# Organic Brønsted Acid Catalysed Cycloadditions of *o*-Quinone Methides with 1, 3-Dicarbonlys: Facile Access to Xanthenones and Chromanones

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**Abstract.**

The *in-situ* generation of *o*-quinone methides and their inverse electron demand Diels-Alder reaction in the presence of pentacarboxycyclopentadiene – an organic Brønsted Acid has been reported. The synthesis of xanthenones and chromanones in good to excellent yields from the [4+2] cycloaddition of quinone methides with 1, 3- dicarbonyls and Meldrum's acid has been accomplished. The development of this method helps in generating a number of biologically potent heterocycles with medicinal applications.

**Keywords:** Organic Brønsted Acid; Pentacarboxycyclopentadiene; *o*-Quinone methide; Inverse Electron Demand Diels Alder reaction; Xanthenones; Chromanones

## Introduction

Quinones are important structural motifs in synthetic organic chemistry with fascinating chemistry and wide distribution in nature [1].Benzoquinones are the simplest form of quinones in which a six-membered ring containing two double bonds in conjugation with one another along with two carbonyl groups either in the 1,2 (ortho) or 1,4 (para) positions. The immense potential of benzoquinones for the synthesis of biologically relevant heterocycles attained the attention of scientific community for the last few decades. Our group was also interested in this area and reported [2] the cycloaddition of benzoquinones with various partners which delivered various novel heterocyclic compounds like spirodioxazoles [3], spirodioxazolines [4], benzodioxinones [5] and azapolyclyes [6]. Our research team has also conducted investigations on the analogues of benzoquinones where one oxygen atom is replaced by a sulphur atom (*o*-thioquinones) [7] or a carbon atom (quinone methides) [8] which drastically expands the horizons of heterocyclic chemistry.

*o*-Quinone methides, analogues of benzoquinones with relative positions of the carbonyl group and the exocyclic double bond – 1, 2 (*o*-quinone methide) are short lived reactive intermediates. These synthons have occupied pivotal role in the field of organic synthesis due to their contribution in the synthesis of varied heterocycles. They usually react in one of the three pathways [9] – (a) as an electron poor diene in an inverse- electron demand Diels-Alder reaction, (b) as a Michael acceptor in conjugate addition or (c) as a part of oxa-6π electrocylisation reaction. There have also been many reports of [4+2], [4+3], [4+4] reactions where *o*-quinone methide is the 4π component that undergoes cyclization with various partners resulting in the formation of expanded heterocycles [10]. There is an extensive amount of literature regarding both the generation as well as the numerous reactions of quinone methides towards the formation of a rich reserve of heterocycles [11].

The generation of quinone methides is a well-explored area involving the use of an impetus to break their aromaticity. Transition metals [12], chemical oxidants [13], fluoride based reagents [14], thermal activation [15], photochemical activation [16] and ionic liquids [17] have been used extensively for generating quinone methides. There are many other methods available in the literature [18], although

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the simplest method available to date is the use of acids/bases to generate *o*-quinone methides. There are innumerable reports of using Lewis acids [17], Brønsted acids [18] and bases [19] to facilitate the formation of *o*-quinone methides and their subsequent reactions. Among the colossal number of publications, a particular report by Gheewala and Lambert [20] attracted our attention, wherein they have used an organic Brønsted acid for making *o*-quinone methide from salicylaldehyde diethyl acetal to effect its cycloaddition with vinyl ethers. The synthesis of pentacarboxycyclopentadiene (PCCP), with a pKa value of 8.85 making use of a potent combination of three factors– induction, resonance and aromaticity was initially reported by Gheewala et al in 2016 [21].

Since our research group has a long standing interest in the chemistry of benzoquinones and an avid interest towards natural products, we were naturally drawn towards the generation of quinone methides and their application to the synthesis of various heterocyclic scaffolds having potential biological applications. In this paper, we have successfully studied the generation of quinone methides and their inverse electron Diels-Alder reaction catalysed by PCCP, an organic Brønsted acid.

## Experimental Section

**General Procedure for the preparation of the *o*-hydroxybenzylalcohols (1a – 1e) [22]**:

An oven dried flask equipped with a magnetic stir bar was charged with Mg turnings (0.717 g, 29.9 mmol), and an iodine crystal. The round bottom was fitted with an oven dried reflux condenser and anhydrous THF (8.2 mL) was added. The mixture stirred for 5 minutes, and was treated dropwise with aryl bromide (24.6 mmol, 3 equiv). The Grignard mixture was allowed to stir at room temperature for 30-45 minutes. A solution of salicylaldehyde (8.2 mmol, 1 equiv) in 41 mL of dry THF was added to the Grignard mixture slowly at 0 °C. The reaction was monitored by TLC until completion and was quenched with $NH_4Cl$ (aq) (30 mL). The reaction mixture was extracted with 2 x 30 mL Ether. The combined organic extracts were washed with brine, and dried over $Na_2SO_4$, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography over silica with hexane: ethyl acetate polarities.

***2-(hydroxy (phenyl) methyl) phenol (1a).*** White solid (4.67 g, 95%), m.p.. 72 °C $^1$H NMR (500MHz, Acetone, TMS): δ 8.72 (s, 1H), 7.47 (d, *J* = 7.5 Hz, 2H), 7.31 (t, *J* = 7.5 Hz, 2H), 7.27 – 7.22 (m, 2H), 7.10 (t, *J* = 7.5 Hz, 1H), 6.82 (d, *J* = 8.0 Hz, 2H), 6.14 (s, 1H), 5.33 (s, 1H) $^{13}$C NMR (125 MHz, Acetone, TMS): δ 156.9, 156.3, 129.6, 129.5, 129.2, 128.4, 128.0, 125.6, 121.2, 119.8, 117.1, 110.9 HRMS(ESI): $C_{13}H_{12}NaO_2$ Calcd $[M+Na]^+$ 223.0735 Found 223.0736

***2-((2,6-dimethylphenyl)(hydroxy)methyl)phenol(1b).*** Green solid (5.27 g, 94%) m.p.. 82 °C $^1$H NMR (500MHz, $CDCl_3$, TMS): δ 8.09 (s, 1H), 6.92 (d, *J* = 8.0 Hz, 1H), 6.75 (t, *J* = 7.5 Hz, 1H), 6.61 (d, *J* = 7.5 Hz, 1H), 6.31 (s, 1H), 2.32 (s, 3H), 2.22 (s, 3H) $^{13}$C NMR (125 MHz, $CDCl_3$, TMS): δ 156.7, 148.9, 136.7, 135.9, 129.8, 126.8, 125.9, 124.8, 116.8, 69.8, 19.5, 19.2. HRMS(ESI): $C_{15}H_{16}NaO_2$ Calcd $[M+Na]^+$ 251.1048 Found 251.1048

***2-((2,3-dimethylphenyl)(hydroxy)methyl)phenol(1c).*** White solid (5.21 g, 93%) m.p.. 74 °C $^1$H NMR (500MHz, $CDCl_3$, TMS): δ 8.06 (d, *J* = 9.6 Hz, 1H), 7.17 (dt, *J* = 14.9, 7.9 Hz, 4H), 6.93 (d, *J* = 8.1 Hz, 1H), 6.76 (t, *J* = 7.5 Hz, 1H), 6.62 (d, *J* = 7.6 Hz, 1H), 6.32 (s, 1H), 2.33 (s, 3H), 2.23 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 156.15, 139.32, 137.72, 134.96, 130.23, 129.42, 128.16, 126.19, 126.10, 125.56, 120.04, 117.16, 74.37, 20.75, 15.34. HRMS(ESI): $C_{15}H_{16}NaO_2$ Calcd $[M+Na]^+$ 251.1048 Found 251.1048

