Experimental Section

1. Chemistry

Melting points were determined on a Fisher-Johns melting apparatus and are uncorrected. ^{1}H-NMR spectra were recorded on a Varian INOVA-400 spectrometer. The chemical shifts are presented in terms of ppm with TMS as the internal reference. Electron-spray ionization mass spectra in positive mode (ESI-MS) data were recorded on a Bruker Esquire 3000$^+$ spectrometer. Column chromatography purifications were carried out on Silica Gel 60 (E. Merck, 70-230 mesh). The purity of all new compounds was checked by thin-layer chromatography (TLC) and ^{1}H-NMR. All reactions were monitored by TLC analyses on pre-coated Silica Gel F254 plates (purchased from Qingdao Marine Chemical Factory, China) by UV detection. 4-fluorobenzaldehyde, 2-bromobenzaldehyde, 3,4-dihydro-α-pyran, 2-fluoro-3-(trifluoromethyl)benzaldehyde, 5-bromofuran-2-aldehyde and 3-bromobenzaldehyde were purchased from Aldrich. Other reagents were purchased from Sinopharm Chemical Reagent Co., Ltd, China.

1.1 General procedure for synthesis of 01, 02, 03, 04, 06, 08, 09, 10 and 12 analogues.

To a solution of 15 mmol arylaldehyde in MeOH (10 ml) was added 7.5 mmol ketone. The solution was stirred at room temperature (RT) for 20 min, followed by added dropwise 20%(w/v) NaOH (1.5 ml, 7.5 mmol). The mixture was stirred at RT and monitored with TLC. When the reaction finished, the residue was poured into saturated NH_4Cl solution and filtered. The precipitate was washed with water, then with cold ethanol, then cold acetone and dried in vacuum. The solid was purified by chromatography over silica gel using CH_2Cl_2 / CH_3OH as the eluent to afford compounds **01, 02, 03, 04,06, 08, 09, 10** and **12**.

(2E,5E)-2,5-bis(4-ethoxybenzylidene)cyclopentanone (A01). The product was recrystallized from ethanol/water (9:1). Orange powder, 76% yield, mp 191~192°C. ^{1}H-NMR ($CDCl_3$) δ: 1.44 (6H, t, *J*=7 Hz, CH_3×2), 3.08 (4H, s, CH_2-CH_2), 4.09 (4H, q, *J*=13.8 Hz, O-CH_2×2), 6.95 (4H, d, *J*=8.8 Hz, Ar-$H^{2,6}$×2), 7.54 (2H, s, Ar-CH=C×2), 7.56 (4H, d, *J*=8.8 Hz, Ar-$H^{3,5}$×2). ESI-MS *m/z*: 349.15 $(M+1)^+$, calcd for $C_{23}H_{24}O_3$: 348.43.

(2E,5E)-2,5-bis(4-fluorobenzylidene)cyclopentanone (A02). The product was recrystallized from ethanol/water(9:1). Yellow crystal, 88% yield, mp 239~240°C. ^{1}H-NMR ($CDCl_3$) δ: 3.10 (4H, s, CH_2-CH_2), 7.14 (4H, t, *J*=8.4 Hz, Ar-$H^{2,6}$×2), 7.58 (2H, d, *J*=8.4 Hz, Ar-CH=C×2), 7.59 (4H, t, *J*=9 Hz, Ar-$H^{3,5}$×2). ESI-MS *m/z*: 297.13 $(M+1)^+$, calcd for $C_{19}H_{14}F_2O$: 296.31.

(2E,5E)-2,5-bis(3,4,5-trimethoxybenzylidene)cyclopentanone (A03). Yellow powder, 90% yield, mp 202~204°C. ^{1}H-NMR ($CDCl_3$) δ: 3.15 (4H, s, CH_2-CH_2), 3.91 (18H, s, O-CH_3×6), 6.85 (4H, s, Ar-$H^{2,6}$×2), 7.53 (2H, s, Ar-CH=C×2). ESI-MS *m/z*: 441.16 $(M+1)^+$, calcd for $C_{25}H_{28}O_7$: 440.49.

(2E,5E)-2,5-bis(4-(dimethylamino)benzylidene)cyclopentanone (A04). Red powder, 71.1%

yield, mp >260°C. ^{1}H-NMR ($CDCl_3$) δ: 2.54 (4H, s, CH_2-CH_2), 2.98 (12H, s, N-CH_3×4), 6.74 (4H, m, *J*=8.8 Hz, Ar-$H^{2,6}$×2), 7.41 (4H, m, *J*=8.8 Hz, Ar-$H^{3,5}$×2), 7.77 (2H, s, Ar-CH=C×2). ESI-MS *m/z*: 347.21 $(M+1)^+$, calcd for $C_{23}H_{26}N_2O$: 346.47.

