}N_4O_4$ requires: M.W. 324.0858). IR ($CHCl_3$): 1780, 1710 cm^{-1}. NMR ($CDCl_3$ + TFA): τ 2.50 (m, 5 arom H); 3.15 (t, 2H, vinylic); 4.35 (br, 2H, CHN); 6.55 (m, 2H, CHC=O). MS M$^+$ 324(35); 227(100); 119(40); 91(10).

Adduct **7a** (46 mg; 53%) had m.p. 337–338° (acetone). (Found: C, 58.67; H, 3.43; N, 17.30; M.W. 324.0856. $C_{16}H_{12}N_4O_4$ requires: C, 59.26; H, 3.73; N, 17.28%; M.W. 324.0858. IR(KBr): 3390, 1780, 1705, 1405 cm^{-1}. NMR ($CDCl_3$ + TFA): τ 2.55 (5 arom H); 3.2 (m, 2 vinylic H); 4.30 (m, 2H, CHN); 6.15 (m, 2H, CHC=O). MS M$^+$ 324(27); 227(100); 119(26); 91(10).

(b) A soln of the dienophile (82 mg) in CH_2Cl_2 (10 ml) was added to **2** (68 mg) in CH_2Cl_2. The reaction was instantaneous. After evaporation of solvent the residue (178 mg) was extracted with benzene. Adduct **8a** did not dissolve. After purification on a preparative silica plate (123 mg; 94%), elution with acetone (2): hexane (1), **8a** had m.p. 239–240° (benzene). (Found: C, 65.58; H, 3.89; N, 14.14; M.W. 400.1155. $C_{22}H_{16}N_4O_4$ requires: C, 65.99; H, 4.03; N, 13.99%; M.W. 400.1171). IR ($CHCl_3$): 1780, 1720 cm^{-1}. NMR ($CDCl_3$): τ 2.55 (br, 5 arom H); 3.30 (t, 2 vinylic H); 4.50 (m, 2H, CHN); 6.70 (m, 2H, CHC=O). MS M$^+$ 400(36); 227(100).

Adduct **9a** was obtained from the benzene-soluble portion. Purification as above on a preparative silica plate afforded the analytical sample (9 mg; 6%), m.p. 318–319° (acetone). (Found: C, 64.77; H, 3.90; N, 14.04; M.W. 400.1199). IR(KBr): 1780, 1700 cm^{-1}. NMR ($CDCl_3$): τ 2.50 (br, 10 arom H); 3.30 (t, 2 vinylic H); 4.45 (m, 2H, CHN); 6.20 (m, 2H, CHCO). MS M$^+$ 400(45); 227(100); 119(35).

(c) A soln of dienophile (118 mg) in $CHCl_3$ (25 ml) was added to a soln of **3** (101 mg) in $CHCl_3$ (25 ml). After instantaneous reaction the product precipitated (196 mg; 90%). It was treated with boiling EtOAc whereupon the major part dissolved (150 mg), still leaving an insoluble fraction of **11a**. Ratio of **10a**:**11a** is 2:1 from NMR data.

The adduct **10a** was crystallized from the soln, m.p. 269–270° (EtOAc). (Found: C, 59.35; H, 3.10; N, 12.76; M.W. 325.0710. $C_{16}H_{11}N_3O_4$ requires: C, 59.08; H, 3.41; N, 12.92%; M.W. 325.0698). IR ($CHCl_3$): 1870, 1790, 1710 cm^{-1}. NMR ($CDCl_3$): τ 2.40 (br, 5 arom H); 3.10 (t, 2 vinylic H); 4.30 (m, 2H, CHN); 6.30 (m, 2H, CHC=O). MS M$^+$ 325(39); 227(100); 119(32).

Adduct **11a** was insoluble in boiling EtOAc, m.p. 282–283°. (Found: C, 57.99; H, 3.42; N, 12.73; M.W. 325.0698). IR ($CHCl_3$): 1870, 1790, 1710 cm^{-1}. NMR ($CDCl_3$ + TFA): 2.40 (br, 5 arom H); 3.10 (t, 2 vinylic H); 4.30 (m, 2H, CHN); 5.90 (m, 2H, CHCO). MS M$^+$ 325(52); 227(100); 119(56).

