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Highly regio- and stereoselective addition of ethyl 3-aminobut-2-enoates to 2-substituted 3-nitro-2*H*-chromenes

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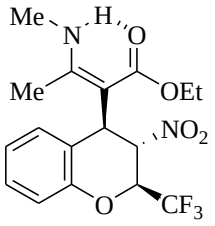
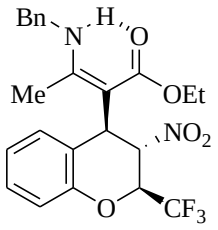
*Characteristics of compounds tt-***3b–h**, *ct-***6a,c,d** *and ct-***7b,c**.

† NMR spectra were recorded for $CDCl_3$ solutions of compounds at 400 MHz for ^1H, 126 MHz for ^{13}C and 376 MHz for ^{19}F.



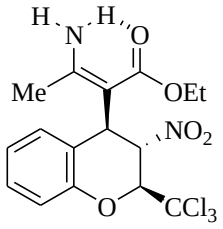
3b

Ethyl tt-(Z)-3-methylamino-2-[3-nitro-2-(trifluoromethyl)-3,4-dihydro-2H-chromen-4-yl]-2-butenoate **3b**. Yield 38%, mp 110–111 °C (decomp.), white powder. IR (KBr): 3228, 3157, 1651, 1596, 1561, 1486, 1457, 1372 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.80 (t, 3H, Me, *J* = 7.1 Hz), 2.03 (s, 3H, Me), 2.97 (d, 3H, MeN, *J* = 5.1 Hz), 3.82 (dq, 1H, OC*H*H, *J* = 10.7, 7.1 Hz), 3.90 (dq, 1H, OCH*H*, *J* = 10.7, 7.1 Hz), 4.63 (d, 1H, H-4, *J* = 10.3 Hz), 4.86 (dq, 1H, H-2, *J* = 10.2, 5.3 Hz), 5.52 (t, 1H, H-3, *J* = 10.2 Hz), 6.92–6.96 (m, 2H, H-6, H-8), 7.03 (br d, 1H, H-5, *J* = 7.6 Hz), 7.15 (br t, 1H, H-7, *J* = 7.6 Hz), 9.82 (br s, 1H, NH); ^{19}F NMR (376 MHz, $CDCl_3$) δ 84.4 (d, CF_3, *J* = 5.3 Hz), 84.6 (d, CF_3, *J* = 4.9 Hz) (6%). Found: C, 52.46; H, 4.90; N, 7.21. Calc. for $C_{17}H_{19}F_3N_2O_5$: C, 52.58; H, 4.93; N, 7.21.



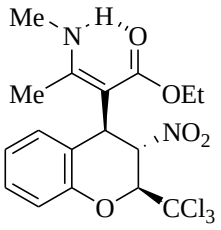
3c

Ethyl tt-(Z)-3-(benzylamino)-2-[3-nitro-2-(trifluoromethyl)-3,4-dihydro-2H-chromen-4-yl]-2-butenoate **3c**. Yield 0.33 g (70%), mp 67–68 °C (decomp.), white powder. IR (KBr): 3257, 1648, 1599, 1583, 1559, 1484, 1454, 1368 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.81 (t, 3H, Me, *J* = 7.1 Hz), 2.02 (s, 3H, Me), 3.83 (dq, 1H, OC*H*H, *J* = 10.7, 7.1 Hz), 3.92 (dq, 1H, OCH*H*, *J* = 10.7, 7.1 Hz), 4.49 (d, 2H, CH_2, *J* = 5.9 Hz), 4.64 (d, 1H, H-4, *J* = 10.3 Hz), 4.86 (dq, 1H, H-2, *J* = 10.1, 5.3 Hz), 5.54 (t, 1H, H-3, *J* = 10.1 Hz), 6.93–6.99 (m, 2H, H-6, H-8), 7.04 (br d, 1H, H-5, *J* = 7.5 Hz), 7.16 (br t, 1H, H-7, *J* = 7.5 Hz), 7.23–7.40 (m, 5H, Ph), 10.24 (t, 1H, NH, *J* = 5.0 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ 84.5 (d, CF_3, *J* = 5.3 Hz), 84.6 (d, CF_3, *J* = 4.9 Hz) (5%). Found: C, 59.58; H, 5.11; N, 5.86. Calc. for $C_{23}H_{23}F_3N_2O_5$: C, 59.48; H, 4.99; N, 6.03.