***2-(hydroxy(3-methoxyphenyl)methyl)phenol (1d).*** White solid (5.15g, 91%) m.p.. 104 °C $^1$H NMR (500MHz, CDCl3, TMS): δ 8.30 (s, 1H), 7.32 (t, *J* = 7.5 Hz, 1H), 7.24 – 7.19 (m, 1H), 6.95 (t, *J* = 8.0 Hz, 3H), 6.92 (s, 1H), 6.81 (s, 2H), 6.20 (d, *J* = 4.0 Hz, 1H), 3.89 (s, 3H). $^{13}$C NMR (125 MHz, CDCl3, TMS): δ 156.93, 156.27, 129.58, 129.53, 129.25, 128.38, 128.03, 125.62, 121.24, 119.81, 117.15, 110.87, 73.25, 55.58 HRMS(ESI): $C_{14}H_{15}O_3$ Calcd $[M+H]^+$ 230.0942 Found 230.0952

***2-(hydroxy(p-tolyl)methyl)phenol (1e)***. White solid ( 5.07 g, 96%) m.p.. 92 °C $^1$H NMR (500 MHz, $CDCl_3$): δ 8.11 (d, *J* = 4.7 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.25 (dd, *J* = 10.8, 4.7 Hz, 3H), 7.01 – 6.84 (m, 3H), 6.01 (s, 1H), 2.42 (s, 3H).$^{13}$C NMR (125 MHz, $CDCl_3$) δ 155.53, 139.07, 138.14, 129.51, 129.29, 128.34, 126.92, 126.86, 120.02, 117.30, 77.41, 21.25. HRMS(ESI): $C_{14}H_{14}NaO_2$ Calcd $[M+H]^+$ 237.0891 Found 237.0892

**General Procedure for the inverse-electron demand Diels-Alder reaction**

*o*-hydroxybenzyl alcohols (1.0 equiv) and 1,3-diketones (2.0 equiv) were added in the reaction tube followed by 2 mL of acetonitrile. The optimal PCCP catalyst (0.05 equiv) was then added and the reaction vial was stirred for 12 hours at 80 °C. Upon completion of the reaction, as monitored by TLC and concentrated in vacuo. The crude mixture was purified by column chromatography eluting with n-hexane-ethyl acetate.

***9-phenyl-2,3,4,9-tetrahydro-1H-xanthen-1-one(3aa).*** Yellow Solid ( 96.6 mg, 70%) m.p. 119 °C
$R_f$ = 0.42 (15% EtOAc/Hexane) $^1$H NMR (500 MHz, $CDCl_3$): δ 7.19 (d, *J* = 8.0 Hz, 2H), 7.17 – 7.14 (m, 2H), 7.08 (dd, *J* = 13.5, 8.0 Hz, 3H), 7.01 (t, *J* = 7.5 Hz, 2H), 5.05 (s, 4H), 2.71 (dt, *J* = 17.5, 5.0 Hz, 1H), 2.64 – 2.58 (m, 1H), 2.42 – 2.29 (m, 2H), 2.05 – 1.94 (m, 2H). $^{13}$C NMR (125 MHz, $CDCl_3$): δ 197.02, 166.33, 149.55, 146.28, 130.14, 128.81, 128.49, 127.99, 127.70, 126.44, 125.50, 125.14, 116.54, 114.86, 37.90, 37.07, 27.97, 20.47. HRMS (ESI) $C_{19}H_{17}O_2$ Calcd $[M+H]^+$: 277.1228 Found :277.1069

***9-(2,6-dimethylphenyl)-2,3,4,9-tetrahydro-1H-xanthen-1-one(3ba).*** White solid (101 mg, 76%) m.p. 181 °C
$R_f$ = 0.55 (15% EtOAc/Hexane) $^1$H NMR (500 MHz, $CDCl_3$): δ 7.13 (t, *J* =7.5 Hz, 1H), 7.08 (d, *J* = 7.5 Hz, 1H), 7.01-6.92 (m, 3H), 6.86(d,*J*=7.5 Hz,1H), 6.82(d, *J*=7.0 Hz, 1H),5.54 (s, 1H), 2.79 (s, 3H), 2.71 – 2.60 (m, 2H), 2.38 – 2.27 (m, 2H), 2.01 – 1.99 (m, 5H). $^{13}$C NMR (125 MHz, $CDCl_3$): δ 197.10, 166.09, 149.40, 141.15, 137.52, 136.66, 130.37, 129.40, 128.41, 127.69, 126.63, 124.93, 124.23, 115.85, 113.08, 37.26, 32.91, 28.01, 21.97, 20.65, 19.43. HRMS (ESI) Calcd $[M+Na]^+$ 327.1361 Found: 327.1368

***9-(2,3-dimethylphenyl)-2,3,4,9-tetrahydro-1H-xanthen-1-one(3ca).*** Yellow solid (96 mg, 72%) m.p. 128 °C $R_f$ = 0.55 (15% EtOAc/Hexane) $^1$H NMR (500 MHz, $CDCl_3$): δ 7.13 (t, *J* = 7.5 Hz, 1H), 7.05 (d, *J* = 8 Hz, 1H), 7.01-6.97 (m,2H), 6.92 (s, 2H), 6.86(t,*J*=4.0 Hz,1H), 5.38 (s, 1H), 2.75 (dt, *J* = 17.5, 5.0 Hz, 1H), 2.67 (dd, *J* =

6.7, 5.5 Hz, 1H), 2.61 (s, 3H), 2.40 – 2.33 (m, 2H), 2.31 (s, 3H), 2.09 – 1.99 (m, 2H). $^{13}$C NMR (125 MHz, $CDCl_3$): δ 197.18, 166.12, 149.08, 145.35, 136.67, 133.69, 129.74, 128.02, 127.47, 126.92, 126.57, 125.79, 125.09, 116.59, 115.72, 37.13, 33.92, 28.03, 21.32, 20.62, 15.56. HRMS(ESI): $C_{21}H_{20}NaO_2$ Calcd $[M+Na]^+$ 327.1361 Found: 327.1368

***9-(3-methoxyphenyl)-2,3,4,9-tetrahydro-1H-xanthen-1-one(3da).*** White solid (104 mg, 78%) m.p. 138 °C $R_f$ = 0.32 (15% EtOAc/Hexane) $^1$H NMR (500 MHz, $CDCl_3$): δ 7.24 (d, *J* = 7.5 Hz, 1H), 7.14 (d, *J* = 7.5 Hz, 1H), 7.11 (t, *J* = 8.0 Hz, 2H), 7.01 – 6.95 (m, 2H), 6.85-6.81 (m, 2H), 5.44 (s, 1H), 3.85 (s, 3H), 2.75(dt, *J*=17.5 Hz,5.5Hz, 1H), 2.68 – 2.62(m,1H),2.44 – 2.30 (m, 2H), 2.10 – 2.02 (m, 2H). $^{13}$C NMR (125 MHz, $CDCl_3$): δ 196.97, 167.05, 156.79, 149.53, 134.83, 129.78, 129.15, 127.73, 127.33, 125.98, 124.82, 120.97, 116.14, 113.87, 111.87, 56.02, 37.19, 31.99, 28.08, 20.75. HRMS (ESI): $C_{20}H_{18}NaO_3$ Calcd $[M+Na]^+$ 329.1154 Found: 329.1146

