Diene-transmissive hetero-Diels–Alder reaction of 2-vinyl $\alpha,\beta$-unsaturated aldimines: stereoselective synthesis of hexahydroquinazolin-2-ones

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Supplementary information

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General information

All melting points were determined on a Yanaco melting point apparatus and are uncorrected. Infrared spectra were recorded on a Hitachi 270-30 or a Horiba FT-710 model spectrophotometer. $^1$H and $^{13}$C NMR spectral data were obtained with a Bruker Avance-600, a JEOL JNM-EX 500, or a JEOL JNM-EX 300 instrument and chemical shifts are reported in ppm down field from tetramethylsilane (TMS) using an internal standard of TMS or CDCl$_3$. HRMS analysis were performed on a Bruker Daltonics microTOF or a Hitachi double-focusing M-80B spectrometer. Elemental analyses were performed with a YANACO CHN-CODER MT-6 model analyzer.

Experimental Procedure

2-Benzylidene-4-phenylbut-3-enal (1a)

A mixture of $\alpha$-bromocinnamaldehyde (10.0 g, 47.4 mmol), tri(o-tolyl)phosphine (1.44 g, 4.73 mmol), styrene (6.17 g, 59.2 mmol), palladium(II) acetate (531 mg, 2.37 mmol), and triethylamine (20.0 g, 198 mmol) was heated at 80 °C for 8 h. The mixture was condensed under reduced pressure, and the residue was purified by column chromatography on silica gel with to give aldehyde 1a (7.32 g, 66%) as yellow solid; mp 66–68 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 6.98 (ddd, 1H, $J$ = 1.0, 2.0, 10.5 Hz), 7.25–7.29 (m, 4H), 7.40 –7.49 (m, 5H), 7.54–7.57 (m, 2H), 7.67 (d, 1H, $J$ = 16.6 Hz), 9.76 (d, 1H, $J$ = 2.0 Hz); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 119.20 (CH), 126.77 (3CH), 128.20 (CH), 128.66 (CH), 128.76 (2CH), 129.82 (CH), 130.29 (2CH), 135.03 (C), 135.90 (CH), 136.19 (C), 137.30 (C), 149.85 (CH), 194.09 (C); LRMS-FAB m/z (ion, % relative intensity): 235 ([M+H]$^+$, 100), 205 (62), 154 (40), 91 (54); HRMS-EI m/z [M$^+$] calcd for C$_{17}$H$_{14}$O: 234.1045, found: 234.1054.

4-Formyl-5-phenylpenta-2,4-dienoic acid methyl ester (1b)

To a solution of $\alpha$-bromocinnamaldehyde (1.0 g, 4.7 mmol) in toluene (50 mL) was added (2E)-3-(tributylstannyl)-2-propenoic acid methyl ester$^{S1}$ (2.11 g, 5.91 mmol) and Pd(PPh$_3$)$_4$ (277 mg, 0.24 mmol, 5 mol %), and the mixture was heated at 110 °C for 45 h. The mixture was condensed under reduced pressure, and the residue was purified by silica gel column chromatography to yield aldehyde 1b (941 mg, 92%) as yellow oil; IR (NaCl): 1678 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.79 (s, 3H, Me), 7.02 (d, 1H, $J$ = 16.1 Hz), 7.47 –7.60 (m, 7H), 9.73 (d, 1H, $J$ = 2.4 Hz); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 51.79 (CH$_3$), 125.12 (CH), 129.00 (2CH), 130.62 (2CH), 130.89 (CH), 133.86 (C), 133.93 (C), 134.37 (CH), 154.69 (CH), 167.56 (C), 192.00 (CH) ; HRMS-ESI calcd for C$_{13}$H$_{12}$O$_3$Na$^+$ [M+Na$^+$]: 239.0678, found: 239.0679.

1,4-Diphenyl-5-styryl-3-(toluene-4-sulfonyl)-3,4-dihydro-1$H$-pyrimidin-2-one (3a)

To a 1,2-dichloroethane (10 mL) solution of aldehyde 1 (100 mg, 0.43 mmol), aniline (48.4 mg, 0.52 mmol), and triethylamine (191 mg, 1.89 mmol) cooled by an ice bath, was added a 1.0 M dichloromethane solution of titanium tetrachloride (0.43 mL, 0.43 mmol). After the ice bath was removed, the mixture was stirred for 30 min, and then tosyl isocyanate (0.10 mL, 0.65 mmol) was added. The mixture was heated at 80 °C for 5 h, and the reaction was quenched by aqueous sodium hydrogen carbonate. The mixture was extracted with dichloromethane, dried over anhydrous magnesium sulfate, and then evaporated. The residue was purified by column chromatography on silica gel with AcOEt/hexane (1/3, v/v) as an eluent to yield 3a (211 mg, 97%) as colorless crystals; mp 204–206 °C; IR (KBr): 1652, 1590, 1484, 1344, 1162 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 2.29 (s, 3H, Me), 6.52 (s, 1H, H-6), 6.53 (d, 1H, $J$ = 13.4 Hz, H-4), 6.61 (d, 2H, $J$ = 13.4 Hz, H-7=H-8), 7.01 (d, 2H, $J$ = 8.1 Hz, Ar), 7.18–7.43 (m, 15H, Ar), 7.53–7.55 (m, 2H, Ar); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 21.51 (CH$_3$), 58.94 (CH), 118.69 (C), 122.97 (CH), 126.13 (2CH), 126.40 (2CH), 127.58 (2CH), 127.60 (CH), 127.61 (CH), 129.00 (2CH), 130.89 (CH), 133.86 (C), 133.93 (C), 134.37 (CH), 154.69 (CH), 167.56 (C), 192.00 (CH) ; HRMS-ESI calcd for C$_{13}$H$_{12}$O$_3$Na$^+$ [M+Na$^+$]: 239.0678, found: 239.0679.