(2E,5E)-2,5-bis(2-bromobenzylidene)cyclopentanone (A06). Yellow powder, 87% yield, mp 163°C. ^{1}H-NMR ($CDCl_3$) δ: 2.98 (4H, s, CH_2-CH_2), 7.23 (2H, q, *J*=15.8 Hz, Ar-H^4×2), 7.37 (2H, q, *J*=14.8 Hz, Ar-H^6×2), 7.53 (2H, q, *J*=7.6 Hz, Ar-H^5×2), 7.66 (2H, q, *J*=8 Hz, Ar-H^3×2), 7.86 (2H, s, Ar-CH=C×2). ESI-MS *m/z*: 418.94 $(M+1)^+$, calcd for $C_{19}H_{14}Br_2O$: 418.12.

(2E,5E)-2,5-bis(2-fluoro-3-(trifluoromethyl)benzylidene)cyclopentanone (A08). Yellow powder, 91% yield, mp 223°C; ^{1}H-NMR ($CDCl_3$) δ: 3.05 (4H, s, CH_2-CH_2), 7.32 (2H, t, *J*=8 Hz, Ar-H_6×2), 7.64 (2H, t, *J*=7 Hz, Ar-H_5×2), 7.66 (2H, t, *J*=7 Hz, Ar-H_4×2), 7.79 (2H, s, Ar-CH=C×2). ESI-MS *m/z*: 430.92 $(M-1)^+$, calcd for $C_{21}H_{12}F_8O$: 432.31.

(2E,5E)-2,5-bis((5-bromofuran-2-yl)methylene)cyclopentanone (A09). Yellow powder, 77% yield, mp 176°C. ^{1}H-NMR ($CDCl_3$) δ: 3.06 (4H, s, CH_2-CH_2), 6.47 (2H, d, *J*=3.6 Hz, Ar-H^4×2), 6.65 (2H, d, *J*=3.6 Hz, Ar-H^3×2), 7.25 (2H, s, Ar-CH=C×2). ESI-MS *m/z*: 398.81 $(M+1)^+$, calcd for $C_{15}H_{10}Br_2O_3$: 398.05.

(2E,5E)-2,5-bis(3-bromobenzylidene)cyclopentanone (A10). Yellow powder, 91% yield, mp 186°C. ^{1}H-NMR ($CDCl_3$) δ: 3.12 (4H, s, CH_2-CH_2), 7.30 (2H, t, *J*=15.6 Hz, Ar-H^5×2), 7.50~7.52 (6H, m), 7.73 (2H, s, Ar-CH=C×2). ESI-MS *m/z*: 418.98 $(M+1)^+$, calcd for $C_{19}H_{14}Br_2O$: 418.12.

(2E,5E)-2,5-bis(4-(3-(dimethylamino)propoxy)benzylidene)cyclopentanone (A12). Yellow powder, 72% yield, mp 154°C. ^{1}H-NMR ($CDCl_3$) δ: 1.98 (4H, m, CH_2×2), 2.26 (12H, s, N-CH_3×4), 2.46 (4H, t, *J*=7.4 Hz, CH_2-N×2), 3.08 (4H, s, CH_2-CH_2), 4.07(4H, t, *J*=6.2 Hz, O-CH_2×2), 6.96 (4H, d, *J*=8.8 Hz, Ar-$H^{2,6}$×2), 7.73 (2H, s, Ar-CH=C×2), 7.56 (4H, d, *J*=8.8 Hz, Ar-$H^{3,5}$×2). ESI-MS *m/z*: 463.33 $(M+1)^+$, calcd for $C_{29}H_{38}N_2O_3$: 462.62.

(2E,5E)-2,5-bis((E)-3-phenylallylidene)cyclopentanone (A15) Yellow powder, 81.1% yield, mp 229°C. ^{1}H-NMR ($CDCl_3$) δ: 2.93 (4H, s, CH_2-CH_2), 6.98 (4H, t, *J*=6.8 Hz, Ar-$H^{3,5}$×2), 7.26~7.39 (8H, m), 7.53(4H, t). ESI-MS *m/z*: 313.11 $(M+1)^+$, calcd for $C_{23}H_{20}O$: 312.40.

