Ni-Catalyzed Ketene Cycloaddition: A System that Resists the Formation of Decarbonylation Side Products

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SUPPORTING INFORMATION

General Experimental:

All reactions were conducted under an atmosphere of N_2 using standard Schlenk techniques or in a N_2 filled glove-box unless otherwise noted. Toluene was dried over neutral alumina under N_2 using a Grubbs type solvent purification system. THF was freshly distilled from Na/benzophenone. $Ni(cod)_2$ was purchased from Strem and used without further purification. The ketenes **a**,[1a] **b**,[1b] **c**,[1c] **d**,[1d] **e**,[1c] **f**,[1d] **g**,[1e] **h**,[1a] **i**,[1f] **j**,[1g] and diynes **1**,[2a] **2**,[2b] **3**,[2c] **5**,[2d] **6**,[2e] **7**,[2a] and **8**[2c] were prepared according to literature procedures. All other reagents were purchased and used without further purification unless otherwise noted.

^1H and ^{13}C Nuclear Magnetic Resonance spectra of pure compounds were acquired at 300 and 125 MHz, respectively unless otherwise noted. All spectra are referenced to a singlet at 7.27 ppm for ^1H and to the center line of a triplet at 77.23 ppm for ^{13}C. The abbreviations s, d, dd, dt, dq, t, q, and quint stand for singlet, doublet, doublet of doublets, doublet of triplets, doublet of quartets, triplet, quartet, and quintet, in that order. All ^{13}C NMR spectra were proton decoupled. Gas Chromatography was performed using the following conditions: initial oven temperature: 100 ºC; temperature ramp rate 50 ºC/min.; final temperature: 300 ºC held for 7 minutes; detector temperature: 250 ºC.

Ligand Screening:

In a nitrogen filled glovebox, a stock solution of diyne (**1,** 1 equiv., 0.05M) in benzene was prepared along with decane as standard in a clean and pre-dried scintillation vial. The stock solution of ketene (**a,** 1.2 equiv.) in benzene was also prepared in a separate vial. In separate vials, stock solutions of catalyst were prepared by mixing $Ni(cod)_2$ and ligands (see Table 1 for the ratio). 5 mol% Catalyst was added to the vial containing diyne and ketene. The vials were

taken out of the glove box and stirred at 60 °C for overnight; after which, all the reaction vials were opened to air and then analyzed by GC.

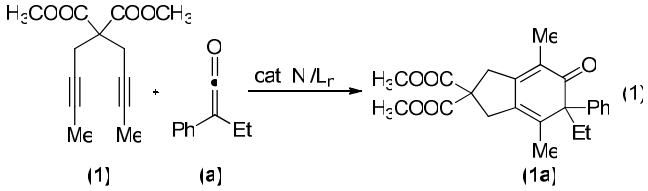


Table 1: Ni-Catalyzed Cycloaddition of Diynes and Ketenes[a]

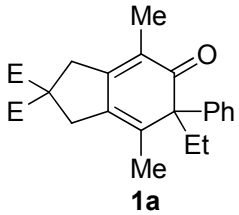
Entry	Ligand (L_n)	Ni:L_n	1 % Conv[b]	1a % Yield[b]
1	Pr^c	1:2	100	12
2	SPr^c	1:2	63	3
3	PPh_3	1:2	100	39
4	PCy_3	1:2	72	20
5	$MePPh_2$	1:2	100	54
6	$CyPPh_2$	1:2	100	31
7	DPPE	1:1	32	2
8	DCPE	1:1	39	-
9	DPPF	1:1	100	>99 (86%)[d]
10	DPPB	1:1	100	86 (86)%[d]

[a]Reaction conditions: 5 mol% Ni–catalyst, diyne (1 equiv, 0.05M), ketene (1.2 equiv), benzene, 60 °C, 12 h, [b] GC yield analyzed using decane as an internal standard. [c]The catalyst solutions were equilibrated for at least 6 h before use. [d]Isolated yields.

General Procedure for Cycloaddition:

In a nitrogen-filled glove box, a 5 mol% catalyst solution (prepared from $Ni(cod)_2$ and DPPB in 1:1 ratio in toluene) was added to the vial containing diyne (1 equiv., 0.1 M) and ketene (1.2 equiv.) in toluene. The vial was taken out of the glove box and stirred at 60 °C for 5h, opened to air, concentrated *in vacuo,* and purified by silica gel flash column chromatography.

Dimethyl 5-ethyl-4,7-dimethyl-6-oxo-5-phenyl-5,6-dihydro-1H-indene-2,2(3H)-dicarboxylate (1a):

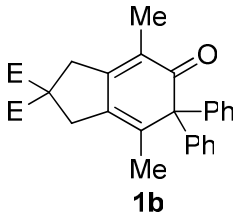


1a

The general procedure was used with 41.8 mg (0.18 mmol, 0.1 M) of diyne **1**, 31.0 mg (0.21 mmol) of ketene **a**, and 5 mol% of catalyst in toluene. The reaction mixture was purified via flash column chromatography using 15% ethyl acetate in hexanes to afford the title compound **1a** as bright yellow sticky oil, 82% yield.

^{1}H NMR (300 MHz,$CDCl_3$): δ (ppm) 7.26-7.10 (m, 5H), 3.79 (s, 3H), 3.77 (s, 3H), 3.32 (s, 2H), 3.24 (d, *J*= 7.2 Hz, 2H), 2.63 (dq, J_1= 7.5 Hz, J_2= 14.9 Hz, 1H), 1.95 (dq, J_1= 7.5 Hz, J_2= 14.9 Hz, 1H), 1.79 (s, 3H), 1.61 (s, 3H), 0.64 (t, *J*= 7.5 Hz, 3H). ^{13}C NMR (75 MHz , $CDCl_3$): δ (ppm) 203.3, 171.6, 154.6, 142.2, 141.6, 132.1, 128.8, 127.1, 126.9, 124.7, 61.4, 58.3, 53.3, 53.2, 39.7, 38.0, 29.9, 16.4, 11.6, 8.8. IR (CH_2Cl_2, cm^{-1}): 2956, 1736, 1648, 1437, 1263, 1204, 1076. HRMS (ESI) calcd for $C_{23}H_{26}O_5Na$ $[M+Na]^+$ 405.1678, found 405.1682.

Dimethyl 4,7-dimethyl-6-oxo-5,5-diphenyl-5,6-dihydro-1H-indene-2,2(3H)-dicarboxylate (1b):

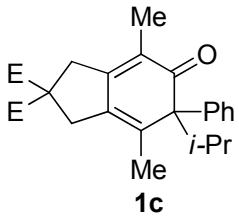


1b

The general procedure was used with 50 mg (0.21 mmol, 0.1 M) of diyne **1**, 49.3 mg (0.25 mmol) of ketene **b**, and 5 mol% of catalyst in toluene. The reaction mixture was purified via flash column chromatography using 20% ethyl acetate in hexanes to afford the title compound **1b** as yellow sticky oil, 50% yield.