(d) A soln of dienophile (187 mg) in CH_2Cl_2 (30 ml) was added to one of **4** (234 mg) in CH_2Cl_2 (30 ml). The reaction was instantaneous. Evaporation of solvent afforded the crude reaction product (422 mg, 100%). It was treated with chloroform in which the adduct **12a** dissolved (54 mg; 12%). The adduct **13a** (368 mg; 88%) was insoluble. Evaporation of the chloroform afforded crude **12a**. It had m.p. 215–217° (benzene). (Found: M.W. 311.0898. $C_{16}H_{13}N_3O_4$ requires: 311.0905). IR ($CHCl_3$): 1780, 1720 cm^{-1}. NMR ($CDCl_3$): τ 2.55 (s, 5 arom H); 3.35 (t, 2 vinylic H); 4.65 (m, 1H, CHN); 5.10 (m, 1H, CHN); 5.40 (m, 2H, CH_2O); 7.00 (m, 2H, CH, CHCO). MS M$^+$ 311(20); 227(87); 177(100); 165(16); 119(100).

The adduct **13a** had m.p. 236–238° (MeOH). (Found: C, 61.06; H, 4.27; N, 13.53; M.W. 311.0935). IR ($CHCl_3$): 1770, 1715 cm^{-1}. NMR ($CDCl_3$ + TFA): τ 2.45 (5 arom H); 3.15 (t, 2 vinylic H), 4.45 (q, 1H, CHN); 4.65 (q, 1H, CHN); 5.30 (q, 1H, CH_2O); 5.90 (dd, 1H, CH_2O); 6.30 (d, 2H, CHCO). MS 311(25); 227(100); 119(29).

(e) A soln of dienophile (48 mg) in CH_2Cl_2 (10 ml) was added to one of impure **5** (66 mg) in CH_2Cl_2 (10 ml). After the instantaneous reaction the solvent was removed and the residue was extracted with hexane and the hexane-insoluble material (74 mg) was chromatographed on a preparative silica plate, elution with $CHCl_3$. Only one adduct, **14a**, was isolated, m.p. 218–219° (ethyl acetate). (Found: C, 64.35; H, 4.76; N, 14.22; M.W. 297.1094. $C_{16}H_{15}N_3O_4$ requires: C, 64.63; H, 5.09; N, 14.14%; M.W. 297.1113). IR ($CHCl_3$): 1760, 1710, 1050 cm^{-1}. NMR ($CDCl_3$): τ 2.50 (5 arom H); 3.45 (t, 2 vinylic H); 5.00 (m, 2H, CHN); 6.00–6.60 (m, 4H, CH_2O); 6.90 (m, 2 CH). MS M$^+$ 297(25); 227(100); 119(36).

Reaction of dienes with 4-methyl-1,2,4-triazoline-3,5-dione

(a) Dienophile (53 mg) in $CHCl_3$ (10 ml) was added to **1** (83 mg) in $CHCl_3$ (10 ml) at room temp. After instantaneous reaction the product mixture precipitated. Separation was effected by chromatography on preparative silica plates using acetone (2): hexane (1) as eluant.

Adduct **6b** (53 mg; 52%) had m.p. 264–265° (acetone). (Found: C, 50.33; H, 3.41; N, 21.43; M.W. 262.0708. $C_{11}H_{10}N_4O_4$ requires: C, 50.38; H, 3.84; N, 21.37%; M.W. 262.0712). IR (KBr): 3380, 1760, 1700 cm^{-1}. NMR ($CDCl_3$ + TFA): τ 3.30 (t, 2 vinylic H); 4.50 (m, 2H, CHN); 6.65 (m, 2H, CHCO); 6.90 (s, 3H, NCH_3). MS M$^+$ 262(14); 165(100).

Adduct **7b** (48 mg; 48%) had m.p. 296–297° (acetone). (Found: C, 50.10; H, 3.75; N, 21.45; M.W. 262.0706). IR(KBr): 3380, 1760, 1700 cm^{-1}. NMR ($CDCl_3$ + TFA): τ 3.35 (t, 2 vinylic H); 4.40 (m, 2H, CHN); 6.20 (m, 2H, CHCO); 6.90 (s, 3H, NCH_3). MS M$^+$ 262(12); 165(100).