(1E,4E)-1,5-bis(4-ethoxyphenyl)penta-1,4-dien-3-one (B01). Yellow powder, 77% yield, mp 123°C. ^{1}H-NMR ($CDCl_3$) δ: 1.39 (6H, t, *J*=8.1 Hz, CH_3×2), 4.10 (4H, q, *J*=16.4 Hz, O-CH_2×2), 6.99 (4H, m, *J*=7.2, Ar-H), 7.14 (2H, d, *J*=16 Hz, CH-C=O×2), 7.68~7.74 (6H, m). ESI-MS *m/z*: 323.16 $(M+1)^+$, calcd for $C_{21}H_{22}O_3$: 322.40.

(1E,4E)-1,5-bis(4-fluorophenyl)penta-1,4-dien-3-one (B02). The product was recrystallized from ethanol/water(9:1). Yellow crystal, 67% yield, mp 152°C [lit.[25] 152-154°C].

(1E,4E)-1,5-bis(3,4,5-trimethoxyphenyl)penta-1,4-dien-3-one (B03). Yellow powder, 81%

yield, mp 136°C. ^{1}H-NMR ($CDCl_3$) δ: 3.89 (18H, s, O-CH_3×6), 6.84 (4H, s, Ar-H), 6.98 (2H, q, *J*=16 Hz, CH-C=O×2), 7.65 (2H, q, *J*=16 Hz, Ar-CH=C×2). ESI-MS *m/z*: 415.14 $(M+1)^+$, calcd for $C_{23}H_{26}O_7$: 414.45.

(1E,4E)-1,5-bis(4-(dimethylamino)phenyl)penta-1,4-dien-3-one (B04). Red powder, 91% yield, mp 185°C. ^{1}H-NMR ($CDCl_3$) δ: 3.04 (12H, s, N-CH_3×4), 6.69 (4H, m, *J*=8.4 Hz, Ar-H), 6.90 (2H, d, *J*=15.6 Hz, C=CH-CO×2), 7.52 (4H, m, *J*=8.4 Hz, Ar-H), 7.68 (2H, d, *J*=15.6 Hz, Ar-CH=C×2). ESI-MS *m/z*: 321.18 $(M+1)^+$, calcd for $C_{21}H_{24}N_2O$: 320.43.

(1E,4E)-1,5-bis(2-bromophenyl)penta-1,4-dien-3-one (B06). Orange powder, 59% yield, mp 97°C ^{1}H-NMR ($CDCl_3$) δ: 7.03 (2H, d, *J*=16 Hz, C=CH-CO×2), 7.22~7.63 (8H, m, Ar-H), 8.09 (2H, d, *J*=16 Hz, Ar-CH=C×2). ESI-MS *m/z*: 393.10 $(M+1)^+$, calcd for $C_{17}H_{12}Br_2O$: 392.08.

(1E,4E)-1,5-bis(5-bromofuran-2-yl)penta-1,4-dien-3-one (B09). Yellow powder, 79% yield, mp 138°C. ^{1}H-NMR ($CDCl_3$) δ: 6.44 (2H, d, *J*=3.6 Hz, Ar-H^4×2), 6.63 (2H, d, *J*=3.6 Hz, Ar-H^3×2), 6.89 (2H, d, *J*=15.6 Hz, C=CH-CO×2), 7.36 (2H, d, *J*=15.6 Hz**,** Ar-CH=C×2). ESI-MS *m/z*: 372.88 $(M+1)^+$, calcd for $C_{13}H_8Br_2O_3$: 372.01.

(1E,4E)-1,5-bis(3-bromophenyl)penta-1,4-dien-3-one (B10). Yellow powder, 63% yield, mp 117°C. ^{1}H-NMR ($CDCl_3$) δ: 7.06 (2H, d, *J*=16 Hz, C=CH-CO×2), 7.22~7.52 (8H, m, Ar-H), 7.65 (2H, d, *J*=16 Hz, Ar-CH=C×2). ESI-MS *m/z*: 392.95 $(M+1)^+$, calcd for $C_{17}H_{12}Br_2O$: 392.08.

(1E,3E,6E,8E)-1,9-diphenylnona-1,3,6,8-tetraen-5-one (B15). Yellow powder, 90% yield, mp 142°C. ^{1}H-NMR ($CDCl_3$) δ: 6.58 (2H, d, *J*=15.2 Hz, C=CH-CO×2), 6.97~7.00 (4H, m, C=CH-CH=C×2), 7.27~7.52 (12H, m, Ar-H). ESI-MS *m/z*: 287.07 $(M+1)^+$, calcd for $C_{21}H_{18}O$: 286.37.