^{1}H NMR (300 MHz,$CDCl_3$): δ (ppm) 7.26 (m, 6H), 7.15 (m, 4H), 3.75 (s, 6H), 3.32 (s, 2H), 3.25 (s, 2H), 1.80 (s, 3H), 1.56 (s, 3H); ^{13}C NMR (75 MHz , $CDCl_3$): δ (ppm) 203.3, 171.7, 153.5, 141.8, 141.5, 131.4, 129.9, 128.3, 127.3, 124.3, 68.3, 58.2, 53.4, 39.6, 38.1, 18.9, 12.0. IR (CH_2Cl_2, cm^{-1}): 2954, 2922, 1736, 1652, 1616, 1438, 1258, 1203, 1072. HRMS (ESI) calcd for $C_{27}H_{26}O_5Na$ $[M+Na]^+$ 453.1678, found 453.1693.

Dimethyl 5-isopropyl-4,7-dimethyl-6-oxo-5-phenyl-5,6-dihydro-1H-indene-2,2(3H)-dicarboxylate (1c):



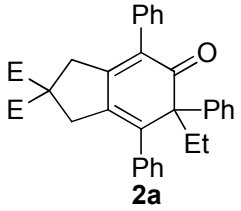
1c

The general procedure was used with 119.0 mg (0.50 mmol, 0.1 M) of diyne **1**, 160 mg (1.0 mmol) of ketene **c**, and 5 mol% of catalyst in toluene. The reaction mixture was purified via flash column chromatography using 15% ethyl acetate in hexanes to afford the title compound **1c** as bright yellow liquid, 50% yield.

^{1}H NMR (300 MHz,$CDCl_3$): δ (ppm) 7.20 (m, 3H), 7.09 (d, *J*= 7.2 Hz, 2H), 3.77 (s, 3H), 3.76 (s, 3H), 3.29 (d, *J*= 6.3 Hz, 2H), 3.20 (s, 2H), 2.92 (septet, *J*= 6.9 Hz, 1H), 1.79 (s, 3H), 1.67 (s, 3H), 0.95 (d, *J*= 7.2 Hz, 3H), 0.86 (d, *J*= 7.2 Hz, 3H). ^{13}C NMR (75 MHz , $CDCl_3$): δ (ppm) 203.7, 171.7, 171.68, 153.7, 141.7, 141.4, 132.4, 128.8, 128.4, 126.7, 125.2, 65.7, 58.3, 53.3,

53.27, 39.6, 38.2, 35.4, 18.8, 17.5, 11.6. IR (CH_2Cl_2, cm^{-1}): 2959, 1737, 1438, 1265, 1074. HRMS (ESI) calcd for $C_{24}H_{28}O_5K$ $[M+K]^+$ 435.1574, found 435.1586.

Dimethyl 5-ethyl-6-oxo-4,5,7-triphenyl-5,6-dihydro-1H-indene-2,2(3H)-dicarboxylate (2a):

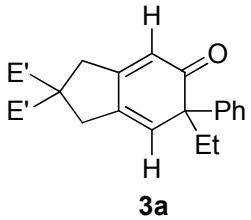


2a

The general procedure was used with 65.4 mg (0.18 mmol, 0.1 M) of diyne **2**, 31.8 mg (0.22 mmol) of ketene **a**, and 5 mol% of catalyst in toluene. The reaction mixture was purified via flash column chromatography using 15% ethyl acetate in hexanes to afford the title compound **2a** as bright yellow sticky oil, 65% yield.

^{1}H NMR (300 MHz,$CDCl_3$): δ (ppm) 7.30 (m, 8H), 7.20 (m, 5H), 6.75 (d, *J*= 8.1 Hz, 2H), 3.77 (s, 3H), 3.72 (s, 3H), 3.23 (m, 4H), 2.72 (dq, J_1= 7.5 Hz, J_2= 14.7 Hz, 1H), 1.75 (dq, J_1= 7.2 Hz, J_2= 14.4 Hz, 1H), 0.84 (t, *J*= 7.2 Hz, 3H). ^{13}C NMR (75 MHz , $CDCl_3$): δ (ppm) 200.7, 171.4, 171.3, 155.1, 147.5, 140.6, 138.0, 134.3, 134.2, 130.4, 129.8, 129.1, 128.5, 128.1, 128.0, 127.9, 127.5, 127.2, 62.3, 58.6, 53.3, 53.2, 40.9, 39.8, 28.6, 9.4. IR (CH_2Cl_2, cm^{-1}): 2956, 1736, 1655, 1594, 1492, 1441, 1265, 1204, 1075. HRMS (ESI) calcd for $C_{33}H_{30}O_5Na$ $[M+Na]^+$ 529.1991, found 529.2004.

Dimethyl 5-ethyl-6-oxo-5-phenyl-5,6-dihydro-1H-indene-2,2(3H)-dicarboxylate (3a):

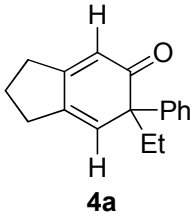


3a

The general procedure was used with 39.3 mg (0.18 mmol, 0.1 M) of diyne **3**, 33.1 mg (0.22 mmol) of ketene **a**, and 5 mol% of catalyst in toluene. The reaction mixture was purified via flash column chromatography using 15% ethyl acetate in hexanes to afford the title compound **3a** as slightly yellow oil, 54% yield.

^{1}H NMR (300 MHz,$CDCl_3$): δ (ppm) 7.25 (m, 5H), 6.25 (s, 1H), 5.95 (s, 1H), 4.24 (m, 4H), 3.30 (m, 4H), 2.50 (dq, J_1= 4.5 Hz, 1H), 1.91 (dq, J_1= 4.5 Hz, 1H), 1.27 (m, 6H), 0.78 (t, *J*= 4.5 Hz, 3H); ^{13}C NMR (75 MHz , $CDCl_3$): δ (ppm) 202.8, 170.7, 159.8, 140.9, 137.1, 135.0, 128.8, 127.4, 127.0, 119.5, 62.2, 59.2, 58.5, 40.3, 38.4, 32.0, 14.2, 9.4. IR (CH_2Cl_2, cm^{-1}): 2975, 1732, 1649, 1446, 1368, 1251, 1190, 1069, 860, 697. HRMS (ESI) calcd for $C_{23}H_{26}O_5Na$ $[M+Na]^+$ 405.1678, found 405.1692.

6-ethyl-6-phenyl-2,3-dihydro-1H-inden-5(6H)-one (4a):

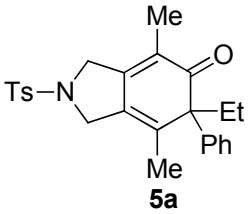


4a

The general procedure was used with 37.0 mg (0.40 mmol, 0.1 M) of diyne **4**, 70.4 mg (0.48 mmol) of ketene **a**, and 5 mol% of catalyst in toluene. The reaction mixture was purified via flash column chromatography using 5-10% ethyl acetate in hexanes to afford the title compound **4a** as slightly yellow oil, 35% yield.