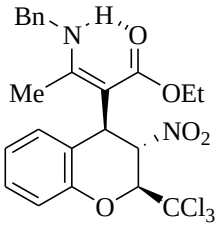
3d

Ethyl tt-(Z)-3-amino-2-[3-nitro-2-(trichloromethyl)-3,4-dihydro-2H-chromen-4-yl]-2-butenoate **3d**. Yield 0.24 g (58%), mp 143–144 °C (decomp.), colourless prisms. IR (KBr): 3449, 3313, 1656, 1613, 1589, 1566, 1552, 1516, 1486, 1456, 1365 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.95 (t, 3H, Me, *J* = 7.1 Hz), 2.01 (s, 3H, Me), 3.96 (dq, 1H, OC*H*H, *J* = 10.7, 7.1 Hz), 4.09 (dq, 1H, OCH*H*, *J* = 10.7, 7.1 Hz), 4.45 (d, 1H, H-4, *J* = 10.8 Hz), 4.7–5.1 (br s, 1H, N*H*H), 5.40 (d, 1H, H-2, *J* = 7.9 Hz), 5.76 (dd, 1H, H-3, *J* = 10.8, 7.9 Hz), 6.95–7.05 (m, 3H, H-5, H-6, H-8), 7.21 (dddd, 1H, H-7, *J* = 8.2, 7.2, 2.0, 0.7 Hz), 8.9–9.2 (br s, 1H, NH*H*). Found: C, 45.39; H, 4.11; N, 6.53. Calc. for $C_{16}H_{17}Cl_3N_2O_5$: C, 45.36; H, 4.04; N, 6.61.



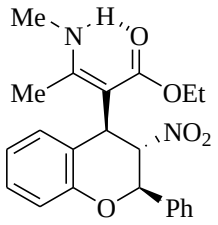
3e

Ethyl tt-(Z)-3-methylamino-2-[3-nitro-2-(trichloromethyl)-3,4-dihydro-2H-chromen-4-yl]-2-butenoate **3e**. Yield 76%, mp 116–117 °C (decomp.), white powder. IR (KBr): 3243, 3152, 1644, 1587, 1561, 1552 1483, 1453, 1366 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.92 (t, 3H, Me, *J* = 7.1 Hz), 1.99 (s, 3H, Me), 2.97 (d, 3H, MeN, *J* = 5.1 Hz), 3.92 (dq, 1H, OC*H*H, *J* = 10.7, 7.1 Hz), 4.06 (dq, 1H, OCH*H*, *J* = 10.7, 7.1 Hz), 4.52 (d, 1H, H-4, *J* = 10.8 Hz), 5.39 (d, 1H, H-2, *J* = 7.9 Hz), 5.76 (dd, 1H, H-3, *J* = 10.8, 7.9 Hz), 6.94–7.05 (m, 3H, H-5, H-6, H-8), 7.19 (t, 1H, H-7, *J* = 7.8 Hz), 9.98 (br s, 1H, NH). Found: C, 46.57; H, 4.25; N, 6.52. Calc. for $C_{17}H_{19}Cl_3N_2O_5$: C, 46.65; H, 4.38; N, 6.40.