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4-Phenyl-5- styryl-3-(toluene-4-sulfonyl)-1-p-tolyl-3,4-di hydro-1H-pyrimidin-2-one (3b)

Colorless crystals; mp 135–137 °C; IR (KBr): 1650, 1344, 1162 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 2.29 (s, 3H, Me (Ts)), 2.34 (s, 3H, Me (Ts)), 6.49 (s, 1H, H-4), 6.54 (s, 1H, H-6), 6.58 (d, 1H, J = 16.2 Hz, H-7), 6.63 (d, 1H, J = 16.2 Hz, H-8), 7.00 (d, 2H, J = 8.2 Hz, Ar), 7.18–7.36 (m, 14H, Ar), 7.51–7.54 (m, 2H, Ar); ¹³C NMR (126 MHz, CDCl₃) δ 21.00 (CH3), 21.44 (CH3), 58.90 (CH), 118.48 (C), 123.06 (CH), 126.12 (CH), 126.17 (CH), 127.49 (CH), 127.53 (CH), 127.56 (2CH), 128.30 (CH), 128.62 (2CH), 128.76 (3CH), 128.92 (2CH), 129.07 (2CH), 129.86 (2CH), 132.62 (C), 136.69 (C), 136.83 (C), 137.88 (C), 139.47 (C), 144.01 (C), 148.79 (C); LRMS-FAB m/z (ion, % relative intensity): 521 ([M+H⁺], 100), 366 ([M–Ts⁻], 12), 324 ([M–TsNCO]⁻, 39), 289 (13), 246 (36), 185 (13), 154 (42); HRMS-FAB m/z [M+H⁺] calcd for C₃₁H₂₇N₂O₃S: 521.1989, found: 521.1989.

1-Benzyl-4-phenyl-5-styryl-3-(toluene-4-sulfonyl)-3,4-di hydro-1H-pyrimidin-2-one (3c)

Colorless crystals; mp 181–183 °C; IR (KBr): 1638, 1594, 1340, 1160 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 2.35 (s, 3H, Me), 4.65 (d, 1H, J = 14.9 Hz, CH₂ (Bn)), 4.76 (d, 1H, J = 14.9 Hz, CH₂ (Bn)), 6.25 (s, 1H, H-4), 6.48 (d, 1H, J = 16.3 Hz, H-7), 6.50 (s, 1H, H-6), 6.57 (d, 1H, J = 16.3 Hz, H-8), 7.10–7.19 (m, 5H, Ar), 7.24–7.39 (m, 10H, Ar), 7.37–7.39 (m, 2H, Ar), 7.47 (d, 2H, J = 8.5 Hz, Ar); ¹³C NMR (100 MHz, CDCl₃) δ 21.57 (CH₃), 50.15 (CH₂), 58.33 (CH), 118.48 (C), 123.20 (CH), 126.08 (2CH), 126.71 (CH), 127.19 (CH), 127.48 (2CH), 127.49 (CH), 127.97 (CH), 128.03 (CH), 128.60 (2CH), 128.65 (CH), 128.72 (2CH), 128.82 (2CH), 128.93 (CH), 128.95 (2CH), 135.89 (2CH), 135.90 (C), 136.36 (C), 136.75 (C), 139.07 (C), 144.18 (C), 149.56 (C); LRMS-FAB m/z (ion, % relative intensity): 521 ([M+H⁺], 93), 366 ([M–Ts⁻], 12), 324 ([M–TsNCO]⁻, 21), 246 (23), 185 (60), 154 (78); HRMS-FAB m/z [M+H⁺] calcd for C₃₂H₂₉N₂O₃S: 521.1989, found: 521.1902.

3-[1-Benzyl-2-oxo-4-phenyl-3-(toluene-4-sulfonyl)-1,2,3,4-tetra hydropropyrimidin-5-yl]acrylic acid methyl ester (3d)

Colorless crystals; mp 178–180 °C; IR (KBr): 1678, 1612, 1344, 1160 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 2.34 (s, 3H, Me (Ts)), 3.67 (s, 3H, Me (CO₂Me)), 4.67 (d, 1H, J = 15.0 Hz, CH₂ (Bn)), 4.78 (d, 1H, J = 15.0 Hz, CH₂ (Bn)), 5.79 (d, 1H, J = 15.9 Hz, H-8), 6.30 (s, 1H, H-4), 6.50 (s, 1H, H-6), 7.07–7.18 (m, 5H, H-7+Ar), 7.25–7.31 (m, 8H, Ar), 7.39 (d, 2H, J = 8.2 Hz, Ar); ¹³C NMR (126 MHz, CDCl₃) δ 21.54 (CH₃), 50.41 (CH₂), 51.53 (CH₃), 58.39 (CH), 115.36 (CH), 115.92 (C), 127.51 (2CH), 128.08 (2CH), 128.34 (CH), 128.81 (2CH), 128.92 (2CH), 128.95 (CH), 128.98 (2CH), 129.04 (2CH), 133.01 (CH), 135.38 (C), 139.97 (C), 138.50 (C), 139.35 (CH), 144.38 (C), 149.13 (C), 167.05 (C); LRMS-EI 502 ([M⁺], 1.4), 471 ([M–OMe]⁺, 3), 425 (3), 347 ([M–Ts⁻], 51), 246 (14), 91 (100); HRMS-EI calcd for C₃₂H₂₉N₂O₃S [M⁺]: 502.1562, found: 502.1568.

