Design, Microwave-assistant Synthesis, Bioactivity and SAR of Novel Substituted 2-Phenyl-2-Cyclohexanedione Enol Ester Derivatives

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Supporting information
3-Hydroxy-2-phenylcyclohex-2-en-1-one (2a)

\[
\text{C}_{12}\text{H}_{12}\text{O}_{2}
\]

**IR**

![IR spectrum](image)

**\(^1\)H NMR**

![\(^1\)H NMR spectrum](image)
$^1$H NMR
3-Hydroxy-5-methyl-2-phenylcyclohex-2-en-1-one (2b)

C_{13}H_{14}O_{2}

IR

\text{Wavenumber cm}^{-1}

3027.50

2929.67

2911.77

2846.69

1592.83

1557.43

1289.57

1246.09

1137.70

1018.59

754.96

690.20

609.43

478.96

500

1000

1500

2000

2500

3000

3500

4000

4500

5000

5500

6000

6500

\text{Transmittance [%]}

1H NMR

\text{H (ppm)}

3.00

1.15

2.10

2.08

0.87

1.94

1.03

2.03

1.17

1.18

1.60

2.36

2.38

2.39

2.39

2.40

2.60

2.64

6.06

7.21

7.23

7.28

7.36

7.38

7.40

7.45

7.47

7.49
3-Hydroxy-5,5-dimethyl-2-phenylcyclohex-2-en-1-one (2c)

\[ \text{C}_{14}\text{H}_{16}\text{O}_{2} \]

**IR**

**\( ^{1}H \) NMR**
$^{13}\text{C NMR}$
3-(Benzoyloxy)-2-phenyl-2-cyclohexen-1-one (S1)

\[
\text{C}_{19}\text{H}_{16}\text{O}_3
\]

IR

\begin{figure}
\centering
\includegraphics[width=\textwidth]{IR_spectrum.png}
\caption{IR spectrum of 3-(Benzoyloxy)-2-phenyl-2-cyclohexen-1-one (S1).}
\end{figure}

\[ \text{IR} \]

\begin{figure}
\centering
\includegraphics[width=\textwidth]{NMR_spectra.png}
\caption{\textsuperscript{1}H NMR spectra of 3-(Benzoyloxy)-2-phenyl-2-cyclohexen-1-one (S1).}
\end{figure}

\[ \text{\textsuperscript{1}H NMR} \]
**13C NMR**

![13C NMR Spectrum]

**HRMS**

![HRMS Spectrum]
3-(Benzoyloxy)-2-phenyl-5-methyl-2-cyclohexen-1-one (S2)

\[ \text{C}_{20}\text{H}_{18}\text{O}_3 \]

**IR**

![IR spectrum graph]

**\(^1\text{H} \text{NMR}\)**

![\(^1\text{H} \text{NMR} \) spectrum graph]
3-(Benzoyloxy)-2-phenyl-5,5-dimethyl-2-cyclohexen-1-one (S3)

C_{21}H_{20}O_{3}

IR

\begin{center}
\includegraphics[width=\textwidth]{IR_spectrum}
\end{center}

\begin{center}
\textbf{^1H NMR}
\end{center}

\begin{center}
\includegraphics[width=\textwidth]{NMR_spectrum}
\end{center}
3-(2,4-Dichlorobenzoyloxy)-2-phenyl-2-cyclohexen-1-one (S4)

\[
\begin{align*}
\text{C}_{19}\text{H}_{14}\text{Cl}_2\text{O}_3
\end{align*}
\]

**IR**

![IR Spectrum](image)

**\(^1\)H NMR**

![\(^1\)H NMR Spectrum](image)
$^{13}$C NMR

HRMS
3-(2,4-Dichlorobenzoyloxy)-2-phenyl-5-methyl-2-cyclohexen-1-one (S5)

\[
\text{C}_{20}\text{H}_{16}\text{Cl}_2\text{O}_3
\]

IR

\[
\begin{array}{c}
\text{Wavenumber cm}^{-1} \\
3500 & 3000 & 2500 & 2000 & 1500 & 1000 & 500 \\
3060.87 & 3035.65 & 3002.72 & 2935.78 & 2905.77 & 2851.72 & 1734.81 & 1667.00 & 1637.10 & 1571.67 & 1544.09 & 1483.63 & 1460.34 & 1364.06 & 1256.28 & 1223.86 & 1194.46 & 1140.20 & 1078.12 & 1029.31 & 951.17 & 864.86 & 834.26 & 753.61 & 693.89 & 598.92 & 511.55 & 500 & 400 & 300 & 200 & 100 & 50 & 0
\end{array}
\]

\[
\text{Transmittance [\%]}
\]

\[
\begin{array}{c}
0 & 10 & 20 & 30 & 40 & 50 & 60 & 70 & 80 & 90 & 100
\end{array}
\]

\[
\text{Page 1/1}
\]

\[
^1\text{H NMR}
\]

\[
\begin{array}{c}
\text{f1 (ppm)} \\
0 & 1 & 2 & 3 & 4 & 5 & 6 & 7 & 8 & 9 & 10 & 11 & 12 & 13 & 14
\end{array}
\]

\[
\begin{array}{c}
3.00 & 1.02 & 1.05 & 1.97 & 0.98 & 2.82 & 3.93 & 0.91 & 1.22 & 1.24 & 2.37 & 2.41 & 2.51 & 2.55 & 2.60 & 2.69 & 2.72 & 2.76 & 2.77 & 2.80 & 7.16 & 7.18 & 7.18 & 7.21 & 7.22 & 7.28 & 7.29 & 7.30 & 7.31 & 7.31 & 7.32 & 7.34 & 7.35 & 7.36 & 7.37 & 7.45 & 7.46
\end{array}
\]