(b) Dienophile (65 mg) in CH_2Cl_2 (10 ml) was added to **2** (117 mg) in CH_2Cl_2 (15 ml). The instantaneous reaction afforded the crude product (197 mg) after evaporation of solvent. This was taken up in benzene. **8b** was soluble and **9b** was insoluble (9 mg; 5%). Chromatography of **8b** on a preparative silica plate using acetone (2): hexane (1) as eluant afforded material (172 mg; 95%) of m.p. 269–270° (benzene). (Found: M.W. 338.1011. $C_{17}H_{14}N_4O_4$ requires: 338.1014). IR ($CHCl_3$): 1780, 1720 cm^{-1}. NMR ($CDCl_3$): τ 2.60 (5 arom H); 3.40 (t, 2 vinylic H); 4.60 (m, 2H, CHN); 6.85 (m, 2H, CHCO), 7.00 (s, 3H, NCH_3). MS M$^+$ 338(18); 165(100).

The adduct **9b** by similar chromatographic purification had m.p. 305–307° (acetone). (Found: M.W. 338.1017). IR ($CHCl_3$): 1790, 1720 cm^{-1}. NMR ($CDCl_3$): τ 2.50 (5 arom H); 3.40 (t, 2 vinylic H); 4.50 (m, 2H, CHN); 6.30 (m, 2H, CHCO); 6.95 (s, 3H, NCH_3). MS M$^+$ 338(37); 165(100).

(c) Dienophile (59 mg) in $CHCl_3$ (10 ml) was added to **3** (75 mg) in $CHCl_3$ (10 ml). After instantaneous reaction crude product precipitated (**10b**; 84 mg). Evaporation of solvent from the mother liquor followed by trituration with $CDCl_3$ gave **11b** (38 mg). Ratio of **10b**:**11b** is 2:1 from NMR data.

The adduct **10b** had m.p. 233–234° (dry C_6H_6). (Found: C, 49.22; H, 3.11; N, 15.97; M.W. 263.0545. $C_{11}H_9N_3O_4$ requires: C, 50.19; H, 3.45; N, 15.97%; M.W. 263.0542). IR(KBr): 1840, 1730, 1700 cm^{-1}. NMR ($CDCl_3$ + TFA): τ 3.30 (t, 2 vinylic H); 4.35 (m, 2H, CHN); 6.35 (m, 2H, CHCO); 6.85 (s, 3H, NCH_3). MS M$^+$ 263(22); 165(100).

The adduct **11b** had m.p. 226–228° (trit. $CDCl_3$). (Found: C, 49.83; H, 3.17; N, 16.01; M.W. 263.0538). IR ($CHCl_3$): 1840, 1740, 1720 cm^{-1}. NMR ($CDCl_3$): τ 3.40 (t, 2 vinylic H); 4.35 (m, 2H, CHN); 6.15 (m, 2H, CHCO); 6.95 (s, 3H, NCH_3). MS M$^+$ 263(28); 165(100).

(d) Dienophile (153 mg) in $CHCl_3$ (30 ml) was added to **4** (113 mg) in $CHCl_3$ (30 ml). The NMR spectrum of the crude mixture obtained after the instaneous reaction appeared to be that of a single product but fractional crystallization afforded the less soluble **12b** (13 mg; 5%), m.p. 235–236° (benzene). A purer sample was obtained by reduction of **10** (see below). (Found: M.W. 249.0769). IR(KBr): 1760, 1700 cm^{-1}. MS. M$^+$ 249(15); 165(100) (see below). The major product **13b** (253 mg; 95%) had m.p. 190–192° (benzene). (Found: C, 52.76; H, 4.33; N, 17.12; M.W. 249.0760. $C_{11}H_{11}N_3O_4$ requires: C, 53.01; H, 4.45; N, 16.86%; M.W. 249.0750). IR ($CHCl_3$): 1780, 1720 cm^{-1}. NMR ($CDCl_3$): τ 3.40 (t, 2 vinylic H); 4.70 (m, 1H, CHN); 4.90 (m, 1H, CHN); 5.50 (m, 1H, CH_2O); 6.00 (m, 1H, CH_2O); 6.50 (m, 2H, CH, CHCO); 6.95 (s, 3H, NCH_3). MS M$^+$ 249(28); 165 (100).