2-Oxo-1,4,6,6-tetraphenyl-3-(toluene-4-sulfonyl)-1,2,3,4,6,8a-hexahydroquinazoline-7,7,8,8-tetracarbonitrile (4a)

To a solution of 3a (100 mg, 0.18 mmol) in dichloromethane (5 mL) was added tetracyanoethylene 38.4 mg (0.30 mmol). The mixture was stirred for 4 h at room temperature, and then condensed under reduced pressure. The residue was purified by column chromatography on silica gel with EtOAc/Hex (1/3, v/v) as an eluent to yield 4a (101.6 mg, 90%) as colorless crystals; mp 166–168 °C; IR (KBr): 1682, 1594, 1488, 1366, 1168 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 2.46 (s, 3H, Me), 4.65 (dd, 1H, J = 2.4, 4.0 Hz, H-6), 4.86 (dd, 1H, J = 2.4, 2.4 Hz, H-8a), 6.57 (s, 1H, H-4), 6.68 (dd, 1H, J = 2.4, 4.0 Hz, H-5), 6.80 (d, 2H, J = 2.4, 4.0 Hz, H-6), 7.26 (s, 1H, J = 8.0 Hz, H-7), 7.39 (d, 2H, J = 8.0 Hz, H-8), 7.46 (d, 2H, J = 8.0 Hz, H-9).
128.17 (CH), 128.43 (CH), 128.51 (2CH), 128.62 (2CH), 128.68 (2CH), 128.85 (2CH), 128.86 (2CH), 128.89 (2CH), 129.25 (2CH), 129.31 (3CH), 129.18 (CH), 129.64 (2CH), 129.92 (3CH), 130.10 (130.19 (CH), 131.47 (2CH), 135.00 (C), 135.40 (C), 136.48 (2C), 145.57 (C), 149.63 (C); LRMS-FAB m/z (ion, % relative intensity): 635 ([M+H]+, 69), 507 ([M–TCNE]–, 16), 310 (27), 246 (18), 232 (17), 185 (30); Anal. Calcd. for C37H26N6O3S: C, 70.02; H, 4.13; N, 13.24; Found: C, 69.62; H, 3.97, N, 13.12.

2-Oxo-4,6-diphenyl-3-(toluene-4-sulfonyl)-1-p-tolyl-1,2,3,4,6,8a-hexahydroquinazoline-7,7,8,8-tetracarbonitrile (4b)

Colorless crystals; mp 152–154 °C; IR (KBr): 1686, 1594, 1390, 1386, 1166 cm–1; 1H NMR (400 MHz, CDCl3) δ 2.29 (s, 3H, Me (p-Tol)), 2.46 (s, 3H, Me (Ts)), 4.64 (dd, 1H, J = 2.4, 3.9 Hz, H-6), 4.82 (dd, 1H, J = 2.4, 2.4 Hz, H-8a), 6.59 (s, 1H, H-4), 6.67 (dd, 1H, J = 2.4, 3.9 Hz, H-5), 6.69 (2H, J = 6.6 Hz, Ar), 7.09 (2H, J = 8.3 Hz, Ar), 7.14 (dd, 2H, J = 1.0, 7.1 Hz, Ar), 7.32 (2H, J = 8.3 Hz, Ar), 7.39–7.57 (m, 8H, Ar), 7.97 (2H, J = 8.3 Hz, Ar); 13C NMR (100 MHz, CDCl3) δ 21.19 (CH3), 21.72 (CH3), 40.82 (C), 43.73 (C), 47.47 (CH), 61.14 (CH), 61.78 (2CH), 107.17 (C), 108.95 (C), 109.11 (C), 111.19 (C), 124.28 (CH), 124.99 (2CH), 128.08 (CH), 128.99 (2CH), 129.10 (2CH), 129.56 (2CH), 129.83 (2CH), 130.15 (C), 130.23 (C), 130.45 (2CH), 130.90 (2CH), 131.43 (2CH), 134.04 (C), 134.99 (C), 135.36 (C), 140.40 (C), 145.47 (C), 149.71 (C); LRMS-FAB m/z (ion, % relative intensity): 649 ([M+H]+, 59), 520 (19), 324 (21), 289 (10), 246 (26), 185 (66); HRMS-FAB m/z [M+H]+ calcd for C38H28N6O3S: 649.2022; found: 649.2025.

1-Benzyl-2-oxo-4,6-diphenyl-3-(toluene-4-sulfonyl)-1,2,3,4,6,8a-hexahydroquinazoline-7,7,8,8-tetracarbonitrile (4c)

Colorless crystals; mp 123–125 °C; IR (KBr): 1688, 1364, 1170 cm–1; 1H NMR (500 MHz, CDCl3) δ 2.49 (s, 3H, Me), 4.34 (d, 1H, J = 15.9 Hz, CH2 (Bn)), 4.36 (dd, 1H, J = 2.8, 2.8 Hz, H-6), 4.58 (dd, 1H, J = 2.8, 2.8 Hz, H-8a), 5.32 (d, 1H, J = 15.9 Hz, CH2 (Bn)), 6.42 (s, 1H, H-4), 6.43 (d, 2H, J = 7.3 Hz, Ar), 6.57 (dd, 1H, J = 2.8, 2.8 Hz, H-5), 6.96 (dd, 2H, J = 7.3, 7.3 Hz, Ar), 7.11–7.14 (m, 3H, Ar), 7.26–7.54 (m, 10H, Ar), 8.09 (2H, J = 8.2 Hz, Ar); 13C NMR (126 MHz, CDCl3) δ 21.79 (CH3), 41.95 (C), 45.44 (C), 47.30 (CH), 48.89 (CH2), 56.26 (CH), 61.58 (CH), 107.54 (C), 108.93 (C), 110.77 (C), 111.54 (C), 125.10 (2CH), 126.55 (CH), 128.28 (CH), 128.73 (2CH), 128.76 (CH), 128.89 (2CH), 129.37 (2CH), 129.41 (2CH), 129.66 (2CH), 129.92 (2CH), 130.45 (2CH), 130.81 (CH), 131.80 (C), 131.92 (C), 132.58 (C), 134.75 (C), 135.41 (C), 145.76 (C), 151.34 (C); LRMS-FAB m/z (ion, % relative intensity): 649 ([M+H]+, 9), 635 (54), 507 ([M–TCNE]–, 16), 310 (31), 232 (24), 185 (35), 154 (100); Anal. Calcd. for C39H29N6O3S: C, 70.35; H, 4.35; N, 12.95. Found: C, 70.38; H, 4.16; N, 13.08.