(2E,6E)-2,6-bis(4-ethoxybenzylidene)cyclohexanone (C01). Yellow powder, 77% yield, mp 147-149°C. ^{1}H-NMR ($CDCl_3$) δ: 1.56 (6H, t, *J*=7.2 Hz, CH_3), 1.81(2H, q, *J*=11.8 Hz, CH_2), 3.08 (4H, t, *J*=6 Hz, C-CH_2×2), 3.89 (4H, q, *J*=15.8 Hz, O-CH_2×2), 6.79~7.21 (8H, m, Ar-H), 7.73 (2H, s, Ar-CH=C×2). ESI-MS *m/z*: 363.18 $(M-1)^+$, calcd for $C_{24}H_{26}O_3$: 362.46.

(2E,6E)-2,6-bis(4-fluorobenzylidene)cyclohexanone (C02). Yellow powder, 69% yield, mp 156°C. ^{1}H-NMR ($CDCl_3$) δ: 1.81 (2H, q, *J*=12 Hz, CH_2), 2.90 (4H, t, *J*=5.4 Hz, CH_2×2), 7.12 (4H, m, Ar-$H^{2,6}$×2), 7.45 (4H, m, Ar-$H^{3,5}$×2), 7.76 (2H, s, Ar-CH=C×2). ESI-MS *m/z*: 311.11 $(M+1)^+$, calcd for $C_{20}H_{16}F_2O$: 310.34.

(2E,6E)-2,6-bis(3,4,5-trimethoxybenzylidene)cyclohexanone (C03). Yellow powder, 71% yield, mp 196°C. ^{1}H-NMR ($CDCl_3$) δ: 1.83 (2H, t, *J*=5.6 Hz, CH_2), 2.97 (4H, t, *J*=5.2 Hz, C-CH_2×2), 3.90 (18H, s, O-CH_3×6), 6.71 (4H, s, Ar-H), 7.73 (2H, s, Ar-CH=C×2). ESI-MS *m/z*: 455.15 $(M+1)^+$, calcd for $C_{26}H_{30}O_7$: 454.51.

(2E,6E)-2,6-bis(4-(dimethylamino)benzylidene)cyclohexanone (C04). Yellow powder, 55% yield, mp 160°C. ^{1}H-NMR ($CDCl_3$) δ: 1.82 (2H, t, *J*=6 Hz, CH_2), 2.93 (4H, t, *J*=5.6 Hz, C-CH_2×2), 3.01 (12H, s, N-CH_3×4), 6.72 (4H, d, *J*=8.8 Hz, Ar-$H_{2,6}$×4), 7.45 (4H, d, *J*=8.8 Hz, Ar-$H_{3,5}$×4), 7.76 (2H, s, Ar-CH=C×2). ESI-MS *m/z*: 361.24 $(M+1)^+$, calcd for $C_{24}H_{28}N_2O$: 360.49.

(2E,6E)-2,6-bis(2-bromobenzylidene)cyclohexanone (C06). Yellow powder, 83% yield, mp 120°C. ^{1}H-NMR ($CDCl_3$) δ: 1.75 (2H, q, *J*=9.3 Hz, CH_2), 2.75 (4H, m, *J*=6.1 Hz, C-CH_2×2), 7.18~7.35 (6H, m, Ar-H), 7.64 (2H, m, Ar-H), 7.86 (2H, s, Ar-CH=C×2). ESI-MS *m/z*: 432.98 $(M+1)^+$, calcd for $C_{20}H_{16}Br_2O$: 432.15.

(2E,6E)-2,6-bis((5-bromofuran-2-yl)methylene)cyclohexanone (C09). Yellow powder, 61% yield, mp 127°C. ^{1}H-NMR ($CDCl_3$) δ: 1.90 (2H, q, *J*=9.4 Hz, CH_2), 2.92 (4H, m, *J*=6.2 Hz, C-CH_2×2), 6.44 (2H, d, *J*=3.6 Hz, Ar-H^4×2), 6.66 (2H, d, *J*=3.6 Hz, Ar-H^3×2), 7.43 (2H, s, Ar-CH=C×2). ESI-MS *m/z*: 412.87 $(M+1)^+$, calcd for $C_{16}H_{12}Br_2O_3$: 412.07.

(2E,6E)-2,6-bis(3-bromobenzylidene)cyclohexanone (C10). Yellow powder, 52% yield, mp 112°C. ^{1}H-NMR ($CDCl_3$) δ: 1.81 (2H, s, CH_2), 2.90 (4H, s, C-CH_2×2), 7.28 (2H, t, *J*=7.8 Hz, Ar-H^5×2), 7.37 (2H, d, *J*=7.6 Hz, Ar-H^6×2), 7.47 (2H, d, *J*=7.6 Hz, Ar-H^4×2), 7.59 (2H, s, Ar-H^2×2), 7.70 (2H, s, Ar-CH=C×2). ESI-MS *m/z*: 433.32$(M+1)^+$, calcd for $C_{20}H_{16}Br_2O$: 432.15.