(e) Dienophile (47 mg) in CH_2Cl_2 (10 ml) was added to crude **5** (104 mg) in CH_2Cl_2 (20 ml). After similar workup to that of the N-phenyl analog a single adduct **14b** was obtained (78 mg; 48%), m.p. 180–181° (EtOAc-hexane). (Found: C, 55.91; H, 5.42; N, 18.07; M.W. 235.0950. $C_{11}H_{13}N_3O_3$ requires: C, 56.16; H, 5.57; N, 17.86%; M.W. 235.0957). IR ($CHCl_3$) 1760, 1710 cm^{-1}. NMR ($CDCl_3$): τ 3.50 (t, 2 vinylic H); 5.10 (m, 2H, CHN); 6.00–6.60 (m, 4H, CH_2O); 7.00 (s, 3H, NCH_3); 7.00 (br, 2H, CH). MS M$^+$ 235(99); 165(100).

Interrelations of Diels-Alder adducts

(a) A soln of **10a** in aniline was allowed to stand overnight at room temp. and the excess aniline was removed in a high vacuum. The residue afforded **8a** exclusively, m.p. 238–239° (benzene) identical with **8** described above by m.m.p. and spectroscopically.

(b) Anhydride **10a** (20 mg) was methanolyzed by reflux in MeOH (10 ml) for 1 hr. The insoluble half ester was dissolved in water (5 ml) and Br_2 was added with stirring until the soln remained yellow. Stirring was continued for 90 min and the whole was extracted with CH_2Cl_2 and the solvent removed.

The dibromo-half methyl ester exhibited the following spectral data. IR ($CHCl_3$): 1780, 1710 cm^{-1}. NMR ($CDCl_3$): τ 2.40 (5 arom H); 3.70 (CO_2H, disappears in D_2O); 4.90 (2H); 5.40 (2H); 6.25 (5H). MS (M$^+$-MeOH), 486(20); 484(38); 483(13); 482(17); 481(7); 413(7); 411(8); 334(48); 332(54); 227(100); 214(13); 212(11); 198(32); 196(38).

(c) Anhydride **11a** (20 mg) was methanolyzed as in (b). Evaporation of solvent afforded an oil. NMR ($CDCl_3$): τ 2.50 (5 arom H); 3.30 (m, 2 vinylic H); 4.70 (m, 2H, CHN); 6.20 (m, 2H, CHCO); 6.35 (s, 3H, OCH_3). Bromination as described in (b) afforded a neutral compound which had no free CO_2H but was a bromolactone-methyl ester. IR ($CHCl_3$): 1770, 1720 cm^{-1} (5-memb. lactone, ureide). NMR ($CDCl_3$): τ 2.35 (5 arom H), 4.90 (2H, CHN); 5.90–6.30 (2H, CHBr; 2H, CHCO; 3H, OCH_3).

Ethanolysis of **11a** gave an oily half ethyl ester. NMR ($CDCl_3$). τ 2.50 (5 arom H); 3.30 (t, 2 vinylic H); 4.70 (m, 2H, CHN); 5.80 (q, 2H, OCH_2CH_3); 6.25 (m, 2H, CHCO); 8.75 (t, 3H, OCH_2CH_3). Analogous bromination gave a bromolactone ethyl ester. IR ($CHCl_3$): 1770, 1720 (5 memb. lactone and ureide), 1410 cm^{-1}. MS (M$^+$-Br), 370(17); 324(95); 300(9); 298(8); 296(8); 256(9); 227(12); 177(18); 151(27); 119(100).

(d) Anhydride **10a** (30 mg) was reduced with LAH (25 mg) in THF (20 ml) at −55° during 2 hr.[a] after acidification and filtration the aqueous mother liquor was evaporated to dryness and the residue was taken up in chloroform. The NMR spectrum showed the presence of the lactone **12a**. Isolation gave the crude sample, m.p. 210° which was identical with the compound described above.