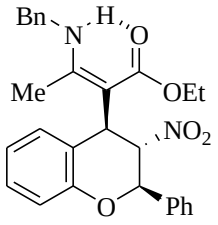
3f

Ethyl tt-(Z)-3-(benzylamino)-2-[3-nitro-2-(trichloromethyl)-3,4-dihydro-2H-chromen-4-yl]-2-butenoate **3f**. Yield 0.37 g (73%), mp 101–102 °C (decomp.), white powder. IR (KBr): 3272, 1639, 1597, 1587, 1559, 1483, 1458, 1432, 1364 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.92 (t, 3H, Me, *J* = 7.1 Hz), 1.98 (s, 3H, Me), 3.93 (dq, 1H, OC*H*H, *J* = 10.7, 7.1 Hz), 4.07 (dq, 1H, OCH*H*, *J* = 10.7, 7.1 Hz), 4.50 (d, 2H, CH_2, *J* = 5.8 Hz), 4.54 (d, 1H, H-4, *J* = 10.7 Hz), 5.39 (d, 1H, H-2, *J* = 8.0 Hz), 5.77 (dd, 1H, H-3, *J* = 10.7, 8.0 Hz), 6.96–7.06 (m, 3H, H-5, H-6, H-8), 7.20 (t, 1H, H-7, *J* = 7.5 Hz), 7.25–7.40 (m, 5H, Ph), 10.40 (t, 1H, NH, *J* = 5.8 Hz). Found: C, 53.79; H, 4.34; N, 5.43. Calc. for $C_{23}H_{23}Cl_3N_2O_5$: C, 53.77; H, 4.51; N, 5.45.



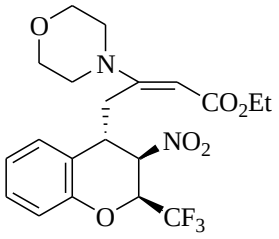
3g

Ethyl tt-(Z)-3-(methylamino)-2-[3-nitro-2-phenyl-3,4-dihydro-2H-chromen-4-yl]-2-butenoate **3g**. Yield 64%, mp 148–149 °C, white powder. IR (KBr): 3251, 1640, 1599, 1549, 1483, 1453, 1372 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.86 (t, 3H, Me, *J* = 7.1 Hz), 2.09 (s, 3H, Me), 2.95 (d, 3H, MeN, *J* = 5.0 Hz), 3.85 (dq, 1H, OC*H*H, *J* = 10.6, 7.1 Hz), 3.90 (dq, 1H, OCH*H*, *J* = 10.6, 7.1 Hz), 4.84 (d, 1H, H-4, *J* = 10.1 Hz), 5.23 (d, 1H, H-2, *J* = 9.8 Hz), 5.52 (t, 1H, H-3, *J* = 10.0 Hz), 6.90 (d, 1H, H-8, *J* = 8.0 Hz), 6.91 (t, 1H, H-6, *J* = 7.2 Hz), 7.08 (d, 1H, H-5, *J* = 8.0 Hz), 7.12 (t, 1H, H-7, *J* = 7.2 Hz), 7.38–7.45 (m, 5H, Ph), 9.73 (br q, 1H, NH, *J* = 5.0 Hz). Found: C, 66.39; H, 5.96; N, 7.02. Calc. for $C_{22}H_{24}N_2O_5$: C, 66.65; H, 6.10; N, 7.07.



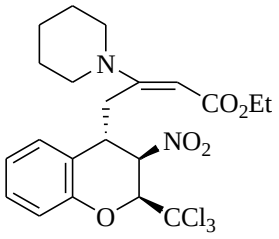
3h

Ethyl tt-(Z)-3-(benzylamino)-2-[3-nitro-2-phenyl-3,4-dihydro-2H-chromen-4-yl]-2-butenoate **3h**. Yield 37%, mp 134–135 °C (decomp.), white powder. IR (KBr): 3241, 1646, 1595, 1581, 1549, 1484, 1452, 1370 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.87 (t, 3H, Me, *J* = 7.1 Hz), 2.08 (s, 3H, Me), 3.86 (dq, 1H, OC*H*H, *J* = 10.7, 7.1 Hz), 3.92 (dq, 1H, OCH*H*, *J* = 10.7, 7.1 Hz), 4.49 (d, 2H, CH_2, *J* = 6.0 Hz), 4.85 (d, 1H, H-4, *J* = 10.2 Hz), 5.23 (d, 1H, H-2, *J* = 9.8 Hz), 5.53 (t, 1H, H-3, *J* = 10.0 Hz), 6.91 (d, 1H, H-8, *J* = 8.2 Hz), 6.93 (t, 1H, H-6, *J* = 7.4 Hz), 7.08 (d, 1H, H-5, *J* = 7.5 Hz), 7.13 (t, 1H, H-7, *J* = 7.8 Hz), 7.25–7.40 (m, 5H, Ph), 7.40–7.45 (m, 5H, Ph), 10.14 (t, 1H, NH, *J* = 6.0 Hz). Found: C, 70.95; H, 5.89; N, 5.86. Calc. for $C_{28}H_{28}N_2O_5$: C, 71.17; H, 5.97; N, 5.93.



