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A Novel Synthesis of Dihydropyranoflavonols

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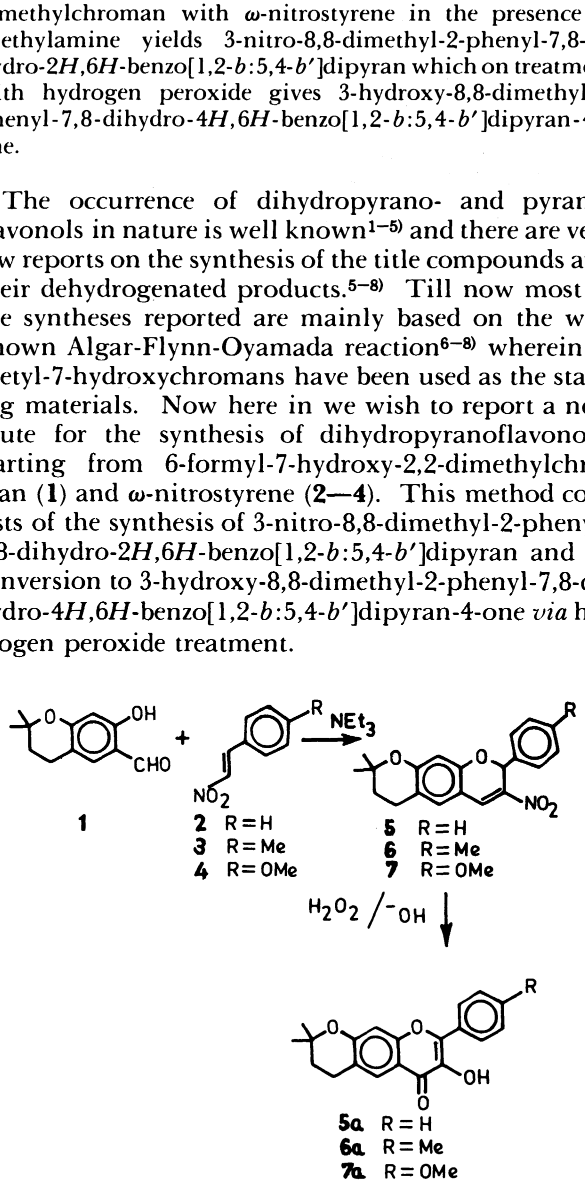
Synopsis. Condensation of 6-formyl-7-hydroxy-2,2-dimethylchroman with ω-nitrostyrene in the presence of triethylamine yields 3-nitro-8,8-dimethyl-2-phenyl-7,8-dihydro-2*H*,6*H*-benzo[1,2-*b*:5,4-*b*′]dipyran which on treatment with hydrogen peroxide gives 3-hydroxy-8,8-dimethyl-2-phenyl-7,8-dihydro-4*H*,6*H*-benzo[1,2-*b*:5,4-*b*′]dipyran-4-one.

The occurrence of dihydropyrano- and pyranoflavonols in nature is well known[1—5)] and there are very few reports on the synthesis of the title compounds and their dehydrogenated products.[5—8)] Till now most of the syntheses reported are mainly based on the well known Algar-Flynn-Oyamada reaction[6—8)] wherein 6-acetyl-7-hydroxychromans have been used as the starting materials. Now here in we wish to report a new route for the synthesis of dihydropyranoflavonols, starting from 6-formyl-7-hydroxy-2,2-dimethylchroman (**1**) and ω-nitrostyrene (**2**—**4**). This method consists of the synthesis of 3-nitro-8,8-dimethyl-2-phenyl-7,8-dihydro-2*H*,6*H*-benzo[1,2-*b*:5,4-*b*′]dipyran and its conversion to 3-hydroxy-8,8-dimethyl-2-phenyl-7,8-dihydro-4*H*,6*H*-benzo[1,2-*b*:5,4-*b*′]dipyran-4-one *via* hydrogen peroxide treatment.



Experimental

Proton NMR spectra were obtained in $CDCl_3$ solution, unless otherwise stated, containing Me_4Si as reference using a Varian XL-100 spectrometer. Infrared spectra were recorded on a Perkin Elmer Model 618 instrument. UV spectra were recorded in $CHCl_3$ on a Varian Superscan-3 spectrometer. Mass spectra were determined on a MAT 112 S mass spectrometer. Melting points were taken in open capillaries and were not corrected.