***9-(p-tolyl)-2,3,4,9-tetrahydro-1H-xanthen-1-one(3ea).*** Yellow solid (95 mg, 70%), m.p.. 109 °C $R_f$ = 0.50 (15% EtOAc/Hexane) $^1$H NMR (500 MHz, $CDCl_3$): δ 7.18 – 7.15 (m,1H), 7.11 (t, *J* = 8.0 Hz, 3H), 7.07 (d, *J* = 8.0 Hz, 1H), 7.03 (d, *J* = 8.0 Hz, 3H), 5.03 (s, 1H), 2.72 (dt, *J* = 17.5, 5.0 Hz, 1H), 2.67 – 2.60 (m,1H), 2.43 – 2.35 (m,2H), 2.25 (s, 3H), 2.07 – 1.99 (m,2H) $^{13}$C NMR (125 MHz, $CDCl_3$): δ 197.09, 166.24, 149.59, 143.51, 136.00, 130.15, 129.26, 127.91, 127.64, 125.76, 125.19, 116.55, 115.05, 37.53, 37.16, 28.03, 21.13, 20.54. HRMS (ESI): $C_{20}H_{18}NaO_2$ Calcd $[M+Na]^+$ 313.1204 Found 313.1210

***9-phenyl-3,9-dihydrocyclopenta[b]chromen-1(2H)-one(3ab).*** Yellow solid (92 mg, 70%) m.p.. 147 °C $R_f$ = 0.25 (15% EtOAc/Hexane) $^1$H NMR (500 MHz, $CDCl_3$): δ 7.23 – 7.13 (m, 7H), 7.08 – 7.06 (m, 2H), 4.93 (s, 1H), 2.83 – 2.72 (m, 2H), 2.47 – 2.45 (m, 2H). $^{13}$C NMR (125 MHz, $CDCl_3$): δ 202.53, 178.03, 150.64, 144.45, 131.21, 128.62, 128.43, 128.29, 126.87, 125.63, 124.18, 117.91, 117.26, 38.49, 33.61, 25.69. HRMS(ESI): $C_{18}H_{14}NaO_2$ Calcd $[M+Na]^+$ 285.0891 Found 285.0896

***9-(2,6-dimethylphenyl)-3,9-dihydrocyclopenta[b]chromen-1(2H)-one(3bb).***Pale yellow solid ( 87 mg, 68%) m.p.. 147 °C $R_f$ = 0.38 (15% EtOAc/Hexane) $^1$H NMR (500 MHz, $CDCl_3$): δ 7.19 (t, *J* = 7.5 Hz, 1H), 7.09 (d, *J* = 7.5 Hz, 1H), 7.05 (dd, *J* = 11.5, 7.5 Hz, 2H), 7.01-6.98 (m,1H), 6.84 (t, *J* = 7.0 Hz, 2H), 5.48 (s, 1H), 2.77 (d, *J* = 5.5 Hz, 2H), 2.68 (s, 3H), 2.45 (dd, *J* = 5.5, 4.5 Hz, 2H), 1.84 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$): δ 202.22, 178.05, 150.85, 138.72, 137.55, 137.00, 130.44, 129.78, 128.43, 128.15, 127.14, 125.55, 124.14, 116.66, 116.59, 33.41, 33.27, 25.65, 22.06, 19.81. HRMS (ESI): $C_{20}H_{18}NaO_2$ Calcd $[M+Na]^+$ 313.1204 Found 313.1210

***9-(2,3-dimethylphenyl)-3,9 dihydrocyclopenta[b]chromen-1(2H)-one(3cb).*** Yellow powder (89 mg, 70%) m.p. 137 °C $R_f$ = 0.30 (15% EtOAc/Hexane) $^1$H NMR (500 MHz, $CDCl_3$): δ 7.20 (t, *J* = 7.5 Hz, 1H), 7.13 (d, *J* = 8.5 Hz, 1H), 7.02 (t, *J* = 7.5 Hz, 1H), 6.98 – 6.94 (m, 3H), 6.78 (s, 1H), 5.25 (s, 1H), 2.86 – 2.74 (m, 2H), 2.48– 2.43 (m, 5H), 2.32 (s, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$): δ 202.33, 177.72, 150.48, 142.93, 136.84, 134.35, 130.78, 128.43, 128.00, 127.78, 125.77, 125.57, 125.40, 118.60, 117.10, 34.93, 33.48, 25.74, 21.18, 15.62. HRMS (ESI): $C_{20}H_{18}NaO_2$ Calcd $[M+Na]^+$ 313.1205 Found 313.1210

***9-(3-methoxyphenyl)-3,9-dihydrocyclopenta[b]chromen-1(2H)-one(3db).*** Pale brown solid (91 mg, 72%) m.p. 117°C $R_f$ = 0.12 (15% EtOAc/Hexane) $^1$H NMR (500 MHz, $CDCl_3$): δ 7.16 (t, *J* = 7.5 Hz, 3H), 7.09 – 7.07 (m, 2H), 7.02 – 6.99 (m, 1H), 6.85 (t, *J* = 8.0 Hz, 2H), 5.32 (s, 1H), 3.80 (s, 3H), 2.84 (dt, *J* = 17.5, 5.0 Hz, 1H), 2.78 – 2.75 (m,1H), 2.48 (t, *J* = 5.0 Hz, 2H). $^{13}$C NMR (125 MHz, $CDCl_3$): δ 202.48, 178.96, 156.93, 150.47, 132.80, 130.52, 129.67, 128.16, 127.79, 125.33, 125.07, 121.02, 117.24, 116.78, 111.75, 55.91, 33.60, 32.29, 25.71. HRMS(ESI): $C_{19}H_{16}NaO_3$ Calcd $[M+Na]^+$ 315.0997 Found 315.0997

***9-(p-tolyl)-3,9-dihydrocyclopenta[b]chromen-1(2H)-one(3eb).*** Cream solid (98 mg, 76%), m.p. 162 °C $R_f$ = 0.25 (15% EtOAc/Hexane) $^1$H NMR (500 MHz, $CDCl_3$): δ 7.24 – 7.20(m, 1H), 7.14 (d, *J* = 8.5 Hz, 1H), 7.10 – 7.05 (m, 6H), 4.90 (s, 1H), 2.81 – 2.76 (m, 2H), 2.49 – 2.46 (m, 2H), 2.27 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$): δ 202.55, 177.91, 150.66, 141.64, 136.46, 131.21, 129.36, 128.30, 128.22, 125.62, 124.43, 118.07, 117.24, 38.11, 33.65, 25.69, 21.16, 0.13. HRMS(ESI): $C_{19}H_{16}NaO_2$ Calcd $[M+Na]^+$ 299.1048 Found 299.1050

***3-methyl-9-phenyl-2,3,4,9-tetrahydro-1H-xanthen-1-one (3ac).*** White solid (127 mg, 88%) m.p. 119 °C $R_f$ = 0.53 (15% EtOAc/Hexane) $^1$H NMR (500 MHz, $CDCl_3$): δ 7.26 – 7.17 (m, 5H), 7.12 – 7.01 (m, 4H), 5.04 (d, *J* = 12.5 Hz, 1H), 2.75 – 2.69 (m, 1H), 2.53 – 2.32 (m, 2H), 2.14 – 2.05 (m, 1H), 1.57(d, *J* = 7.0 Hz,1H) 1.10 (dd, *J* = 9.5, 6.5 Hz, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$): δ 197.02, 165.19, 146.33, 130.22, 128.55, 128.52, 128.05, 128.02, 127.75, 126.50, 125.22, 125.15, 116.64, 45.46, 45.39, 38.16, 37.97, 36.21, 35.85, 28.69, 28.02, 21.00, 20.91. HRMS(ESI): $C_{20}H_{18}NaO_2$ Calcd: $[M+Na]^+$ 313.1204 Found 313.1210