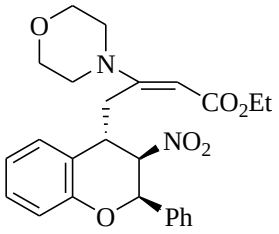
6a

Ethyl ct-(E)-4-[3-nitro-2-(trifluoromethyl)-3,4-dihydro-2H-chromen-4-yl]-3-morpholino-2-butenoate **6a**. Yield 0.36 g (79%), mp 174–175 °C (decomp.), white powder. IR (KBr): 1677, 1585, 1557, 1495, 1481, 1449, 1394, 1379 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.24 (t, 3H, Me, *J* = 7.1 Hz), 2.79 (dd, 1H, H-4′a, *J* = 15.3, 4.4 Hz), 3.22 (dt, 2H, N(C*H*H)$_2$, *J* = 12.8, 4.9 Hz), 3.33 (dt, 2H, N(CH*H*)$_2$, *J* = 12.8, 4.9 Hz), 3.39 (dd, 1H, H-4, *J* = 12.2, 4.4 Hz), 3.76 (t, 4H, O(CH_2)$_2$, *J* = 4.9 Hz), 4.05 (dq, 1H, OC*H*H, *J* = 10.9, 7.1 Hz), 4.12 (dq, 1H, OCH*H*, *J* = 10.9, 7.1 Hz), 4.18 (dd, 1H, H-4′b, *J* = 15.3, 12.2 Hz), 5.06 (s, 1H, H-2′), 5.15 (br s, 1H, H-3), 5.20 (qd, 1H, H-2, *J* = 6.0, 1.4 Hz), 7.06 (td, 1H, H-6, *J* = 7.5, 1.2 Hz), 7.07 (d, 1H, H-8, *J* = 8.2, 1.2 Hz), 7.17 (d, 1H, H-5, *J* = 7.7 Hz), 7.26 (ddd, 1H, H-7, *J* = 8.2, 7.3, 1.5 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ 86.7 (d, CF_3, *J* = 6.0 Hz), 86.9 (d, CF_3, *J* = 5.9 Hz) (3%). Found: C, 54.12; H, 5.11; N, 6.34. Calc. for $C_{20}H_{23}F_3N_2O_6$: C, 54.05; H, 5.22; N, 6.30.



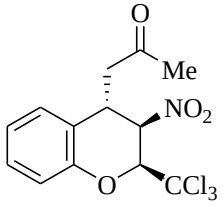
6c

Ethyl ct-(E)-4-[3-nitro-2-(trichloromethyl)-3,4-dihydro-2H-chromen-4-yl]-3-piperidino-2-butenoate **6c**. Yield 0.26 g (54%), mp 171–172 °C (decomp.), white powder. IR (KBr): 1678, 1588, 1554, 1488, 1456, 1397, 1377 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.23 (t, 3H, Me, *J* = 7.1 Hz), 1.54–1.72 (m, 6H, 3CH_2), 2.84 (dd, 1H, H-4′a, *J* = 15.4, 4.5 Hz), 3.26–3.42 (m, 5H, H-4, N(CH_2)$_2$), 4.04 (dq, 1H, OC*H*H, *J* = 10.9, 7.1 Hz), 4.08 (dq, 1H, OCH*H*, *J* = 10.9, 7.1 Hz), 4.45 (br t, 1H, H-4′b, *J* = 13.6 Hz), 5.02 (s, 1H, H-2′), 5.26 (s, 1H, H-2), 5.57 (s, 1H, H-3), 7.06 (t, 1H, H-6, *J* = 7.6 Hz), 7.12 (d, 1H, H-8, *J* = 8.1 Hz), 7.22 (d, 1H, H-5, *J* = 7.6 Hz), 7.26 (t, 1H, H-7, *J* = 7.5 Hz). Found: C, 51.19; H, 5.08; N, 5.67. Calc. for $C_{27}H_{25}Cl_3N_2O_5$: C, 51.29; H, 5.12; N, 5.70.



