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UNUSUAL REACTION OF AN 9,11-UNSATURATED RING A AROMATIC BMD-STEROID WITH N-BROMSUCCINIMIDE

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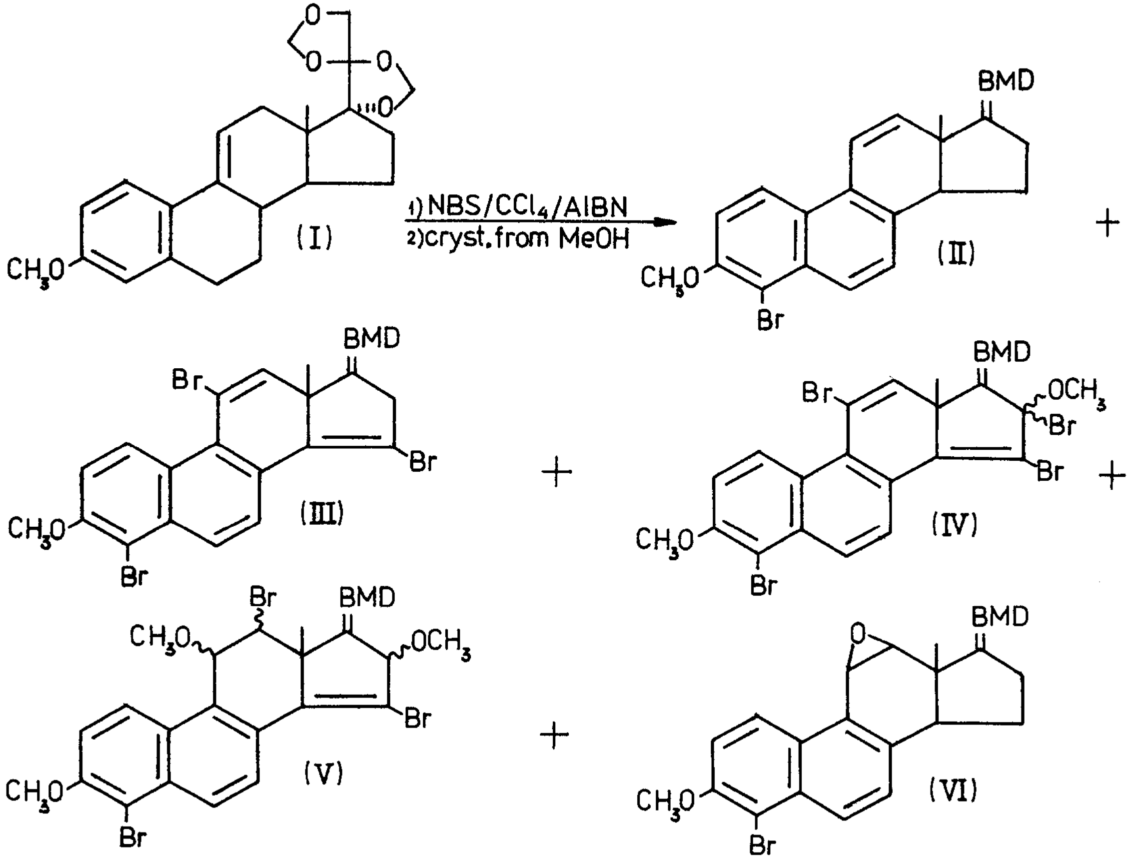
We have been interested[1] in the study of the reactivity of 17α, 20;20,21-bismethylenedioxy-19-norpregna-1,3,5(10),9(11)-tetraen-3-yl methyl ether(I). In the present communication we wish to report an unusual reaction course of(I) with N-bromsuccinimide. When (I) was refluxed with NBS in CCl_4 solution in the presence of azobisisobutyronitrile (AIBN) for 10 minutes a complex mixture was obtained. Repeated chromatography and crystallization from methanol furnished five compounds (II-VI), whose structure could be deduced from their analytical and spectral characteristics. The results are depicted in chart 1, and the physical characteristics of the compounds (II-VI) are summarised below:

<u>Compound (II)</u>: $C_{23}H_{23}O_5Br$(m.p.264-265°), $[\alpha]_D^{20}$ -25°(c 0.6,$CHCl_3$), λ_{max}^{EtOH} 240 nm (ε=58.800), 277(ε=5170), 290(ε=5700), 306(ε=6380), 322(ε=7920)and 348(ε=5750); ν_{max}(KBr):1615,1595,1575,1500,1080 cm^{-1}. PMR($CDCl_3$):δ0.75 ppm (s,3,18-H_3), 4.00("s",5,21-H_2 and CH_3O-), 5.11,5.15,5.24(m,4,BMD),6.83(d,1,J_{12-11}=10 Hz,12-H), 7.11(d,1,J_{11-12}=10 Hz,11-H), 7.22(d,1,J_{2-1}=10 Hz, 2-H), 7.32(d,1,J_{7-6}=9 Hz, 7-H), 8.06(d,1,J_{1-2}=10 Hz, 1-H), 8.12(d,1,J_{6-7}=9 Hz, 6-H).

<u>Compound (III)</u> : $C_{23}H_{19}O_5Br_3$(m.p.192-194°),$[\alpha]_D^{20}$-374°(c.0.9,$CHCl_3$),λ_{max}^{EtOH} 269 nm (ε=41.400), 282.5(ε=37.500), 292(ε=35.700), 363(ε=7650) and 378(ε=6470);ν_{max}(KBr): 1630,1610,1580,1540,1500,1090 cm^{-1}. PMR(CCl_4):δ1.11 ppm(s,3,18-H_3), 2.84(dd,2, J_{gem}=17 Hz, 16-H_2), 3.97(s,2,21-H_2), 4.01(s,3,CH_3O-), 5.02,5.08,5.10,5.21(m,4,BMD) 6.90(s,1,12-H), 7.16(d,1,J_{2-1}=10 Hz, 2-H), 8.17(d,1,J_{7-6}=9,5 Hz, 7-H), 8.41(d,1, J_{6-7}=9,5 Hz, 6-H), 8.80(d,1,J_{1-2}=10 Hz, 1-H); MS(70 eV)m/e:612(78,9%),597(3,1%), 567(17,1%),445(39,4%), 430(36,8%),409(71,0%),366(31,6%), 324(100,0%),281(26,3%)

CHART 1



BMD = Bismethylenodioxy; AIBN = azobisisobutyronitrile

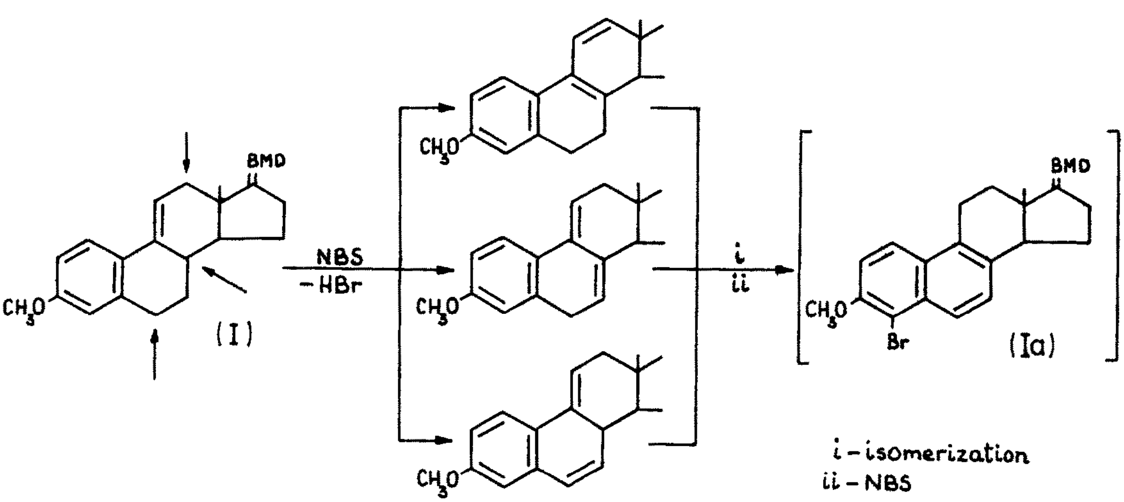
Compound (IV): $C_{24}H_{20}O_6Br_4$ (m.p.250-255°), $[\alpha]_D^{20}$ -236° (c 0.8 $CHCl_3$), λ_{max}^{MeOH} 268 nm (ε=42100), 283(ε=40500), 292(ε=41700) and 363(ε=8650), ν_{max}(KBr): 1630,1610,1590, 1540,1500,1085 cm^{-1}. PMR($CDCl_3$): δ 1.25 ppm(s,3,18-H_3), 3.65(s,3,16-OCH_3), 4.05 (s,3,3-OCH_3), 4.07,4.51(dd,2,J_{gem}=10 Hz,21-H_2), 5.06,5.17,5.22(m,4,BMD), 7.12 (s,1, 12-H), 7.26(d,1,J_{2-1}=10 Hz,2-H), 8.25(d,1,J_{7-6}=9 Hz,7-H), 8.43(d,1,J_{6-7}=9 Hz, 6-H), 8.92(d,1,J_{1-2}=10 Hz,1-H). MS (70 eV) m/e: 720 (12,5%), 676 (2,0%), 675 (1,0%), 642 (15,0%), 641 (12,5%), 611 (13,7%), 532 (22,5%), 445 (22,5%), 381 (30,0%), 103 (100,0%).