***9-(2,6-dimethylphenyl)-3-methyl-2,3,4,9-tetrahydro-1H-xanthen-1-one (3bc).*** White solid (100 mg, 72%) m.p. 173 °C $R_f$ = 0.65 (15% EtOAc/Hexane) $^1$H NMR (500 MHz, $CDCl_3$): δ 7.12 (t, *J* = 7.5 Hz, 1H), 7.09 – 7.06 (m,1H), 7.00 – 6.91 (m, 3H), 6.87 – 6.84 (m, 1H), 6.81 (d, *J* = 7.5 Hz, 1H), 5.53 (d, *J* = 9.5 Hz, 1H), 2.77 (d, *J* = 13.0 Hz, 3H), 2.68 (dd, *J* = 17.0, 4.0 Hz, 1H), 2.44 – 2.17 (m, 3H), 2.11 – 2.02 (m, 1H), 1.97 (d, *J* = 10.0 Hz, 3H), 1.11 (d, *J* = 6.0 Hz, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$): δ 197.49, 166.07, 149.47, 129.46, 127.73, 126.69, 125.00, 115.93, 77.41, 77.16, 76.91, 45.50, 36.17, 32.96, 28.15, 20.97, 0.14.
HRMS (ESI): $C_{22}H_{22}NaO_2$ Calcd $[M+Na]^+$ 341.1517 Found 341.1517

***9-(2,3-dimethylphenyl)-3-methyl-2,3,4,9-tetrahydro-1H-xanthen-1-one(3cc).*** White solid (100 mg, 73%) m.p. 108 °C $R_f$= 0.60 (15% EtOAc/Hexane) $^1$H NMR (500 MHz, $CDCl_3$): δ 7.12 (t, *J* = 7.5 Hz, 1H), 7.07 – 6.93 (m, 3H), 6.91 – 6.90 (m, 2H), 6.86 – 6.80 (m, 1H), 5.35 (d, *J* = 7.0 Hz, 1H), 2.77 – 2.68 (m, 1H), 2.60 (s, 3H), 2.53 – 2.34 (m, 3H), 2.30 (s, 3H), 2.11 – 2.03 (m,1H), 1.10 (t, *J* = 5.5 Hz, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$): δ 197.08, 165.81, 149.18, 136.71, 133.70, 129.76, 128.04, 127.49, 126.96, 125.81, 125.13, 116.65, 77.41, 77.16, 76.91, 45.39, 36.18, 35.86, 33.95, 28.08, 21.33, 20.99, 15.57.
HRMS(ESI): $C_{22}H_{22}NaO_2$ Calcd $[M+Na]^+$ 341.1517 Found 341.1517

***9-(3-methoxyphenyl)-3-methyl-2,3,4,9-tetrahydro-1H-xanthen-1-one(3dc).*** White solid (111 mg, 80%) m.p. 143 °C $R_f$ = 0.39 (15% EtOAc/Hexane) $^1$H NMR (500 MHz, $CDCl_3$): δ 7.23 (dd, *J* = 16.5, 7.5 Hz, 1H), 7.14 – 7.09 (m, 3H), 7.00 – 6.94 (m, 2H), 6.85 – 6.81 (m, 2H), 5.43 (d, *J* = 9.0 Hz, 1H), 3.84 (d, *J* = 1.5 Hz, 3H), 2.77 – 2.68 (m, 1H), 2.53 – 2.28 (m, 3H), 2.13 – 2.05 (m, 1H), 1.13 – 1.11 (m, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$): δ 196.94, 166.73, 165.88, 156.79, 156.74, 149.59, 149.53, 134.79, 129.81, 129.79, 129.21, 129.15, 127.74, 127.70, 127.35, 127.33, 126.04, 125.76, 124.84, 124.79, 120.97, 120.92, 116.18, 116.14, 113.47, 113.29, 111.88, 111.77, 56.01, 56.00, 45.48, 45.36, 36.23, 35.87, 32.14, 31.99, 28.55, 28.23, 21.06, 20.91. HRMS(ESI): $C_{21}H_{20}NaO_3$ Calcd $[M+Na]^+$ 343.1310 Found 343.1310

***3-methyl-9-(p-tolyl)-2,3,4,9-tetrahydro-1H-xanthen-1-one(3ec).*** Pale Yellow solid (81 mg, 57%) m.p. 87 °C $R_f$= 0.58 (15% EtOAc/Hexane) $^1$H NMR (500 MHz, $CDCl_3$): δ 7.18 – 6.99 (m, 8H), 5.00 (d, *J* = 12.0 Hz, 1H), 2.75 – 2.67 (m, 1H), 2.52 – 2.42 (m, 2H), 2.37 – 2.30 (m, 1H), 2.25 (s, 3H), 2.13 – 2.05 (m, 1H), 1.10 (t, *J* = 7.0 Hz, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$): δ 197.10, 165.95, 165.11, 149.64, 149.49, 143.50, 143.40, 136.01, 135.96, 130.17, 129.26, 129.24, 127.87, 127.64, 125.80, 125.57, 125.20, 125.14, 116.59, 116.56, 114.67, 114.33, 45.45, 45.40, 37.72, 37.52, 36.19, 35.84, 28.69, 28.01, 21.12, 21.01, 20.94. HRMS(ESI): $C_{21}H_{20}NaO_2$ Calcd $[M+Na]^+$ 327.1361 Found 327.1358

***3,3-dimethyl-9-phenyl-2,3,4,9-tetrahydro-1H-xanthen-1-one(3ad).*** White solid (121 mg, 80%) m.p. 133 °C $R_f$ = 0.54 (15% EtOAc/Hexane) $^1$H NMR (500 MHz, $CDCl_3$): δ 7.23 – 7.00 (m, 9H), 5.03 (s, 1H), 2.56 (d, *J* = 2.5 Hz, 2H), 2.25 (m, 2H), 1.12 (s, 3H), 1.04 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$): δ 196.93, 164.65, 149.57, 146.23, 130.24, 128.55, 127.99, 127.74, 126.49, 125.54, 125.18, 116.65, 113.60, 50.97, 41.74, 38.06, 32.29, 29.40, 27.56. HRMS(ESI): $C_{21}H_{20}NaO_2$ Calcd $[M+Na]^+$ 327.1361 Found 327.1367

***9-(2,6-dimethylphenyl)-3,3-dimethyl-2,3,4,9-tetrahydro-1H-xanthen-1-one(3bd).*** White solid (106 mg, 73%) m.p. 192 °C $R_f$ =0.59 (15% EtOAc/Hexane) $^1$H NMR (500 MHz, $CDCl_3$): δ 7.13 (t, *J* = 7.5 Hz, 1H), 7.08 (d, *J* = 7.5 Hz, 1H), 7.01 - 6.93 (m, 3H), 6.85 (d, *J* = 8.0 Hz, 1H),6.82(d, *J*=7.0 Hz, 1H), 5.55 (s, 1H), 2.79 (s, 3H), 2.58 – 2.45 (m, 2H), 2.23 (d, *J* = 3.5 Hz, 2H), 1.98 (s, 3H), 1.12 (d, *J* = 5.5 Hz, 6H). $^{13}$C NMR (125 MHz, $CDCl_3$): δ 197.16, 164.27, 149.60, 141.14, 137.64, 136.61, 130.38, 129.46, 128.41, 127.70, 126.66, 124.94, 124.32, 115.89, 112.00, 51.23, 41.79, 32.87, 32.06, 28.79, 28.53, 22.00, 19.31. HRMS(ESI): $C_{23}H_{24}NaO_2$ Calcd $[M+Na]^+$ 355.1674 Found 355.1682