^{1}H NMR (300 MHz,$CDCl_3$): δ (ppm) 7.26 (m, 5H), 6.23 (s, 1H), 5.95 (s, 1H), 2.68 (m, 4H), 2.47 (dq, J_1= 7.5 Hz, 1H), 1.94 (m, 3H), 0.81 (t, J= 7.5, 3H). ^{13}C NMR (75 MHz , $CDCl_3$): δ (ppm) 203.6, 164.5, 141.6, 138.3, 135.9, 128.7, 127.2, 127.1, 119.0, 58.4, 33.5, 32.1, 30.8, 24.9, 9.4. IR (CH_2Cl_2, cm^{-1}): 2964, 1675, 1646, 1597, 1492, 1444, 1369, 1301, 1221, 1168, 1034, 857, 758, 696. HRMS (ESI) calcd for $C_{17}H_{18}ONa$ $[M+Na]^+$ 261.1255, found 261.1270.

6-ethyl-4,7-dimethyl-6-phenyl-2-tosyl-2,3-dihydro-1H-isoindol-5(6H)-one (5a):

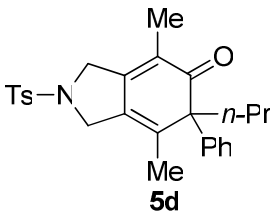


5a

The general procedure was used with 49.1 mg (0.18 mmol, 0.1 M) of diyne **5**, 31.3 mg (0.22 mmol) of ketene **a**, and 5 mol% of catalyst in toluene. The reaction mixture was purified via flash column chromatography using 15-30% ethyl acetate in hexanes to afford the title compound **5a** as a white solid, 50% yield.

Melting Point: 155-158 °C (Decomp.). ^{1}H NMR (300 MHz,$CDCl_3$): δ (ppm) 7.80 (d, J= 8.1 Hz, 2H), 7.39 (d, J= 8.1 Hz, 2H), 7.21 (m, 3H), 7.05 (m, 2H), 4.31 (s, 2H), 4.25 (d, J= 10.8 Hz, 2H), 2.61 (dq, J_1= 7.2 Hz, J_2= 14.7 Hz, 1H), 2.45 (s, 3H), 1.94 (dq, J_1=7.2 Hz, J_2= 14.7 Hz, 1H), 1.72(s, 3H), 1.57 (s, 3H), 0.58 (t, J= , 3H). ^{13}C NMR (75 MHz , $CDCl_3$): δ (ppm) 202.7, 150.0, 144.4, 142.8, 140.8, 133.2, 130.2, 128.99, 128.95, 127.9, 127.4, 126.7, 123.8, 61.6, 52.0, 50.9, 30.0, 21.8, 16.5, 11.5, 8.9. IR (CH_2Cl_2, cm^{-1}): 2926, 1651, 1619, 1493, 1448, 1346, 1272, 1164, 1096, 1061. HRMS (ESI) calcd for $C_{25}H_{27}NO_3SK$ $[M+K]^+$ 460.1349, found 460.1355.

4,7-dimethyl-6-phenyl-6-propyl-2-tosyl-2,3-dihydro-1H-isoindol-5(6H)-one (5d):



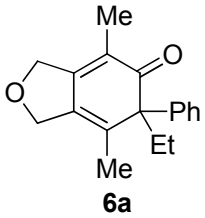
5d

The general procedure was used with 50.6 mg (0.18 mmol, 0.1 M) of diyne **5**, 35.4 mg (0.22 mmol) of ketene **d**, and 5 mol % of catalyst in toluene. The reaction mixture was purified via flash column chromatography using 15-30% ethyl acetate in hexanes to afford the title

compound **5d** as white solid, 55% yield.

Melting Point: 157-160 °C (Decomp.). ^{1}H NMR (300 MHz,$CDCl_3$): δ (ppm) 7.81 (d, *J*= 8.1 Hz, 2H), 7.40 (d, *J*= 8.4 Hz, 2H), 7.22 (m, 3H), 7.07 (m, 2H), 4.24 (m, 4H), 2.55 (m, 1H), 2.48 (s, 3H), 1.88 (m, 1H), 1.73 (s, 3H), 1.58 (s, 3H), 0.87 (m, 5H). ^{13}C NMR (75 MHz , $CDCl_3$): δ (ppm) 202.6, 149.9, 144.4, 143.2, 140.9, 135.4, 133.4, 130.2, 129.0, 128.7, 128.0, 127.5, 126.8, 123.6, 61.2, 52.0, 50.9, 39.5, 21.8, 17.9, 16.6, 14.7, 11.5. IR (CH_2Cl_2, cm^{-1}): 2981, 2936, 1734, 1644, 1511, 1447, 1369, 1269, 1206, 1094, 1048, 914. HRMS (ESI) calcd for $C_{26}H_{29}O_3SNa$ $[M+Na]^+$ 458.1766, found 458.1786.

6-ethyl-4,7-dimethyl-6-phenyl-3,6-dihydroisobenzofuran-5(1H)-one (6a):

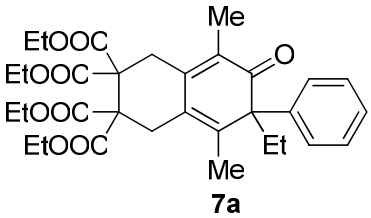


6a

The general procedure was used with 74.2 mg (0.60 mmol, 0.1 M) of diyne **6**, 106.5 mg (0.72 mmol) of ketene **a**, and 5 mol% of catalyst in toluene. The reaction mixture was purified via flash column chromatography using 5-30% ethyl acetate in hexanes to afford the title compound **6a** as yellow sticky oil, 33% yield.

^{1}H NMR (300 MHz,$CDCl_3$): δ (ppm) 7.22 (m, 5H), 4.78 (m, 4H), 2.67 (dq, J_1=4.5 Hz, 1H), 2.00 (dq, J_1=4.5 Hz, 1H), 1.76 (s, 3H), 1.60 (s, 3H), 0.70 (t, *J*=4.5 Hz, 3H). ^{13}C NMR (75 MHz , $CDCl_3$): δ (ppm) 203.4, 153.8, 141.3, 140.2, 132.0, 128.9, 127.3, 126.9, 121.7, 71.5, 71.0, 61.4, 29.9, 16.5, 11.6, 8.9. IR (CH_2Cl_2, cm^{-1}): 2919, 1653, 1623, 1446, 1054, 698. HRMS (ESI) calcd for $C_{18}H_{20}O_2Na$ $[M+Na]^+$ 291.1361, found 291.1374.

Tetraethyl 6-ethyl-5,8-dimethyl-7-oxo-6-phenyl-6,7-dihydronaphthalene-2,2,3,3(1H,4H)-tetracatboxylate (7a) :



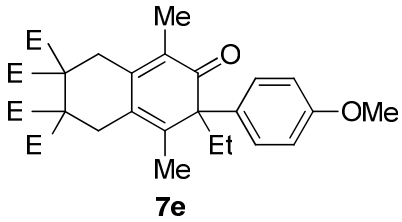
7a

The general procedure was used with 55.3 mg (0.13 mmol, 0.1 M) of diyne **7**, 22.9 mg (0.16 mmol) of ketene **a**, and 5 mol% of catalyst in toluene. The reaction mixture was purified via flash column chromatography using 15% ethyl acetate in hexanes to afford the title compound **7a** as bright yellow sticky oil, 91% yield.