*General Procedure for the Synthesis of 3-Nitro-8,8-dimethyl-2-phenyl-7,8-dihydro-2*H*,6*H*-benzo[1,2-*b*:5,4-*b*′]dipyran (**5**—**7**).* 4 mmol of 6-formyl-7-hydroxychroman (**1**) and 8 mmol of ω-nitrostyrene (**2**—**4**) were taken in a round bottom flask to which 5 ml of triethylamine was added and refluxed for 30 min on a water bath. Then the remaining triethylamine was evaporated off and the resulting solid mass was dissolved in dichloromethane and filtered. The solid residue after repeated washings with dichloromethane was discarded and the combined washings and filtrate on concentration and chromatography (pet. ether) yielded the trace amount of unreacted nitrostyrene, 6-formyl-7-hydroxychroman and 3-nitro-8,8-dimethyl-2-phenyl-7,8-dihydro-2*H*,6*H*-benzo[1,2-*b*:5,4-*b*′]dipyran consecutively. Crystallization was achieved from methanol. The yields of isolated compounds were varying from 30 to 35%.

*3-Nitro-8,8-dimethyl-2-phenyl-7,8-dihydro-2*H*,6*H*-benzo[1,2-*b*:5,4-*b*′]dipyran (**5**):* Mp 210 °C; IR: 1320, 1560 (NO_2) cm^{-1}; NMR: δ=1.32 (3H, s), 1.34 (3H, s), 1.8 (2H, t, J=6 Hz), 2.72 (2H, t, J=7 Hz), 6.3 (1H, s), 6.34 (1H, s), 7.02 (1H, s), 7.36 (5H, s), 8.04 (1H, s); MS m/z (relative intensity) 55 (53), 63 (42), 69 (52), 77 (42), 115 (34), 139 (22), 178 (34), 235 (38), 291 (100), 337 (M^+, 50). Found: C, 71.10; H, 5.58; N, 4.13%. Calcd for $C_{20}H_{19}NO_4$: C, 71.22; H, 5.64; N, 4.15%.

*3-Nitro-8,8-dimethyl-2-(4-methylphenyl)-7,8-dihydro-2*H*,6*H*-benzo[1,2-*b*:5,4-*b*′]dipyran (**6**):* Mp 146—148 °C; IR: 1320, 1560 (NO_2) cm^{-1}; NMR (DMSO-d_6): δ=1.23 (6H, s), 1.65 (2H, t, J=7 Hz), 2.2 (3H, s), 2.46 (2H, t, J=7 Hz), 6.13 (1H, s), 6.46 (1H, s), 7.16 (4H, s, br), 7.26 (1H, s), 8.26 (1H, s); MS m/z (relative intensity) 91 (9), 119 (7), 151 (11), 178 (12), 221 (8), 249 (39), 250 (25), 305 (100), 351 (M^+, 46). Found: C, 71.62; H, 5.88; N, 3.93%. Calcd for $C_{21}H_{21}NO_4$: C, 71.79; H, 5.98; N, 3.99%.

*3-Nitro-8,8-dimethyl-2-(4-methoxyphenyl)-7,8-dihydro-2*H*,6*H*-benzo[1,2-*b*:5,4-*b*′]dipyran (**7**):* Mp 163—164 °C; IR: 1310, 1550 (NO_2) cm^{-1}; NMR: δ=1.32 (3H, s), 1.34 (3H, s), 1.79 (2H, t, J=7 Hz), 2.71 (2H, t, J=7 Hz), 3.78 (3H, s), 6.26 (1H, s), 6.48 (1H, s), 6.84 (2H, d, J=9 Hz), 7.02 (1H, s), 7.32 (2H, d, J=9 Hz), 8.02 (1H, s); MS m/z (relative intensity) 55 (21), 69 (25), 77 (19), 165 (22), 265 (39), 266 (20), 321 (100), 367 (M^+, 19). Found: C, 68.43; H, 5.63; N, 3.76%. Calcd for $C_{21}H_{21}NO_5$: C, 68.66; H, 5.72; N. 3.81%.