***9-(2,3-dimethylphenyl)-3,3-dimethyl-2,3,4,9-tetrahydro-1H-xanthen-1-one(3cd).*** Cream solid (99 mg, 68%) m.p. 143 °C $R_f$ = 0.62 (15% EtOAc/Hexane) $^1$H NMR (500 MHz, $CDCl_3$): δ 7.13 (t, *J* = 7.0 Hz, 1H), 7.06 (d, *J* = 8.0 Hz, 1H), 7.02 (d, *J* = 6.5 Hz, 1H), 6.98 (t, *J* = 7.5 Hz, 1H), 6.93 – 6.92 (m, 2H), 6.87 (d, *J* = 3.0Hz, 1H), 5.38 (s, 1H), 2.64 (s, 3H), 2.58 (d, *J* = 3.5 Hz, 2H), 2.34 (s, 3H), 2.24 (q, *J* = 16.0 Hz, 2H), 1.14 (s, 3H), 1.08 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$): δ 197.05, 164.41, 149.11, 145.22, 136.67, 133.58, 129.74, 127.96, 127.46, 126.79, 126.53, 125.70, 125.08, 116.63, 114.37, 50.92, 41.70, 33.70, 32.26, 29.32, 27.65, 21.32, 15.56. HRMS(ESI): $C_{23}H_{24}NaO_2$ Calcd $[M+Na]^+$ 355.1674 Found 355.1679

***9-(3-methoxyphenyl)-3,3-dimethyl-2,3,4,9-tetrahydro-1H-xanthen-1-one(3dd).*** Yellow solid (128 mg, 88%) m.p. 114 °C $R_f$ = 0.40 (15% EtOAc/Hexane) $^1$H NMR (500 MHz, $CDCl_3$): δ 7.22 (d, *J* = 8.0 Hz, 1H), 7.18 (d, *J* = 8.0 Hz, 1H), 7.12 (t, *J* = 7.5 Hz, 2H), 7.01 (d, *J* = 8.0 Hz, 1H),6.97(t, *J*=7.5 Hz, 1H), 6.84 (d, *J* = 8.0 Hz, 2H), 5.43 (s, 1H), 3.83 (s, 3H), 2.57 (s, 2H), 2.25 (q, *J* = 16.0 Hz, 2H), 1.14 (s, 3H), 1.10 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$): δ 196.78, 165.28, 156.66, 149.55, 134.57, 129.76, 129.32, 127.69, 127.28, 125.79, 124.74, 120.82, 116.10, 112.46, 111.64, 55.83, 50.91, 41.73, 34.76, 32.20, 32.17, 32.02, 31.66, 29.78, 29.42, 27.48, 25.37, 22.72, 14.28, 14.19. HRMS(ESI): $C_{22}H_{22}NaO_3$ Calcd [M+Na] 357.1466 Found 357.1466

***3,3-dimethyl-9-(p-tolyl)-2,3,4,9-tetrahydro-1H-xanthen-1-one(3ed).*** Colourless liquid ( 97 mg, 65%) $R_f$= 0.54 (15% EtOAc/Hexane) $^1$H NMR (500 MHz, $CDCl_3$): δ 7.16 (t, *J* = 7.5 Hz, 1H), 7.11 (t, *J* = 8.5 Hz, 3 H), 7.06 (d, *J* = 8.0 Hz, 1H), 7.02 (t, *J* = 8.5 Hz, 3H), 4.99 (s, 1H), 2.55 (d, *J* = 2.5 Hz, 2H), 2.26 – 2.23 (m, 5H), 1.12 (s, 3H), 1.05 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$): δ 196.95, 164.52, 149.52, 143.40, 135.95, 130.18, 129.26, 127.82, 127.62, 125.74, 125.16, 116.60, 113.68, 50.98, 41.73, 37.64, 32.27, 29.83, 29.38, 27.61, 21.12. HRMS (ESI): $C_{22}H_{22}NaO_2$ Calcd $[M+Na]^+$ 341.1517 Found 341.1524

***1-(2-ethyl-2-hydroxy-4-phenylchroman-3-yl) propan-1-one (3ae).*** White sticky solid (100 mg, 65%), $R_f$ = 0.50
$^1$H NMR (500 MHz, $CDCl_3$) δ 7.27-7.19 (m,3H), 7.09 (d, *J* = 7.0 Hz, 3H), 6.86 (d, *J* = 8.5 Hz, 1H), 6.74 (t, *J* = 7.5 Hz, 1H), 6.63 (d, *J* = 7.5 Hz, 1H), 4.35 (d, *J* = 12.5 Hz, 1H), 4.18 (s, 1H), 3.25 (d, *J* = 12.0 Hz, 1H), 2.20 (dq, *J* = 17.0, 7.0 Hz, 1H), 1.75 – 1.55 (m, 3H), 1.06 (t, *J* = 7.5 Hz, 3H), 0.69 (t, *J* = 7.0 Hz, 3H).
$^{13}$C NMR (125 MHz, $CDCl_3$) δ 216.02, 151.89, 141.60, 130.04, 129.28, 129.09, 128.76, 128.17, 127.64, 127.19, 124.47, 121.31, 117.25, 117.17, 96.86, 58.48, 44.50, 44.35, 40.20, 39.64, 33.70, 24.82, 7.48, 7.15, 6.83, 5.50.

HRMS (ESI): $C_{20}H_{22}NaO_3$ Calcd $[M+Na]^+$ 333.1466 Found 333.1473

***1-(4-(2, 3-dimethylphenyl)-2-ethyl-2-hydroxychroman-3-yl) propan-1-one(3ce).*** Yellow liquid (66 mg, 44%) $R_f$ = 0.52 $^1$H NMR (500 MHz, $CDCl_3$) δ 7.11 (t, *J* = 7.5 Hz, 1H), 7.05 (d, *J* = 4.5 Hz, 2H), 6.91 (d, *J* = 8.0 Hz, 2H), 6.77 (t, *J* = 7.5 Hz, 1H), 6.56 (d, *J* = 7.5 Hz, 1H), 4.90 (d, *J* = 12.0 Hz, 1H), 4.35 (s, 1H), 3.37 (d, *J* = 12.0 Hz, 1H), 2.32 (s, 3H), 2.24 (m, 3H), 1.82 – 1.68 (m, 4H), 1.12 (t, *J* = 7.5 Hz, 3H), 0.73 (t, *J* = 7.0 Hz, 3H).$^{13}$C NMR (125 MHz, $CDCl_3$) δ 216.26, 151.99, 139.83, 137.08, 135.81, 128.92, 128.85, 128.53, 127.84, 126.45, 126.36, 125.38, 121.31, 117.12, 97.11, 77.41, 77.16, 76.91, 57.98, 39.48, 38.48, 36.75, 36.63, 33.67, 27.75, 24.81, 23.46, 21.42, 21.10, 15.16, 14.98, 7.72, 7.53, 6.99. HRMS (ESI): $C_{22}H_{26}NaO_3$ Calcd $[M+Na]^+$ 361.1779 Found 361.1788

***1-(2-ethyl-2-hydroxy-4-(p-tolyl)chroman-3-yl)propan-1-one(3ee).*** Colourless liquid **(**97 mg**,** 64%**)** $R_f$ = 0.50 $^1$H NMR (500 MHz, $CDCl_3$) δ 7.12 (d, *J* = 8.0 Hz, 3H), 7.03 (d, *J* = 8.0 Hz, 2H), 6.91 (d, *J* = 8.0 Hz, 1H), 6.79 (t, *J* = 7.5 Hz, 1H), 6.69 (d, *J* = 7.5 Hz, 1H), 4.37 (d, *J* = 12.0 Hz, 1H), 4.26 (s, 1H), 3.30 (d, *J* = 12.5 Hz, 1H), 2.34 (s, 3H), 2.27 (ddd, *J* = 18.0, 12.5, 5.0 Hz, 1H), 1.78 – 1.67 (m, 3H), 1.12 (t, *J* = 7.5 Hz, 3H), 0.77 (t, *J* = 7.0 Hz, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 216.06, 151.89, 138.43, 137.23, 130.02, 129.75, 129.43, 129.12, 129.08, 128.06, 128.00, 124.74, 121.38, 121.25, 117.20, 117.12, 96.90, 58.48, 44.10, 43.89, 39.56, 33.73, 21.22, 7.46, 6.87. HRMS (ESI): $C_{21}H_{24}NaO_3$ Calcd $[M+Na]^+$ 277.0840 Found 277.0840