(e) Lactone **13a** (130 mg) was treated with LAH (100 mg) in THF (25 ml) at room temp. for 40 hr. After the usual workup and extraction with CH_2Cl_2 a further was obtained showing in the IR bands at 3400 cm^{-1} (OH) and 1770, 1700 cm^{-1} (imide). This was dissolved in toluene (25 ml) and the solution was heated under reflux for 8 hr in the presence of *p*-toluenesulfonic acid. After removal of the acid and evaporation of the solvent chromatography on a preparative silica plate using $CHCl_3$ as eluant, the product **14a** was obtained, m.p. 217–219° (EtOAc) identical to **14a** described above by m.m.p. and spectral data.

(f) The anhydride **10b** was added to an excess of NH_4OH (conc.), allowed to stand for 1 hr at room temp. then heated under reflux for 2 hr. After evaporation to dryness the IR spectrum of the crude product (35 mg) showed the presence of crude and ring-opened product (acid-amide). After separation on a preparative silica plate using acetone (2): hexane (1) as eluant the imide **6b**, m.p. 264–265°, was obtained (11 mg; 37%), identical by m.m.p. and spectroscopically to the product described above.

(g) The anhydride **10b** (35 mg) was dissolved in aniline (2 ml), the whole was allowed to stand overnight and the excess aniline removed in a high vacuum. The crude product (40 mg) was chromatographed on a preparative silica plate using acetone (2): hexane (1) as eluant. The product had m.p. 268–269° and was identical by m.m.p. and spectroscopically to **8b** described above.

(h) Anhydride **10b** (30 mg) was methanolyzed by heating under reflux in MeOH (10 ml) for 1 hr. After removal of solvent the hygroscopic half methyl ester was obtained (31 mg). Trituration with dry benzene gave the pure material, m.p. 115–117°. NMR ($CDCl_3$): τ 3.35 (t, 2 vinylic H); 4.70 (m, 2H, CHN); 6.25 (s, 3H, OCH_3); 6.85 (s, 2H, CHCO); 7.00 (s, 3H, NCH_3). MS (M$^+$-MeOH), 263(40); 165(100). Ethanolysis gave the half ethyl ester, m.p. 210° (trit. $CHCl_3$–EtOH). NMR ($CDCl_3$): τ 3.40 (t, 2 vinylic H); 4.70 (m, 2H, CHN); 5.70 (q, 2H, OCH_2CH_3); 6.95 (s, 2H, CHCO); 7.00 (s, 3H, NCH_3); 8.70 (t, 3H, OCH_2CH_3).

The dibromo-half methyl ester was obtained by treating an aq (10 ml) solution of the half methyl ester (35 mg) with Br_2 (0.5 ml) until the yellow color persisted. After stirring for 45 min at room temp., extraction with CH_2Cl_2 and removal of solvent afforded crude product (39 mg). It had m.p. 250–251° (benzene). IR ($CHCl_3$): 3500 (br, CO_2H), 1770 (sh), 1700 cm^{-1}. NMR ($CDCl_3$): τ 3.00 (CO_2H, disappears in D_2O); 5.00 (2H, CHN); 5.40 (2H, CHBr); 6.30 (5H, OCH_3, CHCO); 6.90 (s, 3H, NCH_3).

(i) Anhydride **11b** (20 mg) was heated under reflux in MeOH (10 ml) for 1 hr. Removal of solvent afforded the half methyl ester (18 mg). Trituration with dry benzene gave hygroscopic material of m.p. 163–164°. (Found: M.W. 295.0817. $C_{12}H_{11}N_3O_6$ requires: 295.0830). NMR ($CDCl_3$): τ 3.40 (t, 2 vinylic H); 4.75 (m, 2H, CHN); 6.30 (s, 3H, OCH_3); 6.35 (2H, CHCO); 6.95 (s, 3H, NCH_3). MS M$^+$ 295(6); 263(16); 165(100). Ethanolysis gave the half ethyl ester, m.p. 239–240°. NMR ($CDCl_3$): τ 3.40 (2 vinylic H); 4.75 (m, 2H, CHN); 5.80 (q, 2H, OCH_2CH_3); 6.30 (m, 2H, CHCO); 6.95 (s, 3H, NCH_3); 8.75 (t, 3H, OCH_2CH_3).