*General Procedure for the Conversion of 3-Nitro-8,8-dimethyl-2-phenyl-7,8-dihydro-2*H*,6*H*-benzo[1,2-*b*:5,4-*b*′]dipyran (**5**—**7**) to 3-Hydroxy-8,8-dimethyl-2-phenyl-7,8-dihydro-4*H*,6*H*-benzo[1,2-*b*:5,4-*b*′]dipyran-4-one (**5a**—**7a**):* To a solution of 3-nitro-8,8-dimethyl-2-phenyl-7,8-dihydro-2*H*,6*H*-benzo[1,2-*b*:5,4-*b*′]-dipyran in methanol (20 ml) were added sodium hydroxide (2 M (1 M=1 mol dm^{-3}), 1 ml) and hydrogen peroxide (2 ml, 15%) while stirring at 35 °C. The stirring was continued for further 18 h. Removal of the solvent and crystallization from ethanol gave the crystalline dihydropyranoflavonol in 70—82% yield. The structures of all the compounds were confirmed by comparison with the literature data.

*3-Hydroxy-8,8-dimethyl-2-phenyl-7,8-dihydro-4*H*,6*H*-benzo-[1,2-*b*:5,4-*b*′]dipyran-4-one (**5a**):* Mp 200—201 °C; lit,[6)] mp 200—201 °C; IR: 1632 (C=O), 3300 (OH) cm^{-1}; NMR: δ=1.42 (6H, s, *gem*-dimethyl), 1.91 (2H, t, J=7 Hz, C_7–H), 2.95 (2H, t, J=7 Hz, C_6–H), 6.95 (1H, s, C_{10}–H), 7.42—7.64 (3H, m, phenyl), 8.0 (1H, s, C_5–H), 8.1—8.32 (2H, m, phenyl); MS m/z (relative intensity) 104 (49), 149 (22), 267 (89), 322 (M^+, 100); UV: λ_{max} (log ε): 263 (4.19), 333 (4.36), 363 (sh) (4.18) nm.

*3-Hydroxy-8,8-dimethyl-2-(4-methylphenyl)-7,8-dihydro-4*H*, 6*H*-benzo[1,2-*b*:5,4-*b*′]dipyran-4-one (**6a**):* Mp 188—190 °C IR: 1635 (C=O), 3250 (OH) cm^{-1}; NMR: δ=1.41 (6H, s, *gem*-dimethyl), 1.9 (2H, t, J=7 Hz, C_7–H), 2.42 (3H, s, methyl), 2.93 (2H, t, J=7 Hz, C_6–H), 6.92 (1H, s, C_{10}–H), 7.34 (2H, d, J=8 Hz, $C_{3'}$–H and $C_{5'}$–H), 9.98 (1H, s, C_5–H), 8.14 (2H, d, J=

8 Hz, $C_{2'}$–H and $C_{6'}$–H); MS *m/z* (relative intensity) 119 (24), 149 (15), 280 (58), 321 (8), 336 (M^+, 100); UV: λ_{max} (log ε) 260 (4.23), 332 (4.26), 351 (4.33), 367 (sh) (4.24) nm.

*3-Hydroxy-8,8-dimethyl-2-(4-methoxyphenyl)-7,8-dihydro-4*H*, 6*H*-benzo[1,2-*b*:5,4-*b*′]dipyran-4-one (**7a**)*: Mp 198—200 °C; lit,[8] mp 199—200 °C; IR: 1630 (C=O), 3300 (OH) cm^{-1}; NMR: δ= 1.42 (6H, s, *gem*-dimethyl); 1.92 (2H, t, *J*=7 Hz, C_7–H), 2.95 (2H, t, *J*=7 Hz, C_6–H), 3.91 (3H, s, methoxy), 6.92 (1H, s, C_{10}–H), 7.03 (2H, d, *J*=9 Hz, $C_{3'}$–H and $C_{5'}$–H), 7.97 (1H, s, C_5–H), 8.2 (2H, d, *J*=9 Hz, $C_{2'}$–H and $C_{6'}$–H); MS *m/z* (relative intensity) 135 (29), 149 (18), 296 (13), 298 (10), 337 (5), 352 (M^+, 100); UV: λ_{max} (log ε): 262 (4.2), 332 (4.35), 358 (4.38) nm.

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