2,4,6,9-Tetraphenyl-7-(toluene-4-sulfonyl)-3a,6,7,9a,9b-hexahydro-4H-2,2,7,9-triazacyclopenta[a]naphthalene-1,3,8-trione (5a)

A solution of 4a (100 mg, 0.20 mmol), N-phenylmaleimide (52 mg, 0.30 mmol) in toluene (5 mL) was heated at 110 °C for 9 h. The mixture was condensed under reduced pressure, and the residue was purified by silica gel chromatography with AcOEt/Hex (1/2, v/v) as an eluent to yield 5a (119.6 mg, 88%) as a colorless solid; mp 293–294 °C; IR (KBr): 1688, 1372, 1260, 1164, 1086, 1014 cm–1; 1H NMR (400 MHz, CDCl3) δ 2.32 (s, 3H, Me (Ts)), 3.36 (m, 2H, H-9b=H-4), 3.62 (dd, 1H, J = 4.2, 4.2 Hz, H-3a), 4.42 (dd, 1H, J = 3.2, 2.7 Hz, H-9a), 6.45 (s, 1H, H-6), 6.63 (dd, 1H, J = 3.2, 2.7 Hz, H-5), 7.03 (d, 2H, J = 8.3 Hz, Ar), 7.12 (d, 2H, J = 7.6 Hz, Ar), 7.21–7.46 (m, 18H, Ar), 7.75 (d, 2H, J = 8.2 Hz, Ar); 13C NMR (100 MHz, CDCl3) δ 21.54 (CH3), 40.88 (CH), 41.56 (CH), 44.59 (CH), 58.67 (CH), 61.34 (CH), 124.42 (CH), 125.75 (2CH), 126.42 (2CH), 127.54 (CH), 127.94 (CH), 128.17 (CH), 128.43 (CH), 128.51 (2CH), 128.62 (2CH), 128.68 (2CH), 128.85 (2CH), 128.86 (2CH), 128.89 (2CH), 129.25 (2CH), 129.31 (2CH), 131.36 (C), 136.01 (C), 137.08 (C), 137.62 (C), 137.92 (C), 139.34 (C), 141.14 (C), 151.46 (C), 173.11 (C), 173.72 (C); LRMS-FAB m/z
2,4,6-Triphenyl-7-(toluene-4-sulfonyl)-9-p-tolyl-3a,6,7,9,9a,9b-hexahydro-4H-2,7,9-triazacyclopenta[a]naphthalene-1,3,8-trione (5b)

Colorless crystals; mp 281–282 °C; IR (KBr): 1696, 1416, 1374, 1162, 1084, 1014 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 2.30 (s, 3H, Me (p-Tol)), 2.33 (s, 3H, Me (Ts)), 3.38 (dd, 1H, J = 6.6, 8.5 Hz, H-9b), 3.43 (dd, 1H, J = 6.6, 8.5 Hz, H-3a), 3.62 (br ddd, 1H, J = 3.2, 3.2, 6.3 Hz, H-4), 4.40 (m, 1H, H-9a), 6.44 (s, 1H, H-6), 6.64 (dd, 1H, J = 3.2, 3.2 Hz, H-5), 7.04 (d, 2H, J = 8.5 Hz, Ar), 7.12 (dd, 4H, J = 4.9, 7.3 Hz, Ar), 7.19–7.47 (m, 15H, Ar), 7.76 (d, 2H, J = 8.3 Hz, Ar); ¹³C NMR (100 MHz, CDCl₃) δ 21.07 (CH₃), 21.57 (CH₃), 40.89 (CH), 41.56 (CH), 44.68 (CH), 58.75 (CH), 61.39 (CH), 124.34 (CH), 125.80 (2CH), 126.44 (3CH), 127.60 (CH), 127.93 (CH), 128.35 (2CH), 128.45 (CH), 128.55 (2CH), 128.70 (2CH), 128.85 (3CH), 128.91 (CH), 129.34 (2CH), 129.96 (2CH), 131.36 (C), 136.01 (C), 137.22 (C), 137.63 (C), 137.96 (C), 138.23 (C), 144.11 (C), 151.61 (C), 173.14 (C), 173.77 (C); LRMS-FAB m/z (ion, % relative intensity): 694 ([M+H]⁺, 100), 456 (10), 366 (13), 324 (28), 289 (14), 246 (35), 243 (29); HRMS-FAB m/z [M+H]⁺ calcd for C₃₂H₂₇N₃O₇S: 694.2376, found: 694.2376; Anal. Calcd. for C₃₂H₂₇N₃O₇S: C, 72.76; H, 5.54; N, 5.92. Found C, 72.35; H, 4.96; N, 6.01.

9-Benzyl-2,4,6-triphenyl-7-(toluene-4-sulfonyl)-3a,6,7,9,9a,9b-hexahydro-4H-2,7,9-triazacyclopenta[a]naphthalene-1,3,8-trione (5c)

Colorless crystals; mp 259–261 °C; IR (KBr): 1672, 1596, 1486, 1428, 1364, 1332, 1162, 1086 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 2.33 (s, 3H, Me (Ts)), 3.43 (dd, 1H, J = 7.3, 9.0 Hz, H-9b), 3.59 (m, 2H, H-3a+H-4), 3.86 (dd, 1H, J = 2.4, 2.4, 6.4 Hz, H-9a), 4.04 (d, 1H, J = 15.9 Hz, CH₂ (Bn)), 5.46 (d, 1H, J = 15.9 Hz, CH₂ (Bn)), 6.34 (s, 1H, H-6), 6.58–6.60 (m, 3H, Ar+H-5), 6.98–7.06 (m, 4H, Ar), 7.12–7.18 (m, 2H, Ar), 7.24–7.45 (m, 14H, Ar), 7.84 (d, 2H, J = 8.3 Hz, Ar); ¹³C NMR (100 MHz, CDCl₃) δ 21.65 (CH₃), 39.64 (CH), 40.80 (CH), 47.57 (CH), 51.83 (CH), 53.41 (CH), 60.67 (CH), 125.33 (CH), 125.81 (2CH), 126.47 (2CH), 127.59 (CH), 127.70 (2CH), 127.83 (CH), 128.13 (CH), 128.42 (CH), 128.54 (2CH), 128.70 (2CH), 128.75 (2CH), 128.90 (2CH), 128.97 (2CH), 129.01 (2CH), 129.28 (2CH), 131.41 (C), 135.16 (C), 135.73 (C), 136.47 (C), 137.30 (C), 137.54 (C), 137.76 (C), 173.82 (C); LRMS-FAB m/z (ion, % relative intensity): 694 ([M+H]⁺, 50), 307 (9), 289 (10), 246 (22), 185 (40), 154 (100); HRMS-FAB m/z [M+H]⁺ calcd for C₃₅H₃₅N₃O₇S: 694.2376, found: 694.2381.