^{1}H NMR (300 MHz,$CDCl_3$): δ (ppm) 7.21-7.09 (m, 5H), 4.27-4.19 (m, 8H), 3.24 (s, 2H), 3.19 (d, *J*= 11.1 Hz, 2H), 2.65 (dq, J_1=7.2 Hz, J_2=14.5 Hz, 1H), 1.90 (dq, J_1=7.2 Hz, J_2= 14.5 Hz,

3H), 1.81 (s, 3H), 1.61 (s, 3H), 1.26 (m, *J*= 7.2 Hz, 12H), 0.62 (t, *J*= 7.2 Hz, 3H). ^{13}C NMR (75 MHz , $CDCl_3$): δ (ppm) 202.0, 170.0, 169.9, 169.8, 169.7, 147.0, 145.6, 141.5, 128.8, 127.1, 127.0, 126.9, 125.3, 62.26, 62.23, 62.21, 61.6, 57.6, 57.2, 34.3, 32.3, 30.3, 16.6, 13.99, 13.98, 13.95, 10.7, 8.7. IR (CH_2Cl_2, cm^{-1}):2981, 1732, 1645, 1446, 1368, 1268, 1205, 1048. HRMS (ESI) calcd for $C_{32}H_{40}O_9Na$ $[M+Na]^+$ 591.2570, found 591.2586.

Tetraethyl 6-ethyl-6-(4-methoxyphenyl)-5,8-dimethyl-7-oxo-6,7-dihydronaphthalene-2,2,3,3(1H,4H)-tetracarboxylate (7e):

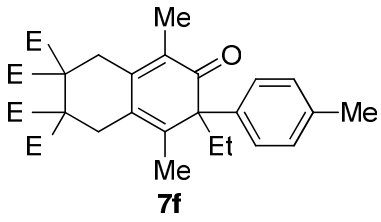


7e

The general procedure was used with 54.1 mg (0.13 mmol, 0.1 M) of diyne **7**, 27.06 mg (0.15 mmol) of ketene **e**, and 5 mol% of catalyst in toluene. The reaction mixture was purified via flash column chromatography using 15% ethyl acetate in hexanes to afford the title compound **7e** as bright yellow sticky oil, 81% yield.

^{1}H NMR (300 MHz,$CDCl_3$): δ (ppm) 7.05 (d, *J*= 9Hz, 2H), 6.77 (d, *J*= 9 Hz, 2H), 4.25 (m, 8H), 3.75 (s, 3H), 3.26 (s, 2H), 3.21 (d, *J*= 12 Hz, 2H), 2.63 (dq, J_1=7.2 Hz, J_2= 15 Hz, 1H), 1.94 (dq, J_1=7.2 Hz, J_2= 14.5 Hz, 1H), 1.83 (s, 3H), 1.64 (s, 3H), 1.28 (m, 12H), 0.63 (t, *J*= 7.2 Hz, 3H); ^{13}C NMR (75 MHz , $CDCl_3$): δ (ppm) 202.4, 170.0, 169.89, 169.84, 169.8, 158.6, 146.8, 145.8, 133.5, 127.9, 127.0, 125.1, 114.2, 62.29, 62.26, 60.9, 57.6, 57.2, 55.4, 34.3, 32.2, 30.4, 16.6, 14.0, 10.7, 8.8. IR (CH_2Cl_2, cm^{-1}): 2981, 1732, 1644, 1447, 1369, 1460, 1368, 1250, 1205, 1093, 1036. HRMS (ESI) calcd for $C_{33}H_{42}O_{10}Na$ $[M+Na]^+$ 621.2676, found 621.2689.

Tetraethyl 6-ethyl-5,8-dimethyl-7-oxo-6-(p-tolyl)-6,7-dihydronaphthalene-2,2,3,3(1H,4H)-tetracarboxylate (7f):

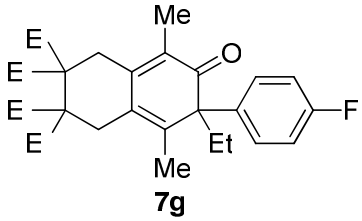


7f

The general procedure was used with 46.4 mg (0.11 mmol, 0.1 M) of diyne **7**, 20.8 mg (0.13 mmol) of ketene **f**, and 5 mol% of catalyst in toluene. The reaction mixture was purified via flash column chromatography using 15% ethyl acetate in hexanes to afford the title compound **7f** as bright yellow sticky oil, 80% yield.

^{1}H NMR (300 MHz,$CDCl_3$): δ (ppm) 7.03 (d, *J*= 3Hz, 4H), 4.26 (m, 8H), 3.26 (s, 4H), 2.66 (dq, J_1= 7.2 Hz, J_2= 14.7 Hz, 1H), 2.42 (s, 3H), 1.96 (dq, J_1= 7.5 Hz, J_2= 14.8 Hz, 1H), 1.83 (s, 3H), 1.65 (s, 3H), 1.29 (m, 12H), 0.64 (t, *J*= 7.2Hz, 3H). ^{13}C NMR (75 MHz , $CDCl_3$): δ (ppm) 202.3, 170.0, 169.9, 169.89, 169.8, 146.9, 145.8, 138.5, 136.8, 129.6, 127.0, 126.8, 125.2, 62.3, 62.28, 61.2, 57.6, 57.2, 34.3, 30.3, 21.2, 16.6, 14.05, 14.05, 14.03, 14.01, 10.8, 8.8. IR (CH_2Cl_2, cm^{-1}): 2982, 2935, 1733, 1644, 1269, 1206, 1049, 1048. HRMS (ESI) calcd for $C_{33}H_{42}O_9Na$ $[M+Na]^+$ 605.2727, found 605.2733.

Preparation of tetraethyl 6-ethyl-6-(4-fluorophenyl)-5,8-dimethyl-7-oxo-6,7-dihydronaphthalene-2,2,3,3(1H,4H)-tetracarboxylate (7g):

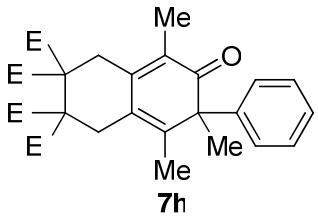


7g

The general procedure was used with 50 mg (0.118 mmol, 0.1 M) of diyne **7**, 23.4 mg (0.14 mmol) of ketene **g**, and 5 mol% of catalyst in toluene. The reaction mixture was purified via flash column chromatography using 15% ethyl acetate in hexanes to afford the title compound **7g** as bright yellow sticky oil, >99% yield.

^{1}H NMR (300 MHz,$CDCl_3$): δ (ppm) 7.11 (m, *2*H), 6.93 (m, 2H), 4.28 (m, 8H), 3.23 (m, 4H), 2.63 (dq, J_1= 7.2 Hz, 1H), 1.95 (dq, J_1= 7.5 Hz, 1H), 1.84 (s, 3H), 1.63 (s, 3H), 1.29 (m, 12H), 0.64 (t, *J*= 7.5Hz, 3H). ^{13}C NMR (75 MHz , $CDCl_3$): δ (ppm) 201.9, 170.0, 169.9, 169.76, 169.7, 163.5, 160.3, 147.1, 145.2, 137.2, 128.6, 128.5, 127.1, 125.5, 115.8, 115.5, 62.3, 60.9, 57.6, 57.1, 34.3, 32.2, 30.6, 16.5, 14.0, 10.7, 8.7. IR (CH_2Cl_2, cm^{-1}): 2983, 2938, 1748, 1644, 1269, 1206, 1055, 1048. HRMS (ESI) calcd for $C_{32}H_{39}O_9FNa$ $[M+Na]^+$ 609.2476, found 609.2477.