***4-phenylchroman-2-one (3af).*** White sticky solid (56 mg, 50%) $R_f$ = 0.54 (15% EtOAc/Hexane) $^1$H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.20 (m, 4H), 7.10 – 7.06 (m, 3H), 7.01 (t, *J* = 7.5 Hz, 1H), 6.90 (d, *J* = 7.5 Hz, 1H), 4.28 (t,*J* = 7.0 Hz, 1H), 2.98 (qd, *J* = 15.0, 6.0 Hz, 2H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 167.80, 151.86, 140.41, 129.29, 128.96, 128.48, 127.82, 127.72, 125.92, 124.81, 117.28, 40.83, 37.16, 29.85. HRMS (ESI): $C_{15}H_{13}O_2$ Calcd $[M+H]^+$ 225.0915 Found 225.0915

***4-(2,6-dimethylphenyl)chroman-2-one (3bf).***

Yellow Sticky Solid (44mg, 40%) $R_f$ = 0.62 (15% EtOAc/Hexane) $^1$H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.25 (m, 1H), 7.17 – 7.11 (m, 3H), 7.06 – 7.00 (m, 2H),6.76 (d, *J* = 8.0 Hz, 1H), 4.94 (dd, *J* = 14.5, 5.5 Hz, 1H), 3.20 (dd, *J* = 16.5, 14.5 Hz, 1H), 2.41 (s, 3H), 2.00 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 168.05, 152.20, 137.90, 137.74, 134.59, 129.56, 129.40, 128.77, 128.27, 126.36, 126.24, 124.85, 124.80, 120.77, 117.15, 114.02, 55.25, 37.07, 36.30, 21.11, 15.26. HRMS(ESI): $C_{17}H_{16}NaO_2$ Calcd $[M+Na]^+$ 275.1048 Found 275.1048

***4-(2,3-dimethylphenyl)chroman-2-one (3cf).*** Yellow sticky solid (53mg, 48%) $R_f$ = 0.54 (15% EtOAc/Hexane) $^1$H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.29 (m, 1H), 7.15 (d, *J* = 8.0 Hz, 1H), 7.11 (d, *J* = 7.5 Hz, 1H), 7.06 (q, *J* = 7.5 Hz, 2H), 6.87 (d, *J* = 7.5 Hz, 1H), 6.74 (d, *J* = 7.5 Hz, 1H), 4.67 (dd, *J* = 8.5, 6.0 Hz, 1H), 3.00 (qd, *J* = 15.5, 8.5 Hz, 2H), 2.35 (s, 3H), 2.29 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 168.05, 152.20, 137.90, 137.74, 134.59, 129.56, 129.40, 128.77, 128.27, 126.36, 126.24, 124.85, 124.80, 120.77, 117.15, 114.02, 55.25, 37.07, 36.30, 21.11, 15.26. HRMS (ESI): $C_{17}H_{16}NaO_2$ Calcd $[M+Na]^+$ 275.1048 Found 275.1047

***4-(3-methoxyphenyl)chroman-2-one (3df).*** Yellow crystalline solid (57mg, 52%) m.p. 117 °C $R_f$ = 0.46 (15% EtOAc/Hexane) $^1$H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.22 (m, 2H), 7.12 (d, *J* = 8.0 Hz, 1H), 7.09 – 7.01 (m, 2H), 6.91 – 6.83 (m, 3H), 4.67 (t, *J* = 6.0 Hz, 1H), 3.82 (s, 3H), 3.10 (dd, *J* = 16.0, 5.5 Hz, 1H), 2.98 (dd, *J* = 16. 0, 7.0 Hz, 1H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 168.16, 156.95, 152.20, 128.93, 128.90, 128.61, 128.57, 128.41, 125.08, 124.61, 120.99, 117.07, 110.89, 55.24, 35.63, 35.28. HRMS (ESI): $C_{16}H_{14}NaO_3$ Calcd $[M+Na]^+$ 277.0840 Found 277.0840

***4-(p-tolyl)chroman-2-one (3ef).*** White sticky solid (55mg, 50%) $R_f$ = 0.65 (15% EtOAc/Hexane) $^1$H NMR (500 MHz, $CDCl_3$) δ 7.29 (t, *J* = 7.5 Hz, 1H), 7.14 (m, 3H), 7.07 (m, 3H), 6.98 (d, *J* = 7.5 Hz, 1H), 4.33 – 4.29 (t, *J* = 7.0 Hz, 1H), 3.08 – 2.98 (m, 2H), 2.34 (s, 3H). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 167.85, 151.85, 137.50, 137.38, 129.92, 128.83, 128.44, 127.57, 126.20, 124.73, 117.21, 40.45, 37.20, 21.15, 0.12. HRMS (ESI): $C_{16}H_{14}NaO_2$ Calcd $[M+Na]^+$ 261.0891 Found 261.0891

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*o*-Hydroxybenzyl alcohols have been readily converted into the respective *o*-quinone methide (*o*-QM) intermediates in the presence of organic Brønsted acid and serve as a suitable diene for inverse electron demand Diels Alder reaction. The reaction proceeds through a similar mechanism as that proposed by Gheewala [21].The plausible mechanism for the reaction has been proposed in Scheme 6. Initially the organic Brønsted acid reacts on *o*-hydroxybenzylalcohol **1a**, to generate the corresponding *o*-quinone methide **I-1**. Subsequently **I-1** reacted with **2a** with the assistance of Brønsted acid to give an adduct **I-2** which underwent the cycloaddition reaction to form **I-3.** Dehydration of **I-3** in presence of Brønsted acid yields the desired product **3aa** and regenerates the Brønsted acid. The utilization of *o*-hydroxybenzyl alcohols as precursors of dienes and 1, 3-diketones as dienophiles, as well as the hydrogen-bonding activation mode of the Brønsted acid catalyst to the substrates delivers the biologically important chroman scaffolds.

Meldrum's acid (2, 2-dimethyl-1, 3-dioxane-4, 6-dione) as a 2π partner gave the corresponding arylchromanones when reacted with **1a** (Scheme 5). Under the heating conditions, Meldrum's acid was converted to its ketene form which then reacted with the quinone methide giving the arylchromanones.

## Results and Discussion

We initiated our efforts with one of the well-known electron rich dienophile 1, 3-diketones and *o*-quinone methides promoted by organic Brønsted acid catalyst based on pentacarboxycyclopentadienes (PCCPs), which are strongly acidic and simple to prepare from alcohol precursors [21].

We commenced the reaction of *o*-hydroxy benzyl alcohol (**1a**) with 5, 5-dimethyl-1, 3-cyclohexadione (**2**) in the presence of catalytic amount of the prepared organic Brønsted acid (20 mol %) in dichloromethane at room temperature. The inverse electron demand Diels-alder reaction proceeded smoothly and generated the 4H- chromene product within 12 h in moderate yield (Scheme 1). The structure of the product was confirmed by various spectroscopic techniques such as $^{1}$H NMR, $^{13}$C NMR and HRMS analyses. (See Supporting Information)

The reaction conditions were optimized by examining various solvents and temperatures. From the optimization studies, a combination of *o*-hydroxy benzyl alcohol (1 equiv), 1, 3-cyclohexadione (2equiv), Brønsted acid (20 mol %), in ACN (2 mL) at 80°C was found to be the best condition under which the product was delivered in 80 % yield. When the reaction was carried out in dry solvents there was a drastic decrease in yield indicating that the presence of moisture plays a major role in maintaining the acidity required for the reaction to produce the quinone methide. The optimization studies are showed in Table 1.