9-Benzyl-1,3,8-trioxo-2,6-diphenyl-7-(toluene-4-sulfonyl)-2,3,3a,4,6,7,8,9,9a,9b-decahydro-1H-2,7,9-triazacyclopenta[a]naphthalene-4-carboxylic acid methyl ester (5d)

Colorless crystals; mp 273–276 °C; IR (KBr): 1702, 1428, 1340, 1168, 1088 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 2.34 (s, 3H, Me (Ts)), 3.05 (dd, 1H, J = 2.7, 3.0, 6.1 Hz, H-4), 3.59 (dd, 1H, J = 7.5, 9.0 Hz, H-9b), 3.66 (dd, 1H, J = 2.7, 2.9, 7.5 Hz, H-9a), 3.82 (dd, 1H, J = 6.1, 9.0 Hz, H-3a), 3.86 (s, 3H, Me (CO₂Me)), 4.05 (d, 1H, J = 15.8 Hz, CH₂ (Bn)), 5.43 (d, 1H, J = 15.8 Hz, CH₂ (Bn)), 6.27 (s, 1H, H-6), 6.54 (d, 2H, J = 7.6 Hz, Ar), 6.71 (dd, 1H, J = 2.9, 3.0 Hz, H-5), 7.01 (m, 3H, Ar), 7.04 (d, 3H, J = 8.0 Hz, Ar), 7.13 (m, 1H, Ar), 7.23 (dd, 2H, J = 7.6, 7.6 Hz, Ar), 7.30 (m, 1H, Ar), 7.39 (d, 3H, J = 7.3 Hz, Ar), 7.45 (dd, 2H, J = 7.3, 7.3 Hz, Ar), 7.82 (d, 2H, J = 8.0 Hz, Ar); ¹³C NMR (126 MHz, CDCl₃) δ 21.78 (CH₃), 39.14 (CH), 39.67 (CH), 41.16 (CH), 47.78 (CH₂), 51.91 (CH₂), 52.89 (CH), 60.69 (CH), 121.28 (CH), 125.90 (2CH), 126.65 (2CH), 127.93 (2CH), 127.95 (CH), 128.01 (CH), 128.84 (CH), 128.91 (2CH), 129.08 (2CH), 129.13 (2CH), 129.19 (2CH), 129.37 (2CH), 131.32 (C), 134.98 (C), 135.88 (C), 136.18 (C), 137.31 (C), 144.59 (C), 152.79 (C), 169.95 (C), 172.41 (C), 175.04 (C); LRMS-ESI 675 ([M⁺]⁺, 5), 611 (34), 520 ([M–Ts⁺]⁺, 61), 347 (31), 91 (100); HRMS-ESI calcd for C₁₆H₁₃NO₂S [M⁺]: 675.2039, found: 675.2032.
8-Acetyl-1,4,6-triphenyl-3-(toluene-4-sulfonyl)-3,4,6,7,8a-hexahydro-1H-quinazolin-2-one (6a)

To a solution of 3a (100 mg, 0.20 mmol) and methyl vinyl ketone (21 mg, 0.30 mmol) in dichloromethane (5 mL) was added 1.0 M dichloromethane solution of trimethylsilyl trifluoromethanesulfonate (40 µL, 40 µmol) at –20 °C. The resulting mixture was warmed to 0 °C and stirred for 36 h. The mixture was quenched by sodium hydrogen carbonate, extracted with dichloromethane, and dried over magnesium sulfate. The solvent was evaporated, and the residue was purified by column chromatography on silica gel with AcOEt/Hex (1/2, v/v) to yield 6a (61.1 mg, 53%) as colorless crystals; mp 254–256 °C; IR (KBr): 1668, 1592, 1436, 1242, 1150 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 1.35 (s, 3H, Me (COMe)), 2.31 (m, 2H, H-7=H-7), 2.39 (dd, 1H, J = 4.3, 8.5 Hz, H-8), 2.42 (s, 3H, Me (Ts)), 3.76 (ddd, 1H, J = 3.2, 3.2, 9.5 Hz, H-6), 4.11 (ddd, 1H, J = 3.2, 3.4, 8.5 Hz, H-8a), 6.27 (dd, 1H, J = 3.2, 3.4 Hz, H-5), 6.50 (s, 1H, H-4), 6.76 (d, 2H, J = 7.9 Hz, Ar), 7.18 (d, 2H, J = 7.2 Hz, Ar), 7.22 (d, 3H, J = 7.3, 7.8 Hz, Ar), 7.25 (d, 3H, J = 4.2, 8.1 Hz, Ar), 7.32–7.38 (m, 7H, Ar), 7.95 (d, 2H, J = 8.2 Hz, Ar); ¹³C NMR (151 MHz, CDCl₃) δ 21.65 (CH₂), 27.47 (CH₃), 31.83 (CH₃), 38.20 (CH), 45.47 (CH), 58.19 (CH), 63.03 (CH), 124.51 (CH), 125.83 (2CH), 126.68 (CH), 127.51 (CH), 127.76 (CH), 127.94 (2CH), 128.47 (2CH), 128.84 (2CH), 129.03 (4CH), 129.14 (2CH), 133.60 (C), 136.39 (C), 137.17 (C), 137.42 (C), 151.30 (C), 205.32 (C); LRMS-FAB m/z (ion, % relative intensity): 577 ([M+H⁺]⁺, 23), 307 (17), 289 (14), 246 (52), 219 (17), 185 (86), 154 (100); HRMS-EI m/z [M⁺] calculated for C₃₆H₃₄N₂O₄S: 576.2083, found: 576.2081.