Preparation of tetraethyl 5,6,8-trimethyl-7-oxo-6-phenyl-6,7-dihydronaphthalene-2,2,3,3(1H,4H)-tetracarboxylate (7h):

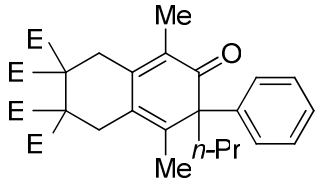


7h

The general procedure was used with 100 mg (0.24 mmol, 0.1 M) of diyne **7**, 37.4 mg (0.28 mmol) of ketene **h**, and 5 mol% of catalyst, in toluene. The reaction mixture was purified via flash column chromatography using 15% ethyl acetate in hexanes to afford the title compound **7h** as bright yellow sticky oil, 65%.

^{1}H NMR (300 MHz,$CDCl_3$): δ (ppm) 7.23 (m, 3H), 7.12 (m, 2H), 4.26 (m, 8H), 3.27 (s, 2H), 3.18 (m, 2H), 1.84 (s, 3H), 1.65 (s, 3H), 1.60 (s, 3H), 1.27 (m, 12H). ^{13}C NMR (75 MHz , $CDCl_3$): δ (ppm) 202.0, 169.9, 169.8, 169.78, 146.8, 146.5, 141.4, 128.7, 127.0, 126.8, 125.9, 122.9, 62.2, 62.1, 57.6, 57.2, 56.9, 34.3, 32.2, 30.4, 29.8, 22.8, 17.0, 13.9, 10.9. IR (CH_2Cl_2, cm^{-1}): 2983, 1732, 1647, 1445, 1367, 1269, 1205, 1094, 1038. HRMS (ESI) calcd for $C_{31}H_{38}O_9Na$ $[M+Na]^+$ 577.2414, found 577.2419.

Tetraethyl 5,8-dimethyl-7-oxo-6-phenyl-6-propyl-6,7-dihydronaphthalene-2,2,3,3(1H,4H)-tetracarboxylate (7d):

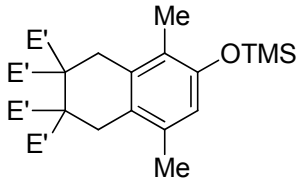


7d

The general procedure was used with 209.1 mg (0.49 mmol, 0.1 M) of diyne **7**, 95.0 mg (0.59 mmol) of ketene **d**, and 5 mol% of catalyst in toluene. The reaction mixture was purified via flash column chromatography using 15% ethyl acetate in hexanes to afford the title compound **7d** as bright yellow sticky oil, 76% yield.

^{1}H NMR (300 MHz,$CDCl_3$): δ (ppm) 7.19 (m, 5H), 4.25 (m, 8H), 3.18 (m, 4H), 2.59 (m, 1H), 1.91 (m, 1H), 1.82 (s, 3H), 1.62 (s, 3H), 1.27 (m, 12H), 0.97 (m, 2H), 0.85 (m, 3H). ^{13}C NMR (75 MHz , $CDCl_3$): δ (ppm) 202.0, 170.0, 169.86, 169.82, 169.8, 146.8, 146.0, 141.5, 128.8, 128.7, 127.1, 126.8, 124.8, 62.3, 62.2, 61.2, 57.6, 57.3, 39.7, 34.3, 32.1, 17.6, 16.7, 14.7, 14.0, 10.7. IR (CH_2Cl_2, cm^{-1}): 2982, 1735, 1646, 1446, 1368, 1267, 1208, 1096, 1033. HRMS (ESI) calcd for $C_{33}H_{42}O_9Na$ $[M+Na]^+$ 605.2727, found 605.2726.

Tetraethyl 5,8-dimethyl-6-((trimethylsilyl)oxy)naphthalene-2,2,3,3(1H,4H)-tetracarboxylate (7i):



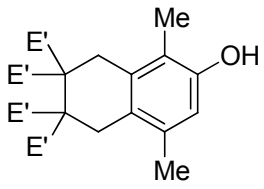
7i

The general procedure was used with 104.5 mg (0.25 mmol, 0.1 M) of diyne **7**, 41.7 mg (0.30 mmol) of ketene **i**, and 5 mol% of catalyst in toluene. The reaction mixture was purified via flash column chromatography using 10-15% ethyl acetate in hexanes to afford the title compound **7i** as colorless oil, 63% yield.

^{1}H NMR (300 MHz,$CDCl_3$): δ (ppm) 6.45 (s, 1H), 4.15 (m, 8H), 3.33 (s, 2H), 3.25 (s, 2H), 2.15 (s, 3H), 2.05 (s, 3H), 1.16 (t, J_1= 7.2 Hz, 12H), 0.19 (s, 9H). ^{13}C NMR (75 MHz , $CDCl_3$): δ (ppm) 193.7, 170.4, 170.36, 151.0, 133.5, 132.7, 124.3, 123.5, 119.1, 76.1, 61.84, 61.8, 57.612, 57.3, 33.3, 32.4, 19.8, 13.9, 12.0, 7.9, 0.6. IR (CH_2Cl_2, cm^{-1}): 2982, 1736, 1579, 1475, 1367,

1257, 1203, 1096, 1052, 913, 843. HRMS (ESI) calcd for $C_{27}H_{40}O_9SiNa$ $[M+Na]^+$ 559.2339, found 559.2340.

Tetraethyl 6-hydroxy-5,8-dimethylnaphthalene-2,2,3,3(1H,4H)-tetracarboxylate (7i'):[3]

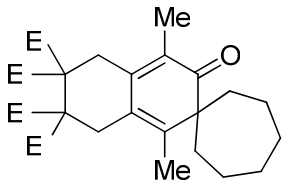


7i'

On eluting the column with 15-20% ethyl acetate in hexanes the title compound **7i'** was obtained as a white solid, 19% yield.

Melting Point: 120-123 °C (Lit:[3] 121.5-122 °C). ^{1}H NMR (300 MHz,$CDCl_3$): δ (ppm) 6.41 (s, 1H), 5.29 (s, 1H), 4.19 (m, 8H), 3.36 (s, 2H), 3.29 (s, 2H), 2.12 (s, 3H), 2.07 (s, 3H), 1.21 (t, J_1= 7.2 Hz, 12H). ^{13}C NMR (75 MHz , $CDCl_3$): δ (ppm) 170.5, 170.4, 151.6, 133.7, 132.4, 123.2, 118.8, 115.2, 61.99, 61.95, 57.5, 57.3, 33.2, 32.4, 19.6, 13.9, 11.0. IR (CH_2Cl_2, cm^{-1}): 3452, 2983, 1733, 1463, 1270, 1205, 1085, 1052. HRMS (ESI) calcd for $C_{24}H_{32}O_9Na$ $[M+Na]^+$ 487.1944, found 487.1953.