1.2 General procedure of 07 and 11

A solution of 3,4-dihydro-α-pyran (22 mmol) in dichloromethane (20 mL) was added dropwise onto a well-stirred suspension of hydroxyl benzaldehyde (14.4mmol) and pyridinium *p*-toluenesulfonate (0.16 mmol) in the same solvent (40 mL). The mixture was stirred at room temperature and monitored by TLC, then was washed with saturated $NaHCO_3$ solution (50mL×3) and brine (50mL×3) and dried over Na_2SO_4. Evaporation of the solvent gave crude product which was purified by column chromatography on silica gel (hexane/ethyl acetate, 7:3, as eluent) to obtain the mediate 4-(tetrahydropyran-2-yloxy) benzaldehyde as a lightly yellow oil (69~78% yield).

A mixture of protected derivative (6.94 mmol) and ketone (3.47 mmol) in C_2H_5OH (10mL) was stirred at rt for 20min; then 20%(w/v) NaOH (0.7ml, 3.47 mmol) was added dropwise. After stirring for 60min, the mixture was treated with 100 ml cold water and filtered. The residue was washed with ethanol and acetone and dried in vacuum. The product was purified by recrystallization from ethanol/water(9:1) to obtain **07** and **11**.

(2E,5E)-2,5-bis(4-(tetrahydro-2H-pyran-2-yloxy)benzylidene)cyclopentanone (A07). Yellow powder, 72% yield, mp 209°C. ^{1}H-NMR ($CDCl_3$) δ: 1.60~1.90 (12H, m), 3.09 (4H, s, CH_2×2), 3.61 (2H, q, *J*=5.2 Hz, O-CH_2^e×2), 3.90 (2H, q, *J*=10.7 Hz, O-CH_2^a×2), 5.50 (2H, t, O-CH-O×2), 7.11 (4H, m, *J*=8.8 Hz, Ar-$H^{2,6}$×2), 7.56 (6H, m). ESI-MS *m/z*: 460.92 (M^+), calcd for $C_{29}H_{32}O_5$: 460.56.

(2E,5E)-2,5-bis(3-methoxy-4-(tetrahydro-2H-pyran-2-yloxy)benzylidene)cyclopentanone

(A11). Yellow powder, 67% yield, mp 138°C. ^{1}H-NMR ($CDCl_3$) δ: 1.70~1.95 (12H,m), 3.11 (4H, s, CH_2-CH_2), 3.63 (2H, q, *J*=7.2 Hz, O-CH_2^e×2), 3.90 (2H, q, *J*=11.6 Hz, O-CH_2^a×2), 3.91 (6H, s, O-CH_3×2), 5.50(2H, s, O-CH-O×2), 7.09~7.23 (6H, m), 7.54 (2H, s, Ar-CH=C×2). ESI-MS *m/z*: 520.86 (M^+), calcd for $C_{31}H_{36}O_7$: 520.61.

(1E,4E)-1,5-bis(4-(tetrahydro-2H-pyran-2-yloxy)phenyl)penta-1,4-dien-3-one (B07). Yellow powder, 71% yield, mp 146~150°C. ^{1}H-NMR ($CDCl_3$) δ: 1.65 (4H, m), 1.76 (4H, m), 1.94 (4H, m), 3.61 (2H, q, *J*=11 Hz, O-CH_2^e×2), 3.88 (2H, q, *J*=14.8 Hz, O-CH_2^a×2), 5.49 (2H, s, O-CH-O×2), 6.95 (2H, d, *J*=16 Hz, C=CH-CO×2), 7.08 (4H, m), 7.56 (4H, m), 7.70 (2H, d, *J*=16 Hz, Ar-CH=C×2). ESI-MS *m/z*: 434.95 (M^+), calcd for $C_{27}H_{30}O_5$: 434.52.

(1E,4E)-1,5-bis(3-methoxy-4-(tetrahydro-2H-pyran-2-yloxy)phenyl)penta-1,4-dien-3-one (B11). Red oil, 66% yield. ^{1}H-NMR ($CDCl_3$) δ: 1.65~1.95 (12H, m), 3.63 (2H, d, *J*=12 Hz, O-CH_2^e×2), 3.86 (2H, q, *J*=15.2 Hz, O-CH_2^a×2), 3.94 (6H, s, O-CH_3×2), 5.49(2H, s, O-CH-O×2), 6.90 (2H, d, *J*=13.2 Hz, C=CH-CO×2), 6.91~7.26 (6H, m), 7.68 (2H, d, *J*=16 Hz, Ar-CH=C×2). ESI-MS *m/z*: 494.88 (M^+), calcd for $C_{29}H_{34}O_7$: 494.57.