8-Acetyl-4,6-diphenyl-3-(toluene-4-sulfonyl)-1-p-tolyl-3,4,6,7,8a-hexahydro-1H-quinazolin-2-one (6b)

Colorless crystals; mp 228–230 °C; IR (KBr): 1672, 1412, 1346, 1244, 1156 cm⁻¹; ¹H NMR (600 MHz, C₆D₆) δ 0.96 (s, 3H, Me (COMe)), 1.44 (ddd, 1H, J = 5.2, 7.6, 15.0 Hz, H-7), 1.65 (dd, 1H, J = 3.1, 15.0 Hz, H-7), 1.86 (s, 3H, Me (p-Tol)), 1.94 (s, 3H, Me (Ts)), 1.96 (ddd, 1H, J = 3.1, 5.2, 7.4 Hz, H-8), 3.13 (ddd, 1H, J = 3.4, 3.8, 7.6 Hz, H-6), 3.93 (ddd, 1H, J = 2.2, 3.4, 7.4 Hz, H-8a), 5.79 (dd, 1H, J = 2.2, 3.8 Hz, H-5), 6.72 (d, 2H, J = 8.4 Hz, Ar), 6.76 (d, 2H, J = 8.4 Hz, Ar), 6.79 (s, 1H, H-4), 6.88 (d, 2H, J = 8.1 Hz, Ar), 7.00 (d, 2H, J = 7.4 Hz, Ar), 7.04 (dd, 1H, J = 7.3, 7.3 Hz, Ar), 7.10–7.15 (m, 5H, Ar), 7.59 (d, 2H, J = 7.4 Hz, Ar), 8.37 (d, 2H, J = 8.1 Hz, Ar); ¹³C NMR (151 MHz, CDCl₃) δ 21.03 (CH₃), 21.66 (CH₃), 27.53 (CH₃), 31.83 (CH₃), 38.21 (CH), 45.49 (CH), 58.13 (CH₃), 63.08 (CH), 124.45 (CH), 125.85 (2CH), 126.65 (CH), 127.62 (2CH), 127.75 (CH), 128.46 (2CH), 128.82 (2CH), 128.90 (2CH), 129.07 (2CH), 129.77 (2CH), 133.65 (C), 136.39 (C), 137.17 (C), 137.42 (C), 138.60 (C), 142.52 (C), 143.75 (C), 151.40 (C), 205.40 (C); LRMS-FAB m/z (ion, % relative intensity): 591 ([M+H⁺]⁺, 45), 307 (14), 289 (11), 246 (26), 219 (11), 185 (20), 154 (100); HRMS-EI m/z [M⁺] calculated for C₃₆H₃₄N₂O₄S: 590.2239, found: 590.2240.

8-Acetyl-1-benzyl-4,6-diphenyl-3-(toluene-4-sulfonyl)-3,4,6,7,8a-hexahydro-1H-quinazolin-2-one (6c)

Colorless crystals; mp 204–206 °C; IR (KBr): 1662, 1342, 1162 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 1.27 (s, 3H, Me (COMe)), 2.28–2.29 (m, 1H, H-7), 2.29–2.35 (m, 1H, H-7), 2.47 (s, 3H, Me (Ts)), 2.72 (dd, 1H, J = 3.8, 6.9 Hz, H-8), 3.50 (d, 1H, J = 15.5 Hz, CH₂ (Bn)), 3.50–3.53 (m, 1H, H-6), 3.69 (ddd, 1H, J = 3.2, 3.4, 6.9 Hz, H-8a), 4.94 (d, 1H, J = 15.6 Hz, CH₂ (Bn)), 6.16 (dd, 1H, J = 3.1, 3.2 Hz, H-5), 6.36 (s, 1H, H-4), 6.49 (d, 2H, J = 7.5 Hz, Ar), 6.97 (dd, 2H, J = 7.5, 7.7 Hz, Ar), 7.02–7.13 (m, 3H, Ar), 7.22 (dd, 2H, J = 7.2, 7.8 Hz, Ar), 7.30 (dd, 2H, J = 7.4, 7.5 Hz, Ar), 7.34–7.41 (m, 6H, Ar), 8.11 (d, 2H, J = 8.3 Hz, Ar); ¹³C NMR (76 MHz, CDCl₃) δ 21.87 (CH₃), 27.38 (CH₃), 31.94 (CH₂), 38.00 (CH), 44.01 (CH), 47.48 (CH₂), 52.86 (CH), 62.71 (CH), 125.32 (CH), 125.89 (2CH), 126.78 (CH), 127.40 (CH), 127.71 (3CH), 128.44 (2CH), 128.55 (2CH), 128.84 (2CH), 129.09 (2CH), 129.18 (2CH), 129.25 (2CH), 133.67 (C), 135.50 (C), 136.88 (C), 138.41 (C), 142.54 (C), 144.21 (C), 153.01 (C), 205.16 (C); LRMS-EI m/z (ion, % relative intensity): 590 (M⁺, 15), 520 (M⁺–MVK, 34), 435 (M⁺–Ts, 20), 393 (M⁺–TsNCO, 4), 331 (27), 91 (100); HRMS-EI m/z [M⁺]
8-Acetyl-1-benzyl-2-oxo-4-phenyl-3-(toluene-4-sulfonyl)-1,2,3,4,6,7,8,8a-octahydroquinazoline-6-carboxylic acid methyl ester (endo-6d)