The bromolactone-methyl ester was obtained by bromination as above of the half methyl ester (30 mg) in aq (10 ml) solution. Similar workup gave crude product (33 mg). Crystallization gave the pure product, m.p. 238–239° (benzene). IR ($CHCl_3$): 1775, 1710 cm^{-1}. NMR ($CDCl_3$): τ 4.70–5.20 (4H; 2 CHN, 1 CHBr, 1 CHO); 6.20 (s, 3H, OCH_3); 6.50 (m, 2H, CHCO); 6.90 (s, 3H, NCH_3). MS M$^+$ 375(46); 373(47); 265(34); 251(15); 249(16); 184(100).

The bromo-lactone ethyl ester was obtained similarly as a gum. (Found: M.W. 389.0037. $C_{13}H_{14}N_3O_6Br$ requires: 389.0046). MS M$^+$ 389(20); 387(25); 308(11); 262(61); 244(11); 236(9); 179(5); 177(5); 165(29); 133(16); 127(11); 115(100).

(j) Anhydride **10b** (37 mg) was reduced as described above for **10a** using LAH (30 mg) at −55°C. After analogous workup, evaporation of the chloroform gave the lactone **12b** (24 mg), m.p. 261–263° (benzene). (Found: C, 52.80; H, 4.65; N, 17.09; M.W. 249.0731. $C_{11}H_{11}N_3O_4$ requires: C, 53.01; H, 4.45; N, 16.86%; M.W. 249.0749). IR(KBr): 1760, 1700 cm^{-1}. NMR ($CDCl_3$): τ 3.40 (t, 2 vinylic H); 4.70 (m, 1H, CHN); 5.15 (m, 1H, CHN); 5.40 (m, 2H, CH_2O); 7.00 (br, 2H, CHCO); 7.00 (s, 3H, NCH_3). MS M$^+$ 249(21); 165(100).

(k) Reduction of **13b** (120 mg) with LAH (100 mg) in THF (25 ml) during 40 hr at room temp. followed by the usual workup as described above under (e) gave after chromatography and crystallization (EtOAc) material identical to **14b**.

Reaction of **2** *with N-phenylmaleimide.* A mixture of **2** (225 mg), dienophile (173 mg) and benzene (100 ml) was heated under reflux for 5 hr. A product precipitated (390 mg; 97%), m.p. >310°. (Found: C, 71.82; H, 4.35; N, 7.18; M.W. 398.1249. $C_{24}H_{18}N_2O_4$ requires: C, 72.35; H, 4.55; N, 7.03%; M.W. 398.1266). IR(KBr): 1775, 1710, 1380 cm^{-1}. NMR ($CDCl_3$): τ 2.50 (br, 10 arom H); 3.50 (t, 2 vinylic H); 6.00 (m, 2 CH); 6.80 (m, 4 CH). MS M$^+$ 398(100); 173(44); 129(8); 119(45).

From the mother liquor was obtained the isomeric adduct (9 mg; 2.5%) (configurations not proved); m.p. 120–121° (benzene). (Found: M.W. 398.1271). IR(KBr): 1770, 1720, 1380 cm^{-1}. NMR ($CDCl_3$): τ 2.50 (br, 10 arom H); 3.40 (t, 2 vinylic H); 6.10 (m, 2 CH); 6.85 (m, 4 CH). MS M$^+$ 398(100); 173(49); 129(13); 119(68).

Reaction of **3** *with N-phenylmaleimide.* A mixture of **3** (90 mg) with dienophile (104 mg) in benzene (50 ml) was heated under reflux for 5 hr. The product (60 mg; 31%) precipitated on cooling, m.p. >300°. (Found: C, 66.84; H, 3.81; N, 4.34; M.W. 323.0790. $C_{18}H_{13}NO_4$ requires: C, 66.87; H, 4.05; N, 4.33%; M.W. 323.0793). IR(KBr): 1850, 1775, 1700, 1390 cm^{-1}. NMR ($CDCl_3$, TFA): τ 2.50 (br, 5 arom H); 3.50 (m, 2 vinylic H); 6.00 (m, 2 CH); 6.50 (2, 4 CH). MS M$^+$ 323(100); 173(42); 133(24); 119(32).

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