With the optimal conditions in hand, we investigated the scope of reaction with substituted *o*-hydroxy benzyl alcohols (Scheme 2 - 4). The attempt to prepare o-hydroxy benzyl alcohols with electron-withdrawing groups on both the aldehyde as well as the aryl halide did not succeed hence only o-hydroxy benzyl alcohols bearing diverse electron donating groups were taken up for the substrate scope. These substrates afforded the corresponding products in moderate to good yields.

Initially, the quinone methides were subjected to unsubstituted cyclic 1, 3- diketones which yielded the corresponding xanthenones in good yields. There was no appreciable difference in the products of cyclopentadione as well as cyclohexadiones.

To further check the substrate scope of the reaction, substituted cyclic 1, 3- diketones were taken under consideration, which gave almost the same yields as those of unsubstituted analogues.

We next moved on to the acyclic 1, 3-diketones. 3, 5- heptadione was taken as the representative for the above mentioned class and allowed to react with the quinone methides which afforded the cycloaddition product without elimination of a water molecule giving the corresponding chromanones with a hydroxyl group.

## Conclusion

In conclusion, the hydroxyl benzyl alcohols were converted into their respective ortho quinone methides in the presence of a novel organic Brønsted acid and their reactivity as a 4π partner in an inverse electron demand– Diels Alder reaction was explored with a variety of scaffolds giving biologically useful heterocyclic compounds. The further study of this reaction to give steroselective products in the presence of chiral Brønsted Acids are currently under progress in our laboratory.

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**ARTICLE**

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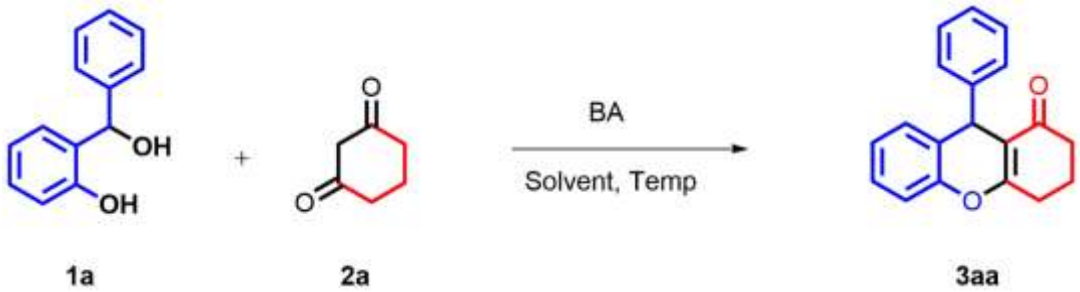


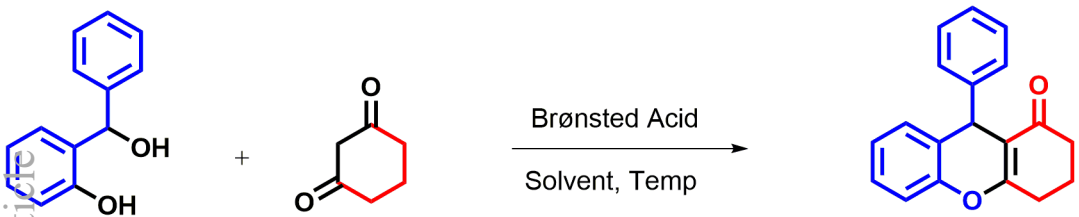

1a 2a 3aa

**Table 1.** Optimization of the Bronsted Acid catalysed inverse –electron demand Diels Alder reaction[a]

| Sl No | Solvent | Temperature (°C) | Catalyst (mol %) | Yield (%) |
|---|---|---|---|---|
| 1 | $CHCl_3$ | rt | 5 | NR |
| 2 | $CHCl_3$ | rt | 10 | 6 |
| 3 | $CH_2Cl_2$ | rt | 5 | 20 |
| 4 | $CH_2Cl_2$ | rt | 10 | 70 |
| 5 | DMF | rt | 10 | NR |
| 6 | ACN | rt | 10 | NR |
| 7 | Ethanol | rt | 10 | Trace |
| 8 | Benzene | rt | 10 | Trace |
| 9 | Toluene | rt | 10 | 60 |
| 10 | Toluene | 70 | 10 | 50 |
| 11 | Toluene | 120 | 10 | 53 |
| **12** | **ACN** | **80** | **10** | **80** |
| 13 | ACN | 80 | 20 | 81 |
| 14 | DCE | 80 | 10 | 60 |
| 15 | Xylene | 140 | 10 | 54 |
| 16 | EtOAc | 70 | 10 | 15 |
| 17 | THF | 70 | 10 | Trace |
| 18 | Benzene | 70 | 10 | 37 |
| 19[b] | DCE | 80 | 10 | NR |
| 20 | ACN | 80 | No Catalyst | NR |

[a] Reaction conditions: **1a** (1 equiv), **2a** (2 equiv), organic Brønsted acid, solvent (2 mL), rt - room temperature, NR - No reaction

[b] $Sc(OTf)_3$ was used in place of the organic Brønsted acid.




1a 2a 3aa



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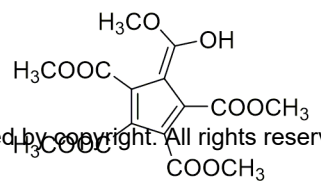
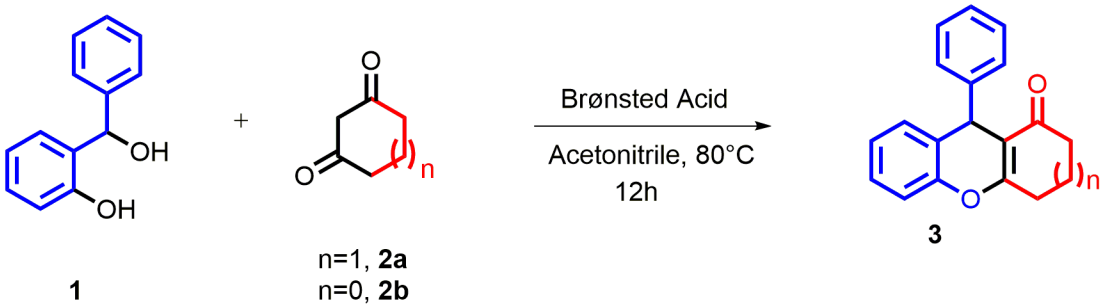


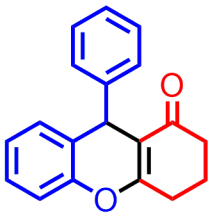



**1**

n=1, **2a**
n=0, **2b**

**3**



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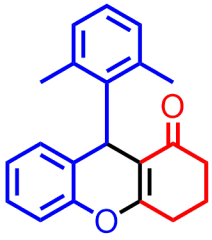


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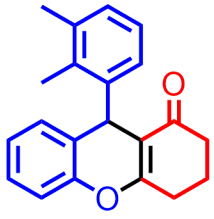


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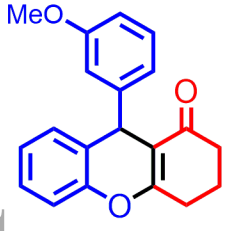


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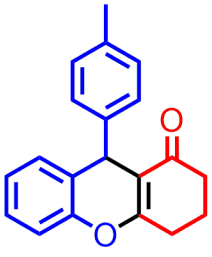