(2E,6E)-2,6-bis(4-(tetrahydro-2H-pyran-2-yloxy)benzylidene)cyclohexanone (C07). Yellow powder, 63% yield, mp 160°C. ^{1}H-NMR ($CDCl_3$) δ: 1.65~2.00 (12H, m), 2.04 (2H, m), 2.92 (4H, t, *J*=5.4 Hz, C-CH_2×2), 3.62 (2H, d, *J*=11.6 Hz, O-CH_2^e×2), 3.90 (2H, t, *J*=9.2 Hz, O-CH_2^a×2), 5.48 (2H, t, O-CH-O×2), 7.03 (4H, d, *J*=8.4 Hz, Ar-$H^{2,6}$×2), 7.43 (4H, d, *J*=8.4 Hz, Ar-$H^{3,5}$×2), 7.82 (2H, s, Ar-CH=C×2). ESI-MS *m/z*: 475.03 (M^+), calcd for $C_{30}H_{34}O_5$: 474.59.

(1E,4E)-1,5-bis(3-methoxy-4-(tetrahydro-2H-pyran-2-yloxy)phenyl)penta-1,4-dien-3-one (C11). Yellow powder, 59% yield, mp 138°C. ^{1}H-NMR ($CDCl_3$) δ: 1.64~2.01 (14H, m), 2.94 (4H, t, *J*=5.2 Hz, C-CH_2×2), 3.62 (2H, d, *J*=11.2 Hz, O-CH_2^e×2), 3.89 (6H, s, O-CH_3×2), 3.97 (2H, t, *J*=9.0 Hz, O-CH_2^a×2), 5.47(2H, s, O-CH-O×2), 6.98~7.17 (6H, m), 7.74 (2H, s, Ar-CH=C×2). ESI-MS *m/z*: 534.88 (M^+), calcd for $C_{32}H_{38}O_7$: 534.64.

1.3 General procedure of 13 and 14

The protected product(**07** or **11**, 10 mmol) was suspended in methanol (40 mL) and treated with a catalytic amount of *p*-toluenesulfonic acid. After stirring at room temperature for 10 h the solvent was removed. The residue was treated with water and neutralized with a saturated solution of $NaHCO_3$. The suspension was extracted with ethyl acetate (50 mL×3) and the collected organic extract was washed with brine (100 mL×3), followed by dring with Na_2SO_4. Evaporation of the solvent gave crude product and then recrystallization from C_2H_5OH/H_2O to obtain pure **13** or **14**.

(2E,5E)-2,5-bis(4-hydroxybenzylidene)cyclopentanone (A13) Yellow crystal, 89.3% yield, mp >300°C. ^{1}H-NMR (DMSO-d_6) δ: 2.89 (4H, t, *J*=20 Hz, CH_2-CH_2), 6.88 (4H, d, *J*=8.4 Hz, Ar-$H^{2,6}$×2),7.33 (2H, s, Ar-CH×2), 7.53 (4H, d, *J*=8.4 Hz, Ar-$H^{3,5}$×2), 10.01 (2H, br, Ar-OH×2). ESI-MS *m/z*: 291.13 $(M\text{-}1)^+$, calcd for $C_{19}H_{16}O_3$: 292.33.

(2E,5E)-2,5-bis(4-hydroxy-3-methoxybenzylidene)cyclopentanone (A14) Yellow powder, 76% yield, mp 214°C [lit.[17] 212-214°C]. ^{1}H-NMR (DMSO-*d*$_6$) δ: 3.57 (4H, s, CH_2-CH_2), 4.45 (6H, s, O-CH_3×2), 7.41~7.72 (6H, m, Ar-H), 7.97 (2H, s, -CH=C×2), 8.83 (2H, br, Ar-OH×2). ESI-MS *m/z*: 350.98 $(M-1)^+$, calcd for $C_{21}H_{20}O_5$: 352.4.

(1E,4E)-1,5-bis(4-hydroxyphenyl)penta-1,4-dien-3-one (B13) Orange crystal, 92% yield, mp 246~248°C [lit.[17] 243-245°C]. ^{1}H-NMR (DMSO-*d*$_6$) δ: 6.83 (4H, d, *J*=8.4 Hz, Ar-$H^{2,6}$×2), 7.07 (2H, d, *J*=16 Hz, C=CH-O×2), 7.58 (4H, d, *J*=8.4 Hz, Ar-$H^{3,5}$×2), 7.66 (2H, d, *J*=16 Hz, Ar-CH=C×2), 10.03 (2H, s, OH×2). ESI-MS *m/z*: 267.09 $(M+1)^+$, calcd for $C_{17}H_{14}O_3$: 266.29.