Colorless crystals; $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 1.81 (ddd, 1H, $J$ = 5.1, 7.5, 15.5 Hz, H-7), 1.97 (s, 3H, Me (COMe)), 2.44 (s, 3H, Me (Ts)), 2.75 (ddd, 1H, $J$ = 1.6, 2.9, 15.5 Hz, H-7'), 2.99 (dd, 1H, $J$ = 3.4, 8.2 Hz, H-8), 3.22 (ddd, 1H, $J$ = 3.4, 3.6, 7.3 Hz, H-9a), 3.47 (m, 1H, H-6), 3.56 (d, 1H, $J$ = 15.5 Hz, CH$_2$ (Bn)), 3.76 (s, 3H, Me (CO$_2$Me)), 4.95 (d, 1H, $J$ = 15.5 Hz, CH$_2$ (Bn)), 6.23–6.25 (m, 1H, H-5), 6.24 (s, 1H, H-4), 6.54 (d, 2H, $J$ = 7.7 Hz, Ar), 6.99 (dd, 2H, $J$ = 7.4, 7.5 Hz, Ar), 7.09 (dd, 1H, $J$ = 7.0, 7.4 Hz, Ar), 7.29–7.36 (m, 7H, Ar), 7.99 (d, 2H, $J$ = 8.4 Hz, Ar); $^{13}$C NMR (151 MHz, CDCl$_3$) $\delta$ 21.86 (CH$_3$), 24.46 (CH$_2$), 29.20 (CH$_3$), 37.99 (CH), 44.35 (CH), 47.85 (CH$_2$), 52.55 (CH$_3$), 52.79 (CH), 62.41 (CH), 121.91 (CH), 125.90 (2CH), 127.64 (CH), 127.84 (2CH), 127.86 (CH), 128.72 (2CH), 129.16 (2CH), 129.20 (2CH), 129.33 (2CH), 132.19 (C), 135.23 (C), 136.50 (C), 138.17 (C), 144.25 (C), 152.58 (C), 172.17 (C), 205.24 (C); HRMS-ESI calcd for C$_{32}$H$_{32}$N$_2$O$_6$SNa [M+Na]$^+$: 595.1877, found: 595.1873.

8-Acetyl-1-benzyl-2-oxo-4-phenyl-3-(toluene-4-sulfonyl)-1,2,3,4,6,7,8,8a-octahydroquinazoline-6-carboxylic acid methyl ester (exo-6d)

Colorless crystals; $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 1.87 (ddd, 1H, $J$ = 4.2, 12.2, 15.8 Hz, H-7), 1.99 (s, 3H, Me (COMe)), 2.34–2.40 (m, 1H, H-7'), 2.47 (s, 3H, Me (Ts)), 3.12 (dd, 1H, $J$ = 4.2, 8.3 Hz, H-8), 3.31–3.37 (m, 1H, H-9a), 3.55–3.59 (m, 1H, H-6), 3.66 (d, 1H, $J$ = 15.5 Hz, CH$_2$ (Bn)), 3.77 (s, 3H, Me (CO$_2$Me)), 5.01 (d, 1H, $J$ = 15.5 Hz, CH$_2$ (Bn)), 6.12 (dd, 2H, $J$ = 2.7, 7.7 Hz, Ar), 6.22 (s, 1H, H-4), 6.51 (d, 2H, $J$ = 7.7 Hz, Ar), 6.99 (dd, 1H, $J$ = 7.5, 7.5 Hz, Ar), 7.11 (dd, 1H, $J$ = 6.9, 7.2 Hz, Ar), 7.24–7.27 (m, 2H, Ar), 7.31–7.38 (m, 5H, Ar), 8.03 (d, 2H, $J$ = 8.0 Hz, Ar); $^{13}$C NMR (151 MHz, CDCl$_3$) $\delta$ 21.87 (CH$_3$), 26.34 (CH$_2$), 28.60 (CH$_3$), 39.42 (CH), 46.03 (CH), 47.85 (CH$_2$), 52.61 (CH$_3$), 52.69 (CH), 62.25 (CH), 122.67 (CH), 125.82 (2CH), 127.73 (CH), 127.84 (2CH), 127.88 (CH), 128.75 (2CH), 129.20 (2CH), 129.25 (2CH), 129.41 (2CH), 132.42 (C), 135.00 (C), 136.68 (C), 137.73 (C), 144.45 (C), 152.56 (C), 173.10 (C), 205.15 (C); HRMS-ESI calcd for C$_{32}$H$_{32}$N$_2$O$_6$SNa [M+Na]$^+$: 595.1869, found: 595.1873.

calcd for C$_{33}$H$_{3}$_N$_2$O$_4$S: 590.2239, found: 590.2249.
$^{1}H$ NMR (1b)

Ph

CO$_2$Me

Date: Fri Apr 12 16:21:41 2002

Filename: auto_H.mndata
Comment:
Siliconhistory: new
EMODE: non

POINT: 36768 points
SAMPO: 36768 points
FREQU: 7963.6 Hz
FILTR: 5000 Hz
DELAY: 50.0 usec
DEADT: 72.3 usec
JNUK: 125.1 usec
TIMES: 8 times
EDPRT: 0 times
PD: 2.9007 usec
ACDOH: 4069.7693 usec
ACDOL: 0.000000 usec
ACDOL: 0.000000 usec
RESOL: 0.24 Hz
PRT: 5.50 usec
CRN: 1H
CSFRQ: 398.65 kHz
CSET: 13400.00 Hz
RAGAIN: 19
SCAMS: 8 times
SLNVT: CDCl3
SPINN: 11 Hz
TEMP: 21.7 C
**1H NMR (3a)**