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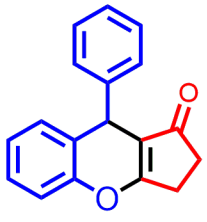


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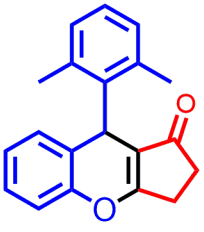


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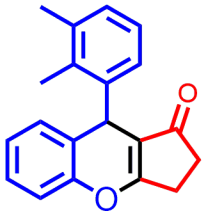


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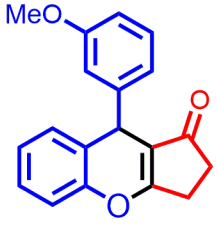


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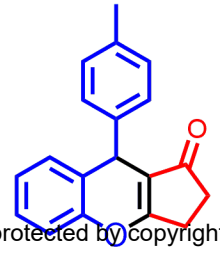




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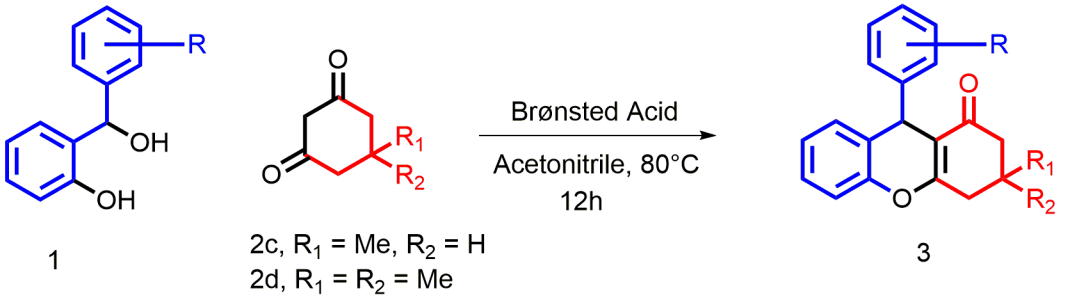
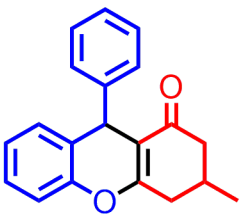



1

2c, $R_1$ = Me, $R_2$ = H
2d, $R_1$ = $R_2$ = Me

3



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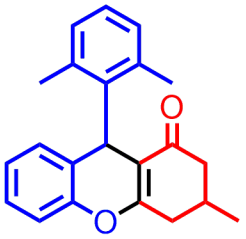


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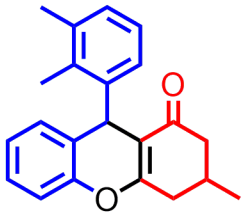


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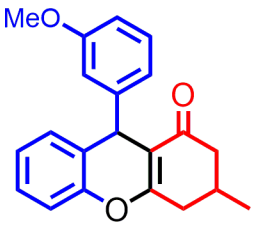


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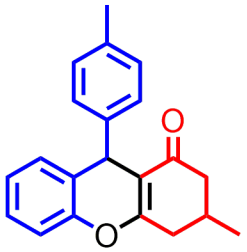


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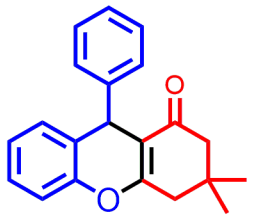


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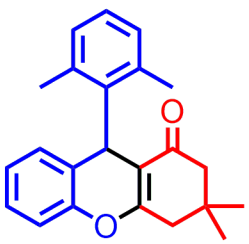


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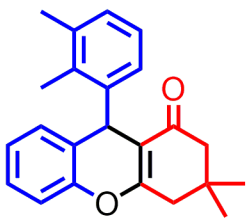


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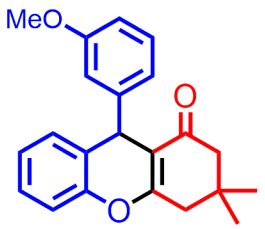


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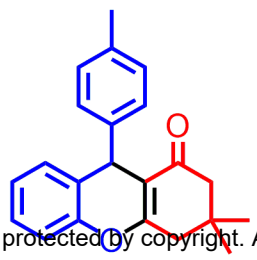




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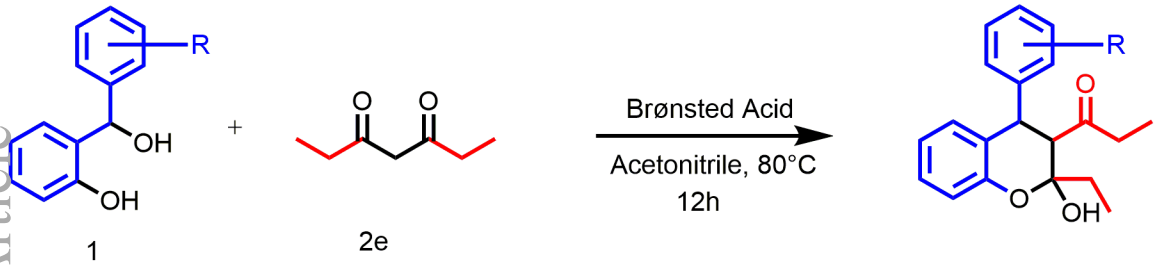


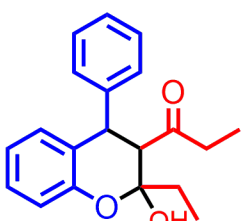


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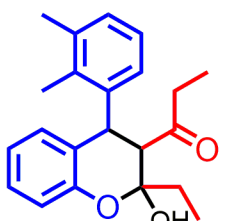


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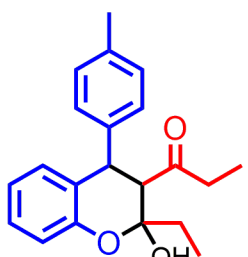


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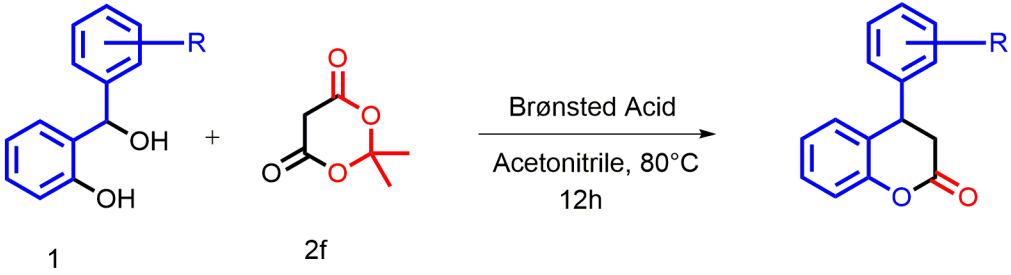


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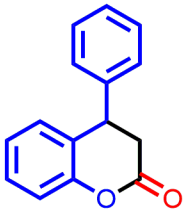

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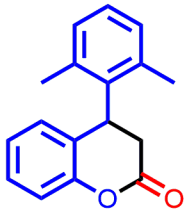

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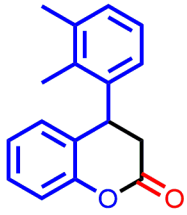

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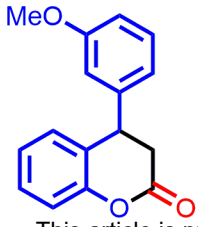


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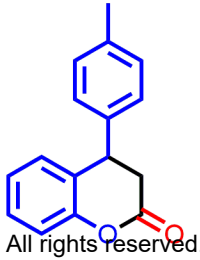

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