Preparation of tetraethyl 1',4'-dimethyl-3'-oxo-3'H-spiro[cycloheptane-1,2'-naphthalene]-6',6',7',7'(5'H,8'H)-tetracarboxylate (7j):

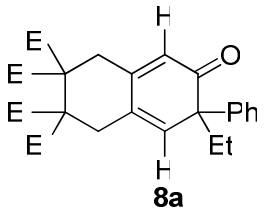


7j

The general procedure was used with 40.2 mg (0.095 mmol, 0.1 M) of diyne **7**, 14.1 mg (0.11 mmol) of ketene **j**, and 5 mol% of catalyst in toluene. The reaction mixture was purified via flash column chromatography using 15% ethyl acetate in hexanes to afford the title compound **7j** as pale oil, 76% yield.

^{1}H NMR (300 MHz,$CDCl_3$): δ (ppm) 4.20 (m, 8H), 3.15 (s, 2H), 3.04 (s, 2H), 1.91 (s, 3H), 1.86 (s, 3H), 1.59 (m, 12H), 1.25 (m, 12H). ^{13}C NMR (75 MHz , $CDCl_3$): δ (ppm) 204.2, 169.96, 169.93, 149.0, 143.6, 125.8, 120.6, 62.2, 62.1, 57.7, 57.6, 57.2, 35.2, 33.9, 32.2, 31.9, 29.8, 24.9, 15.8, 14.02, 14.00, 11.4. IR (CH_2Cl_2, cm^{-1}): 2956, 1736, 1648, 1437, 1263, 1204, 1076. HRMS (ESI) calcd for $C_{31}H_{38}O_9Na$ $[M+Na]^+$ 569.2727, found 569.2737.

Tetraethyl 6-ethyl-7-oxo-6-phenyl-6,7-dihydronaphthalene-2,2,3,3(1H,4H)-tetracarboxylate (8a):



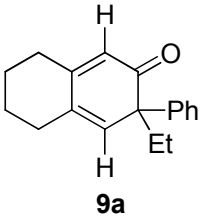
8a

The general procedure was used with 48.2 mg (0.12 mmol, 0.1 M) of diyne **8**, 21.4 mg (0.14 mmol) of ketene **a**, and 5 mol% of catalyst in toluene. The reaction mixture was purified via flash column

chromatography using 15% ethyl acetate in hexanes to afford the title compound **8a** as yellow sticky oil, 78% yield.

^{1}H NMR (300 MHz,$CDCl_3$): δ (ppm) 7.24 (m, 5H), 6.21 (s, 1H), 5.85 (s, 1H), 4.23 (m, 8H), 3.30 (m, 4H), 2.48 (dq, *J*= 7.2 Hz, 1H), 1.90 (dq, J_1= 7.2 Hz, 1H), 1.27 (m, 12H), 0.78 (t, *J*= 7.5 Hz, 3H). ^{13}C NMR (75 MHz , $CDCl_3$): δ (ppm) 202.3, 169.56, 169.5, 169.4, 169.3, 151.7, 141.6, 140.5, 128.8, 128.2, 127.4, 126.9, 123.0, 62.4, 62.34, 62.31, 58.9, 58.2, 57.3, 35.4, 34.2, 31.8, 14.0, 9.4. IR (CH_2Cl_2, cm^{-1}): 2981, 1733, 1662, 1445, 1367, 1268, 1093, 1044, 863, 689. HRMS (ESI) calcd for $C_{30}H_{36}O_9Na$ $[M+Na]^+$ 563.2257, found 563.2253.

3-ethyl-3-phenyl-5,6,7,8-tetrahydronaphthalen-2(3H)-one (9a):

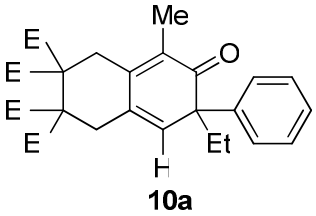


9a

The general procedure was used with 42.9 mg (0.40 mmol, 0.1 M) of diyne **9**, 70.8 mg (0.48 mmol) of ketene **a**, and 5 mol% of catalyst in toluene. The reaction mixture was purified via flash column chromatography using 5-10% ethyl acetate in hexanes to afford the title compound **9a** as bright yellow oil, 33% yield.

^{1}H NMR (300 MHz,$CDCl_3$): δ (ppm) 7.26 (m, 5H), 6.14(s, 1H), 5.80 (s, 1H), 2.58 (m, 4H), 2.45 (dq, J_1= 7.5 Hz, 1H), 1.93 (dq, J_1= 7.5 Hz, 1H), 1.75 (m, 4H), 0.81(t, *J*= 7.2 Hz, 3H). ^{13}C NMR (75 MHz , $CDCl_3$): δ (ppm) 203.2, 157.0, 141.2, 140.37, 132.4, 128.7, 127.2, 127.1, 122.9, 58.5, 32.1, 30.8, 29.1, 23.1, 22.1, 9.5. IR (CH_2Cl_2, cm^{-1}): 2934, 1658, 1492, 1448, 1382, 1231, 853, 764, 697. HRMS (ESI) calcd for $C_{18}H_{20}ONa$ $[M+Na]^+$ 275.1412, found 275.1419.

Tetraethyl 7-ethyl-5-methyl-6-oxo-7-phenyl-6,7-dihydronaphthalene-2,2,3,3(1H,4H)-tetracarboxylate (10a):

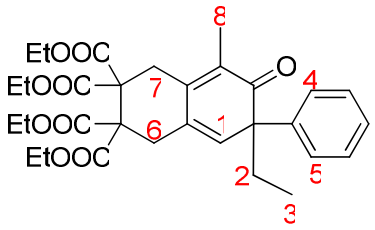


10a

The general procedure was used with 50.7 mg (0.12 mmol, 0.1 M) of diyne **10**, 21.7 mg (0.14 mmol) of ketene **a**, and 5 mol% of catalyst in toluene. The reaction mixture was purified via flash column chromatography using 15% ethyl acetate in hexanes to afford the title compound **10a** as yellow sticky oil, 66% yield.

^{1}H NMR (300 MHz,$CDCl_3$): δ (ppm) 7.25 (m, 5H), 6.12 (s, 1H), 4.25 (m, 8H), 3.30 (m, 4H), 2.48 (dq, *J*= 7.2 Hz, 1H), 1.90 (dq, J_1= 7.2 Hz, 1H), 1.83 (s, 3H), 1.28 (m, 12H), 0.75 (t, *J*= 7.5 Hz, 3H). ^{13}C NMR (75 MHz , $CDCl_3$): δ (ppm) 202.0, 169.9, 169.6, 169.5, 145.2, 140.9, 138.5,

128.9, 128.3, 128.1, 127.3, 127.0, 62.3, 62.2, 57.68, 57.62, 57.5, 34.8, 34.0, 32.1, 14.0, 10.9, 9.4. IR (CH_2Cl_2, cm^{-1}): 2981, 1733, 1645, 1445, 1368, 1269, 1092, 1044, 914, 863, 689. HRMS (ESI) calcd for $C_{31}H_{38}O_9Na$ $[M+Na]^+$ 577.2414, found 577.2411.

