REDUCTIVE CYCLIZATION OF α-(6-NITROVERATRYLIDENE)-γ-BUTYROLACTONE WITH TRIETHYL PHOSPHITE

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The reaction of triethyl phosphite with α-(6-nitroveratrylidene)-γ-butyrolactone (5) produced a mixture of 3,4-dihydro-7,8-dimethoxy-[1,3]oxazino[3,4-a]indol-1-one (8), 2,3-dihydro-6,7-dimethoxy-furo[2,3-b]quinoline (9) and ethyl 5,6-dimethoxyindole-2-carboxylate (10).

Recently we reported that the triethyl phosphite reduction of α-(2-nitrobenzoyl)-(1) and α-(α-methoxy-2-nitrobenzylidene)-(2) γ-butyrolactones affords the spiroindolinone 3 and the oxazinoindole 4, respectively, rather than furo[2,3-b]quinolines.[2] These studies have now been extended to the reduction of α-(6-nitroveratrylidene)-γ-butyrolactone (5).

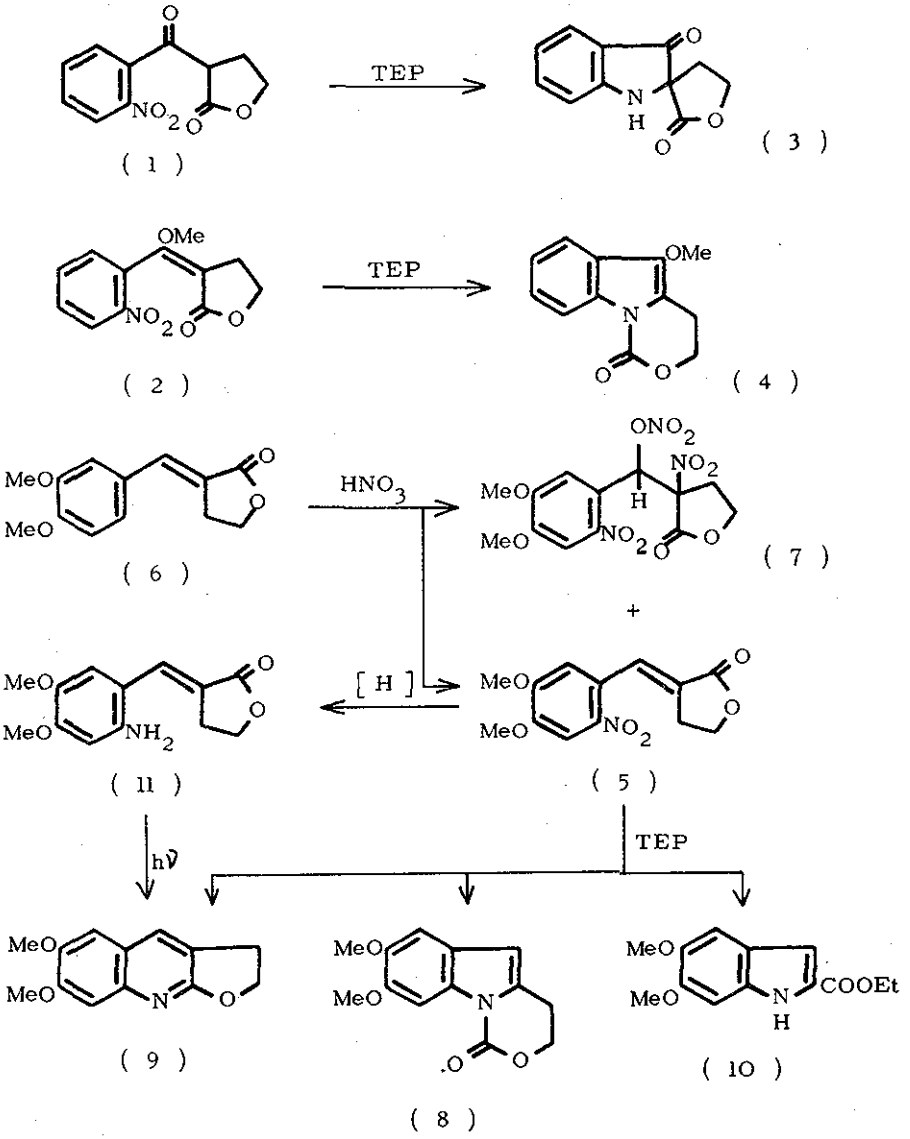
Lactone 5 was prepared, by modifications of known methods,[3] from veratraldehyde and γ-butyrolactone, followed by nitration with concentrated nitric acid (d 1.42) at 0°C. Nitration at the recommended temperature of -10°C resulted in recovery of α-veratrylidene-γ-butyrolactone (6). In addition to 5, an ether soluble polynitrated compound, mp 123 - 125°C, was isolated in low yield (ca. 10 %). The infrared spectrum ($CHCl_3$) exhibited carbonyl absorption at 1790 cm^{-1} and an intense

band at 1660 cm^{-1}, indicating the presence of a saturated lactone and a nitrate group. Microanalytical and spectral data [uv (MeOH) 247, 305 sh, 340 nm; nmr ($CDCl_3$) δ 2.46 - 3.05 (2H, m, $OCH_2C\underline{H}_2$), 3.97 (6H, s, 2 x $OC\underline{H}_3$), 4.16 - 4.50 (2H, m, $OC\underline{H}_2CH_2$), 7.26, 7.68 and 7.85 (each 1H, s, 2 x Ar$\underline{H}$ and Ar$C\underline{H}$); m/e 387 (M^+), 211, 210, 181 and 136] supported assignment of structure 7 to the product.