Compound (V): $C_{25}H_{25}O_7Br_3$ (m.p.188-192°), $[\alpha]_D^{20}$ -10.2° (c 1.2 $CHCl_3$), λ_{max}^{EtOH} 244 nm (ε=24500), shoulder, 264(ε=50800), 305(ε=10900), 312(ε=10500), 335(ε=4500), 354(ε=2850), ν_{max}(KBr): 1630,1600,1575,1510,1100 cm^{-1}. PMR($CDCl_3$): δ 1.35 ppm (s,3,18-H_3), 3.28 (s,3,16ξ-OCH_3), 3.71 (s,3,11ξ-OCH_3), 4.08(s,3,3-OCH_3), 4.10(s,1,12ξ-H), 4.11,4.65(dd,2,J_{gem}=10 Hz,21-H_2), 5.10(s,1,16ξ-H), 5.22(s,1,11ξ-H), 5.35,5.60 (m,4,BMD), 7.39(d,1,J_{2-1}=9,5 Hz,2-H), 8.15(d,1,J_{7-6}=9 Hz,7-H), 8.29(d,1,J_{6-7}=9 Hz, 6-H), 8.43(d,1,J_{1-2}=9,5 Hz,1-H). MS (70 eV) m/e: 674 (37,5%), 594 (10,0%), 564 (5,5%), 447 (10,0%), 355 (25,0%), 276 (15,0%), 131 (100,0%)

Compound (VI): $C_{23}H_{23}O_6Br$(m.p.224-225°),$[\alpha]_D^{20}$=-80°(c,0.6,$CHCl_3$), λ_{max}^{EtOH} 240 nm (ε=76.300),281(ε=5090),293(ε=6680),348(ε=3500); ν_{max}^{KBr}: 1615,1590,1550,1500, 1100 cm^{-1},PMR($CDCl_3$): δ 0.61 ppm(s,3,18-H_3),4.05("s",5,21-H_2 and CH_3O-),4.10 (d,1,J=4,5 Hz,12α-H),4.60(d,1,J=4,5 Hz,11α-H),5.13,5.18,5.30(m,4,BMD),7.30(d,1, J_{7-6}=9,5 Hz,7-H),7.32(d,1,J_{2-1}=10 Hz,2-H),8.24(d,1,J_{6-7}=9,5 Hz,6-H)8.30(d,1,J_{1-2} =10 Hz,1-H).

The tentative mechanism of formation of compounds (II-VI) is outlined in charts 2 and 3.