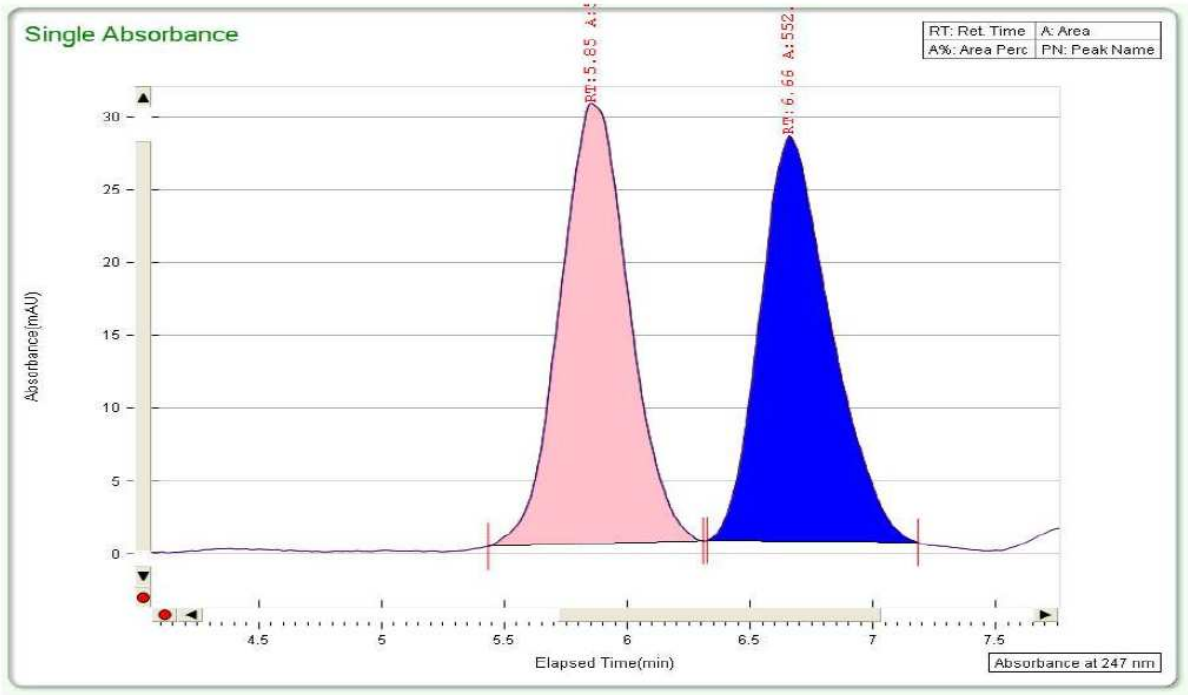


Regioselectivity was assigned on the basis of (a). nOe of proton on C-1 with protons on C-2 (only one H), C-3, C-4, C-5, and C6; (b). nOe of proton on C-8 with protons on C-7.

General Procedure for the Asymmetric Cycloaddition:

In a nitrogen-filled glove box, a 5 mol% catalyst solution (prepared from $Ni(cod)_2$ and (*R)*-BINAP in 1:1 ratio in toluene) was added to the solution of 55.3 mg (0.13 mmol) of diyne **7**, 22.9 mg (0.16 mmol) of ketene **a**. The resulting reaction mixture was then stirred at 80 °C for 5h or 100 °C for 12h, opened to air and concentrated *in vacuo.* The remaining residue was purified via flash column chromatography using 15% ethyl acetate in hexanes to afford the title compound **7a*** as bright yellow sticky oil, 38% (99% ee @ 80°C) and 58% (95% ee @ 100°C) yields. SFC (supercritical fluid chromatography) analysis was performed at 40 °C, using a Thar instrument fitted with a chiral stationary phase (Cellucoat).

ThARSFC



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Log Author		Report Date	1/14/2010
Log Date	9/24/2008 9:38:09 AM	Method Name	ISO_3_3mLmin.met
Report By	current_User	Notes	

Injection Info			
Inj Vol	5	Temp	-40
Solvent	Methanol	Flow	3
Column	Cellucoat	% Modifier	3
Sample	Rac-128	Pressure	201
Well location	P1: 1F		

Peak Info

Peak No	% Area	Area	RT (min)	Height (mV)	K'
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Total:	100	1136.52			

ThARSFC

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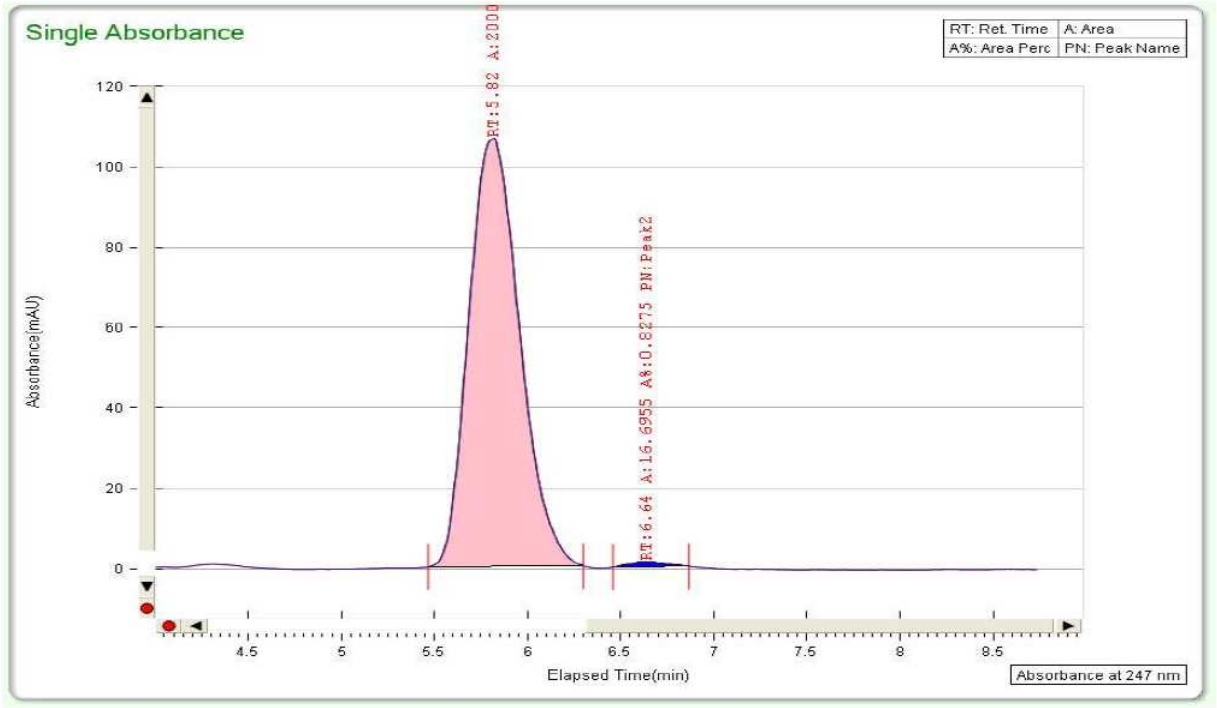
TharSFC