MO Ph TsNCO

Date: Sat Jul 13 17:33 06 2002

Comment: MO Ph TsNCO

**EXMODE**: non

**POINT**: 32768 points

**FREQU**: 7933.6 Hz

**FILTR**: 4000 Hz

**DELAY**: 50.0 usec

**CRD**: 72.3 usec

**INTVL**: 125.1 usec

**TIMES**: 8 times

**RUN**: 0 times

**PD**: 2.9607 sec

**AQT**: 4859.2769 msec

**PRESL**: 10.800000 msec

**INT**: 0.500000 msec

**RESOL**: 0.24 Hz

**PHI**: 5.50 usec

**OBNUC**: 1H

**GPREF**: 399.65 kHz

**ORSET**: 134300.0 Hz

**RGAIN**: 16

**SCANS**: 8 times

**SLNW**: 12 Hz

**SPAN**: CDCl3

**TEMP**: 23.3 C
$^{1}H$ NMR (3b)
$^{13}$C NMR (4a)

Date: 17 50 08 2004

File Name: auto_13C nndata
Command: bcm
ENCODE: bcm

P1NT: 32768 points
SAMPO: 32768 points
FREQU: 33888.3 Hz
FILTR: 16000 Hz
DELAY: 11.8 usec
DSKT: 10.0 usec
INVL: 29.5 usec
TIMES: 128 times
DUMPY: 1 times
PD: 2.0333 sec
ACQIM: 956.6560 msec
PKCL: 10.0000 msec
INNT: 10.0000 usec
RESOL: 1.03 Hz
PM: 5.50 usec
CHURC: 13C
OFFFL: 125.65 MHz
OBSET: 127958.00 Hz
AGAIN: 32
PAUSE: 1.0 MHz
INFIP: 162160.00 Hz
IRHPW: 48.0 usec
INRNS: 0
SCANS: 128 times
SLVNT: CHLOR
SPINNING: 13 Hz
TEMP: 27.5 C
$^1$H NMR (4b)
$^1$H NMR (5b)

p-Tol N-PhM1

Date: Tue Oct 1 12:29:05 2002

Filename: auto_HNmrdata

Comment: p-tol N-PhM1

Spectrum History:

EXMODE: non

RPM: 32768 points

FREQ: 7.050 MHz

FILTR: 4000 Hz

DELAY: 50.0 usec

END: 72.1 usec

INTVL: 125.1 usec

TINES: 0 Lines

DUMMY: 0 Lines

SP: 2.4000 sec

ACQ: 4096 27688 mean

PREDL: 10.00000 mean

INTR: 0.2000 mean

RESL: 0.04 Hz

PM: 5.00 usec

OBDIC: 1H

ODST: 409.95 Hz

ODSET: 13.4580.00 Hz

GAIN: 1B

SCANS: 8 times

SLWN: COOL.3

SPINNING: 14 Hz

TEMP: 22.7 C
$^{13}$C NMR (5b)
$^1$H NMR (5c)

{}
$^1$H NMR (5d)
$^{13}$C NMR (5d)

$\text{OBFRQ } 125.77 \text{ MHz}$

$\text{SLVNT CHLOROFORM-D}$

$\text{OBFIN } 301.0403 \text{ Hz}$

[Image of 13C NMR spectrum with chemical structure and peak assignments]
$^1$H NMR (6a)
$^{13}$C NMR (6a)
$^1$H NMR (6b)

**Chemical Shifts:**
- 0.43 ppm
- 0.95 ppm
- 1.25 ppm
- 1.42 ppm
- 1.43 ppm
- 1.44 ppm
- 1.45 ppm
- 1.63 ppm
- 1.65 ppm
- 1.83 ppm
- 1.85 ppm
- 1.93 ppm
- 1.95 ppm
- 1.95 ppm
- 3.12 ppm
- 3.93 ppm
- 5.78 ppm
- 6.71 ppm
- 6.72 ppm
- 6.74 ppm
- 6.75 ppm
- 6.78 ppm
- 6.86 ppm
- 6.88 ppm
- 6.99 ppm
- 7.00 ppm
- 7.02 ppm
- 7.03 ppm
- 7.04 ppm
- 7.08 ppm
- 7.10 ppm
- 7.10 ppm
- 7.11 ppm
- 7.13 ppm
- 7.13 ppm
- 7.15 ppm
- 7.18 ppm
- 7.28 ppm
- 7.57 ppm
- 7.58 ppm
- 8.35 ppm
- 8.36 ppm

**Spectroscopic Parameters:**
- OBFRQ: 600.13 MHz
- SLVNT: CDCl$_3$
- OBFIN: 3701.166 Hz

**Structure Diagram:**

![Chemical Structure](image)
$^{13}$C NMR (6b)
$^1$H NMR (6c)

![NMR Spectrum Image]

$^1$H NMR (6c) in CDCl$_3$.

- Chemical shifts (ppm): 0.00, 1.27, 2.26, 2.30, 2.47, 2.72, 2.73, 3.48, 3.51, 3.69, 4.92, 4.95, 6.16, 6.36, 6.48, 6.50, 6.95, 6.96, 6.98, 7.06, 7.07, 7.09, 7.10, 7.11, 7.21, 7.22, 7.24, 7.25, 7.29, 7.30, 7.32, 7.35, 7.36, 7.37, 7.38, 8.11, 8.13.

- Peak assignments:
  - Ts
  - H$_{4}$
  - H$_{8a}$
  - Ph
  - O
  - N
  - MeOC
  - H$_{7}$
  - H$_{7'}$
  - H$_{6}$
  - Ph
  - H$_{5}$

S38
$^{13}$C NMR (6c)
$^1$H NMR (endo-6d)
$^{13}$C NMR (endo-6d)
$^1$H NMR (exo-6d)

![NMR spectrum diagram]

ppm $^1$H

0.00 1.25 1.54 1.86 1.97 2.34 2.44 2.46 3.10 3.11 3.31 3.55 3.56 3.63 3.66 3.76 4.98 5.01 6.10 6.20 6.49 6.50 6.96 6.97 6.98 7.08 7.09 7.10 7.23 7.24 7.26 7.26 7.29 7.31 7.32 7.34 7.35 8.00 8.02

OBFRQ 600.13 MHz
SLVNT CDCl$_3$
OBFIN 3701.166 Hz

N
N
Ph
Ts
O
Bn
H4
H8
H7
H9a
MeOC
H7
H7'
CO$_2$Me
$^{13}$C NMR (exo-6d)