The reaction of triethyl phosphite with purified 5 at 160 - 165°C for 20 h produced a dark red viscous residue after distillation. Chromatography resulted in the separation of the following three cyclic compounds: 3,4-dihydro-7,8-dimethoxy-[1,3]oxazino[3,4-a]indol-1-one (8), mp 162.5 - 163.5°C; uv (MeOH) 246, 254 sh, 270, 295 nm; ir ($CHCl_3$) 1730 cm^{-1} (C = O); nmr ($CDCl_3$) δ 3.16 (2H, dt, J 6 and 1.5 Hz, $OCH_2C\underline{H}_2$), 3.90 and 3.95 (each 3H, s, 2 x OCH_3), 4.52 (2H, t, J 6 Hz, $OC\underline{H}_2CH_2$), 6.27 (1H, br, 5 - H), 6.94 (1H, s, 6 - H), 7.81 (1H, s, 9 - H); m/e 247 (M^+), 232 (M^+ - Me), 188 (232 - CO_2), 160 (188 - CH_2CH_2), 145 (160 - Me), 117 (145 - CO); 2,3-dihydro-6,7-dimethoxyfuro[2,3-b]quinoline (9), mp 195 - 196°C (subl) (lit.[4] mp 192 - 193°C); uv (MeOH) 222, 240 sh, 328, 343 nm; ir ($CHCl_3$) 1630 cm^{-1}; and ethyl 5,6-dimethoxyindole-2-carboxylate (10), mp 155 - 175°C (lit.[5] mp 172°C; lit.[6] mp 160°C, softened at 155°C); uv (MeOH), 212, 322 nm; ir ($CHCl_3$) 3470 (NH), 1690 cm^{-1} (C = O); nmr ($CDCl_3$ δ 1.38 (3H, t, J 7 Hz, $CH_2C\underline{H}_3$), 3.88 (6H, s, 2 x OCH_3), 4.36 (2H, q, J 7 Hz, $C\underline{H}_2CH_3$), 6.81 (1H, s, 7 - H), 6.99 (1H, s, 4 - H), 7.08 (1H, distorted d, J 2 Hz, 3 - H), 8.77 (1H, br, NH exchangeable with D_2O); m/e 249 (M^+), 234 (M^+ - Me), 204 (M^+ - EtO), 203 (M^+ - EtOH), 188 (234 - EtOH), 175 (203 - CO), 160 (188 - CO or 175 - Me), 149 (175 - CN).

Oxazinoindole 8 probably arises through a mechanism similar to that involved in the formation of 4:[2] nitrene addition to the lactone carbonyl and olefinic carbons followed by rearrangement of the aziridine intermediate.

The structural assignment of furoquinoline 9 was further supported by an independent synthesis. Catalytic hydrogenation of the nitro compound 5 over 5 % Pd/C



in methanolic hydrochloric acid afforded the amino derivative 11 rather than the furoquinoline 9. The same reductive procedure effected cyclization of 2 to the furo-[2,3-b]quinoline, dihydrodictamnine. Nmr spectral analysis of the nitro-(2)(β - H δ 7.91) and amino-(11)(β - H δ 7.58) benzylidenelactones indicated a trans configuration of carbonyl and phenyl groups (β proton of α-substituted trans-cinnamates δ = 7.4 - 7.5).[7]

Photolysis of amine 11 in ethanol caused isomerization and cyclization to furoquinoline 9 (15 % yield), mp 195 - 196°C (subl); uv (MeOH) 222, 240 sh, 328, 343 nm; ir ($CHCl_3$) 1630 cm^{-1}; nmr ($CDCl_3$) δ 3.29 (2H, dt, J 8 and 1.5 Hz, $OCH_2\underline{CH}_2$), 3.93 and 3.96 (each 3H, s, 2 x OCH_3), 4.62 (2H, t, J 8 Hz, $OC\underline{H}_2CH_2$), 6.91 (1H, s, 5 - H), 7.19 (1H, s, 8 - H), 7.65 (1H, br, 4 - H).

The unexpected and unusual formation of the ethyl indolecarboxylate 10 from 5 could be accounted for by nitrene addition to the double bond followed by reductive fission of a carbon-carbon bond. Normally, one of the substituents in β,β-disubstituted o-nitrostyrenes migrates during deoxygenation with triethyl phosphite to produce 2,3-disubstituted indoles.[8]

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