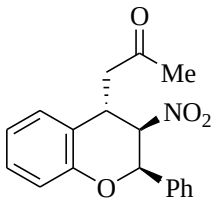
6d

Ethyl ct-(E)-3-morpholino-4-(3-nitro-2-phenyl-3,4-dihydro-2H-chromen-4-yl)-2-butenoate **6d**. Yield 63%, mp 178–179 °C (decomp.), white powder. IR (KBr): 1685, 1584, 1549, 1489, 1451, 1391, 1377 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.31 (t, 3H, Me, *J* = 7.1 Hz), 2.83 (dd, 1H, H-4′a, *J* = 15.3, 4.0 Hz), 3.20 (m, 2H, $N(CHH)_2$, *J* = 12.8, 5.0 Hz), 3.36 (dt, 2H, $N(CHH)_2$, *J* = 12.8, 5.0 Hz), 3.45 (dd, 1H, H-4, *J* = 12.3, 4.0 Hz), 3.68–3.78 (m, 4H, $O(CH_2)_2$), 4.15 (dq, 1H, OC*H*H, *J* = 10.8, 7.1 Hz), 4.20 (dq, 1H, OCH*H*, *J* = 10.8, 7.1 Hz), 4.43 (dd, 1H, H-4′b, *J* = 15.3, 12.3 Hz), 5.06 (d, 1H, H-2, *J* = 1.9 Hz), 5.07 (s, 1H, H-2′), 5.78 (d, 1H, H-3, *J* = 1.9 Hz), 7.03 (t, 1H, H-6, *J* = 7.6 Hz), 7.06 (d, 1H, H-8, *J* = 8.4 Hz), 7.20–7.27 (m, 2H, H-5, H-7), 7.34–7.53 (m, 5H, Ph). Found: C, 66.42; H, 6.34; N, 6.24. Calc. for $C_{25}H_{28}N_2O_6$: C, 66.36; H, 6.24; N, 6.19.



7b

ct-1-[3-Nitro-2-(trichloromethyl)-3,4-dihydro-2H-chromen-4-yl]acetone **7b**. Yield 0.20 g (56%), mp 79–80 °C (hexane), white powder. IR (KBr): 1717, 1591, 1559, 1487, 1371 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.25 (s, 3H, Me), 2.78 (dd, 1H, C*H*HAc, *J* = 18.8, 9.8 Hz), 3.06 (dd, 1H, CH*H*Ac, *J* = 18.8, 3.8 Hz), 3.96 (dd, 1H, H-4, *J* = 9.8, 3.5 Hz), 4.46 (s, 1H, H-2), 5.56 (s, 1H, H-3), 7.04–7.18 (m, 3H, Ar), 7.24–7.30 (m, 1H, Ar); ^{13}C NMR (126 MHz, $CDCl_3$) δ 30.2, 35.5, 50.4, 79.6, 80.7, 95.5, 117.3, 120.9, 123.2, 128.5, 128.7, 152.7, 204.0 (C=O). Found: C, 44.31; H, 3.23; N, 3.72. Calc. for $C_{13}H_{12}Cl_3NO_4$: C, 44.28; H, 3.43; N, 3.97.



7c

ct-1-[3-Nitro-2-phenyl-3,4-dihydro-2H-chromen-4-yl]acetone **7c**. Yield 0.26 g (82%), mp 185–186 °C (dichloromethane–hexane, 2:1), white powder. IR (KBr): 1710, 1587, 1545, 1490, 1371 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.27 (s, 3H, Me), 2.92 (dd, 1H, C*H*HAc, *J* = 18.4, 9.8 Hz), 3.13 (dd, 1H, CH*H*Ac, *J* = 18.4, 4.0 Hz), 3.98 (dd, 1H, H-4, *J* = 9.8, 4.0 Hz), 5.04 (t, 1H, H-3, *J* = 2.0 Hz), 5.26 (d, 1H, H-2, *J* = 2.1 Hz), 7.00–7.06 (m, 2H, H-6, H-8), 7.17 (dd, 1H, H-5, *J* = 8.3, 1.4 Hz), 7.23 (ddd, 1H, H-7, *J* = 8.7, 7.3, 1.4 Hz), 7.35–7.45 (m, 5H, Ph). Found: C, 69.40; H, 5.54; N, 4.44. Calc. for $C_{18}H_{17}NO_4$: C, 69.44; H, 5.50; N, 4.50.