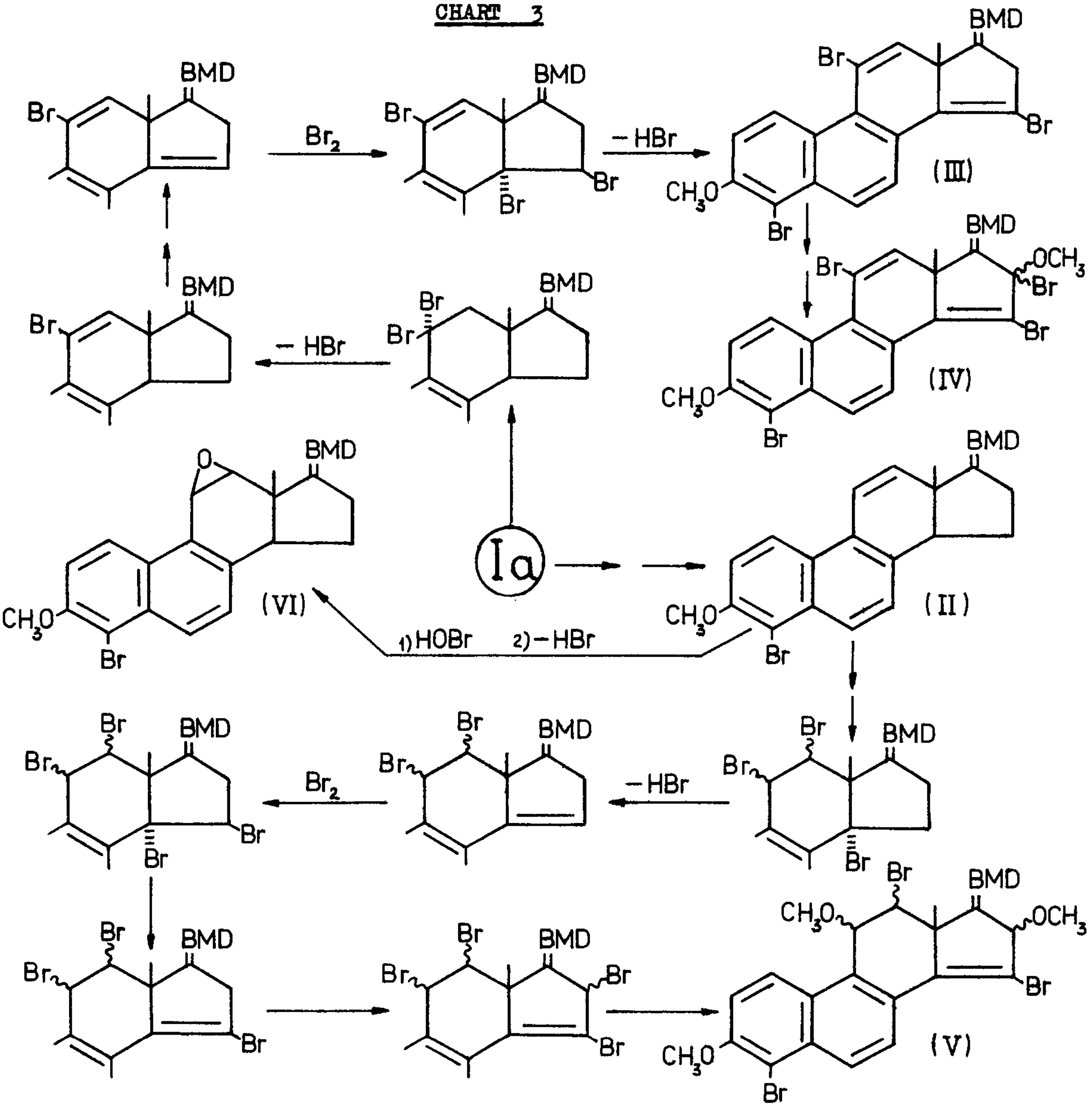
CHART 2



Bromination of (I) at any of the three reactive positions (6,8 and 12) furnishes labile bromoderivative, which eliminates hydrobromic acid and forms a diene, capable of isomerization into the aromatic steroid of equilenine type (cf.ref.2). Under the reaction conditions this undergoes easy bromination at the position 4 yielding the intermediary (Ia). Compound (II) results from bromination of the intermediary (Ia) at C_{11} followed by elimination of HBr. A series of bromination, bromine addition reactions followed by HBr eliminations and solvolysis of reactive bromoderivatives, crystallizing products from methanol gives rise to the compound (V) as outlined in chart 3.

Compound (Ia) however can be transformed into the bis-bromosubstituted benzylic derivative (cf ref.3) which undergoes reaction sequences as outlined in chart 3 and furnishes compounds (III) and (IV). Similar bromination/dehydrobromination and solvolytic displacement of reactive bromines under reaction conditions have been observed in other cases.[3-6] The epoxide (VI) seems to be an artefact of one experiment in which probably not strictly anhydrous conditions were observed. It possibly results from the compound (II) as a consequence of hypobromous acid addition and HBr-elimination reaction. Accordingly, it is formulated as the 11β, 12β-epoxide.

CHART 3



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