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Injection Info			
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Column	Cellucoat	% Modifier	3
Sample	Binap-74	Pressure	200
Well location	P1: 2F		

Peak Info

Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	99.1725	2000.9569	5.82	106.5301	0.0099
2	0.8275	16.6955	6.64	1.2383	0.0113
Total:	100	2017.6524			

TharSFC

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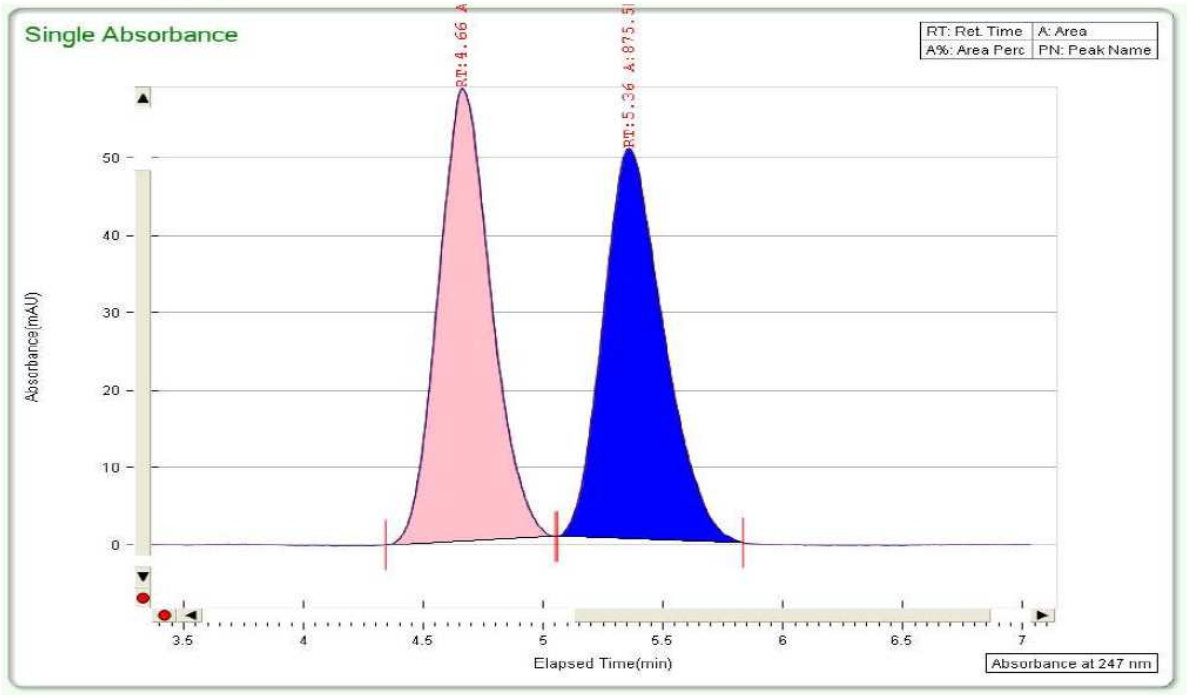
TharSFC



General Info		**Report Date**	1/14/2010
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Log Date	10/3/2008 6:39:10 PM	**Notes**	
Report By	current_User		

Injection Info		**Temp**	29.4
Inj Vol	5	**Flow**	3
Solvent	Methanol	**% Modifier**	3
Column	Column 7	**Pressure**	199
Sample	RC-86-Rac		
Well location	P1: 1F		

Peak Info

Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	50.3668	888.5299	4.66	58.5394	0.0042
2	49.6332	875.5878	5.36	50.4699	0.0048
Total:	100	1764.1177			

TharSFC

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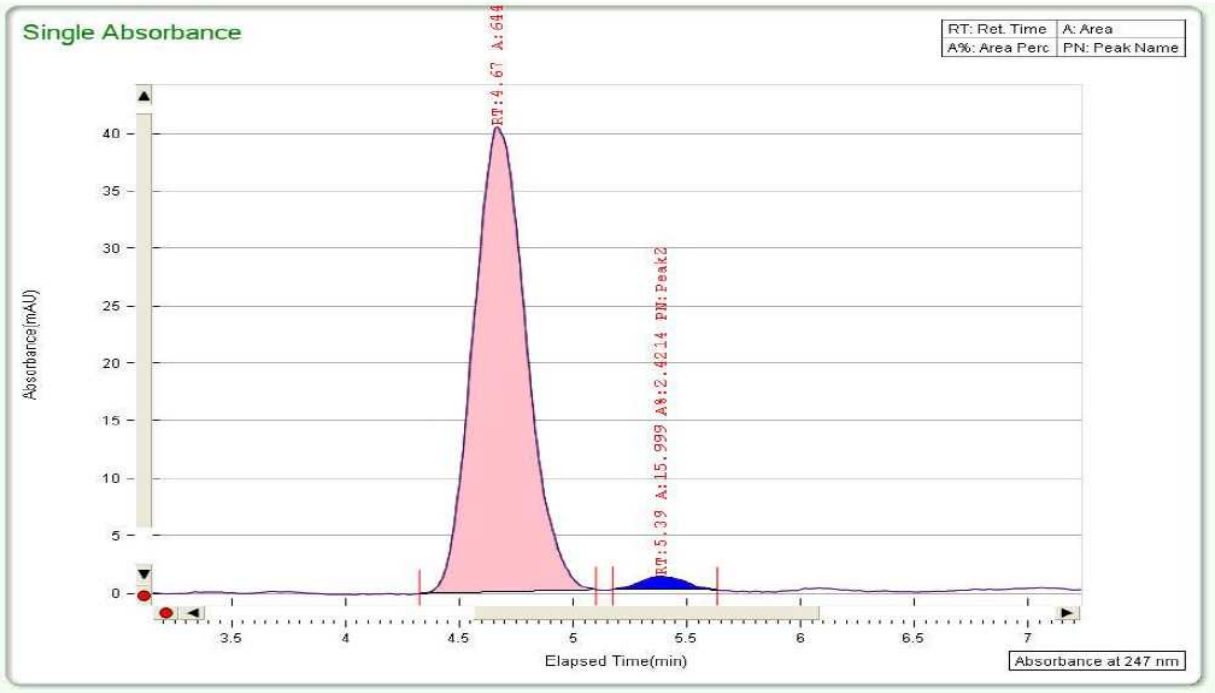
TharSFC



General Info			
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Report By	current_User	Notes	

Injection Info			
Inj Vol	5	Temp	29.7
Solvent	Methanol	Flow	3
Column	Column 7	% Modifier	3
Sample	RC-86-Toluene	Pressure	200
Well location	P1: 3F		

Peak Info

Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	97.5786	644.7462	4.67	40.4509	0.0043
2	2.4214	15.999	5.39	1.1757	0.0049
Total:	100	660.7452			

TharSFC

C:\Program Files\SuperChrom\logs\data\RC\RC-86-Toluene_10-3-2008_6_13_40 PM_1.tta

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