(1E,4E)-1,5-bis(4-hydroxy-3-methoxyphenyl)penta-1,4-dien-3-one (B14) Yellow powder, 85% yield, mp 88~90°C [lit.[22] 84-86°C]. ^{1}H-NMR (DMSO-*d*$_6$) δ: 4.61 (6H, s, O-CH_3×2), 7.02 (4H, d, *J*=8.0 Hz, Ar-$H^{2,6}$×2), 7.27 (2H, d, *J*=16 Hz, C=CH-O×2), 7.61 (4H, d, *J*=8.0 Hz, Ar-$H^{3,5}$×2), 7.98 (2H, d, *J*=16 Hz, Ar-CH=C×2), 9.11 (2H, br, OH×2). ESI-MS *m/z*: 327.27$(M+1)^+$, calcd for $C_{19}H_{18}O_5$: 326.12.

(2E,6E)-2,6-bis(4-hydroxybenzylidene)cyclohexanone (C13) Yellow crystal, 59% yield, mp >300°C. ^{1}H-NMR (DMSO-*d*$_6$) δ: 1.71 (2H, m), 2.84 (4H, s, C-CH_2×2), 6.83 (4H, d, *J*=6.0 Hz, Ar-$H^{2,6}$×2), 7.40 (4H, d, *J*=6.0 Hz, Ar-$H^{3,5}$×2), 7.53 (2H, s, Ar-CH=C×2), 9.50 (2H, br, Ar-OH×2). ESI-MS *m/z*: 305.18 $(M-1)^+$, calcd for $C_{20}H_{18}O_3$: 306.36.

(2E,6E)-2,6-bis(4-hydroxy-3-methoxybenzylidene)cyclohexanone (C14) Yellow powder, 67% yield, mp 172~173°C [lit.[17] 178-179°C]. ^{1}H-NMR (DMSO-*d*$_6$) δ: 2.00 (2H, m), 2.99 (4H, m), 4.11 (6H, s, O-CH_3×2), 7.42 (4H, d, *J*=8.0 Hz, Ar-$H^{2,6}$×2), 7.74 (4H, d, *J*=8.0 Hz, Ar-$H^{3,5}$×2), 8.06 (2H, s, Ar-CH×2), 8.56 (2H, br, Ar-OH×2). ESI-MS *m/z*: 365.13 $(M-1)^+$, calcd for $C_{22}H_{22}O_5$: 366.41.

1.4 General procedure of 16 and 17

A stirred suspension of 4-hydroxylbenzaldehyde (or 3-methoxyl-4-hydroxylbenzaldehyde, 10mmol) and anhydrous K_2CO_3 (1.39 g, 10 mmol) in dry acetone (30 mL) was refluxed for 30 min under nitrogen atmosphere. Then, a solution of allylbromide (15 mmol) in acetone (10 mL) was added and refluxed for 3.5 h under nitrogen atmosphere and monitored by TLC. The resulting solution was evaporated to remove most of acetone and then poured with AcOEt (100ml). The combined organic layers were washed with brine (100 mL×3), dried over Na_2SO_4 and evaporated in vacuo to afford the crude product 4-(allyloxy)benzaldehyde (or 4-(allyloxy)-3-methoxybenzaldehyde) as a colorless oil.

Compounds **16** (or **17**) was prepared according the procedure of **01** starting from 4-(allyloxy)benzaldehyde (or 4-(allyloxy)-3-methoxybenzaldehyde) and ketones, respectively.

(2E,5E)-2,5-bis(4-(allyloxy)benzylidene)cyclopentanone (A16). Yellow powder, 67% yield, mp 192°C. ^{1}H-NMR ($CDCl_3$) δ: 3.09 (4H, s, C-CH_2×2), 4.60 (4H, d, *J*=5.2 Hz, CH_2-O×2), 5.33 (2H, q, *J*=10.8 Hz, CH_2^{α}=C×2), 5.44 (2H, m, *J*=17.2 Hz, CH_2^{β}=C×2), 6.07 (2H, m), 6.98

(4H, d, *J*=8.8 Hz, Ar-$H^{2,6}$×2), 7.51 (2H, s, Ar-CH=C×2), 7.57 (4H, d, *J*=8.8 Hz, Ar-$H^{3,5}$×2). ESI-MS *m/z*: 372.89 (M^+), calcd for $C_{25}H_{24}O_3$: 372.5.

(2E,5E)-2,5-bis(4-(allyloxy)-3-methoxybenzylidene)cyclopentanone (A17). Yellow powder, 67% yield, mp 116~117°C. ^{1}H-NMR ($CDCl_3$) δ: 3.02 (4H, s, CH_2-CH_2), 4.10 (6H, s, O-CH_3×2), 4.59 (4H, d, *J*=6.4 Hz, O-CH_2×2), 5.27 (2H, t, *J*=9.8 Hz, CH_2^{α}=C×2), 5.44 (2H, m, *J*=15.4 Hz, CH_2^{β}=C×2), 6.10 (2H, m), 6.71~7.32 (6H, m), 7.78 (2H, s, CH=C×2). ESI-MS *m/z*: 431.41 $(M-1)^+$, calcd for $C_{27}H_{28}O_5$: 432.5.

(1E,4E)-1,5-bis(4-(allyloxy)phenyl)penta-1,4-dien-3-one (B16). Yellow powder, 67% yield, mp 123~124°C. ^{1}H-NMR ($CDCl_3$) δ: 4.55 (4H, t, J=4.2, CH_2-O×2), 5.33 (2H, d, *J*=10.4 Hz, CH_2^{α}=C×2), 5.44 (2H, m, *J*=17.6 Hz, CH_2^{β}=C×2), 6.08 (2H, m), 6.92 (2H, d, *J*=15.6 Hz, CH-C=O×2), 6.97 (4H, d, J=10 Hz, Ar-$H^{2,6}$×2), 7.57 (4H, d, *J*=10 Hz, Ar-$H^{3,5}$×2), 7.70 (2H, d, *J*=15.6 Hz, Ar-CH=C×2). ESI-MS *m/z*: 245.66 $(M-1)^+$, calcd for $C_{23}H_{22}O_3$: 346.4.

(2E,6E)-2,6-bis(4-(allyloxy)benzylidene)cyclohexanone (C16). Yellow powder, 67% yield, mp 120~122°C. ^{1}H-NMR ($CDCl_3$) δ: 1.81 (2H, t, *J*=5.6 Hz, CH_2), 2.92 (4H, t, *J*=5.6 Hz, C-CH_2×2), 4.59 (4H, d, *J*=5.2 Hz, O-CH_2×2), 5.32 (2H, d, *J*=10.4 Hz, CH_2^{α}=C×2), 5.44 (2H, m, *J*=16 Hz, CH_2^{β}=C×2), 6.09 (2H, m), 6.95 (4H, d, J=8.8 Hz, Ar-$H^{2,6}$×2), 7.45 (4H, d, *J*=8.8 Hz, Ar-$H^{3,5}$×2), 7.76 (2H, s, CH=C×2). ESI-MS *m/z*: 387.81 $(M+1)^+$, calcd for $C_{26}H_{26}O_3$: 386.5.

(2E,6E)-2,6-bis(4-(allyloxy)-3-methoxybenzylidene)cyclohexanone (C17) Yellow powder, 67% yield, mp 141°C. ^{1}H-NMR ($CDCl_3$) δ: 1.88 (2H, s, CH_2), 2.89 (4H, t, *J*=5.6 Hz, C-CH_2×2), 3.91 (6H, s, O-CH_3×2), 4.66 (4H, m), 5.31 (2H, t, *J*=10.2 Hz, CH_2^{α}=C×2), 5.42 (2H, m, *J*=16.4 Hz, CH_2^{β}=C×2), 6.09 (2H, m), 6.59~7.26 (6H, m), 7.40~7.75 (2H, s, CH=C×2). ESI-MS *m/z*: 446.67 (M^+) , calcd for $C_{28}H_{30}O_5$: 446.5.

2. Enzyme-linked immunosorbent assays (ELISA) of cytokines.

Mouse J774A.1 macrophages were pre-treated with curcumin or its analogues (10 μM) or vehicle control for 2 h, then treated with LPS (0.5 μg/ml) for 24 h. At the end of the treatment, the culture media were collected and centrifuged at 14,000 x rpm for 5 min. The supernatants were stored in aliquots at -70°C. TNF-α and IL-6 levels in the media were determined by ELISA using mouse TNF-α and mouse IL-6 ELISA Max^{TM} Set Deluxe Kits (BioLegend). The total protein concentrations of the viable cell pellets were determined using Bio-Rad Protein Assay reagent. Total amounts of the TNF-α and IL-6 in media were normalized to the total protein amounts of the viable cell pellets.