\[
0 & 10000 & 20000 & 30000 & 40000 & 50000 & 60000 & 70000 & 80000 & 90000 & 100000
\]

\[
\begin{array}{c}
14 & 15 & 16 & 17 & 18 & 19 & 20 & 21 & 22 & 23 & 24 & 25 & 26 & 27 & 28 & 29 & 30 & 31 & 32 & 33 & 34 & 35 & 36 & 37 & 38 & 39 & 40
\end{array}
\]

\[
\text{W} (\text{ppm})
\]

\[
\begin{array}{c}
0 & 1000 & 2000 & 3000 & 4000 & 5000 & 6000 & 7000 & 8000 & 9000 & 10000
\end{array}
\]
\[ \text{\( ^{13}C \) NMR} \]

\[ \text{HRMS} \]

\[ \text{FTMS + p ESI Full ms} \]

\[ \text{C}_{20} \text{H}_{16} \text{Cl}_{2} \text{O}_{3} \text{Na}^{+} \]

\[ \text{RT: 0.06 \ AV: 1} \]
3-(2,4-Dichlorobenzoyloxy)-2-phenyl-5,5-dimethyl-2-cyclohexen-1-one (S6):

\[
\text{C}_{21}\text{H}_{18}\text{Cl}_{2}\text{O}_{3}
\]

IR

\begin{figure}
\centering
\includegraphics[width=\textwidth]{IRスペクトル}
\caption{IRスペクトル}
\end{figure}

\[\text{\textsuperscript{1}H NMR}\]

\begin{figure}
\centering
\includegraphics[width=\textwidth]{\textsuperscript{1}H NMRスペクトル}
\caption{\textsuperscript{1}H NMRスペクトル}
\end{figure}
$^{13}\text{C} \text{ NMR}$

HRMS
3-(Chloroacetoxy)-2-phenyl-5-methyl-2-cyclohexen-1-one (S7)

C\textsubscript{14}H\textsubscript{13}ClO\textsubscript{3}

IR

\textbf{\(^1H\) NMR}
\[ ^{13}\text{C} \text{NMR} \]

\[
\begin{array}{cccccccc}
17.55 & 20.60 & 28.70 & 37.44 & 40.30 & 76.62 & 77.04 & 77.47 & 128.06 & 128.10 & 129.46 & 130.79 & 164.14 & 164.16 & 197.53
\end{array}
\]

\[ \text{HRMS} \]

\[
\begin{array}{cccccccc}
230 & 240 & 250 & 260 & 270 & 280 & 290 & 300 & 310 & 320 & 330 & 340 & 350 & 360 & 370 & 380 & 390 & 400 & 410 & 420 & 430
\end{array}
\]

\[
\begin{array}{cccccccc}
287.0449 & 265.0630 & 303.0188 & 289.0419 & 267.0600 & 305.0160 & 301.1414 & 360.3242 & 290.0452 & 268.0632 & 284.0365 & 338.3421 & 306.0192 & 245.0488 & 330.3370 & 317.1152 & 229.0976 & 365.1060 & 253.0839 & 261.1316 & 355.0706 & 265.0626 & 267.0596 & 268.0630
\end{array}
\]

\[
\begin{array}{cccccccc}
NL: 7.82E5 & fuying-63_160331212500#1 & RT: 0.10 & AV: 1 & T: FTMS + p ESI Full ms [100.00-2000.00]
\end{array}
\]

\[
\begin{array}{cccccccc}
6.46E5 & C 14 H13 Cl1 O3 +H: C 14 H14 Cl1 O3 & pa Chrg 1
\end{array}
\]
3-(Chloroacetyloxy)-2-phenyl-5-methyl-2-cyclohexen-1-one (S8)

C₁₅H₁₅ClO₃

IR

¹H NMR
The image contains a 13C NMR spectrum and a HRMS spectrum. The 13C NMR spectrum shows chemical shifts ranging from approximately 0 to 200 ppm, with peaks at various ppm values. The HRMS spectrum displays mass-to-charge ratios (m/z) and their corresponding relative abundances. The HRMS spectrum includes mass/charge ratios and their intensities, indicating the molecular composition and structure of the compound. The spectra provide valuable information for the identification and characterization of the compound under study.
3-(Chloroacetyloxy)-2-phenyl-5,5-dimethyl-2-cyclohexen-1-one (S9)

\[
\begin{align*}
\text{C}_{16}\text{H}_{17}\text{ClO}_3
\end{align*}
\]

IR

\[
\begin{align*}
\text{Wavenumber cm}^{-1} \\
3058.61 & 3025.63 & 2960.08 & 2872.02 & 1776.72 & 1680.84 & 1598.56 & 1355.82 & 1301.48 & 1232.61 & 1186.72 & 1141.32 & 1007.16 & 921.27 & 761.21 & 700.01 & 606.28 & 525.90 & 489.73 & 458.47 & 440.38 & 500
\end{align*}
\]

\[
\begin{align*}
\text{Transmittance } \% \\
100 & 90 & 80 & 70 & 60 & 50 & 40 & 30 & 20 & 10 & 0
\end{align*}
\]

\[
\begin{align*}
\text{f1 (ppm)} \\
6.00 & 1.97 & 1.98 & 1.98 & 1.94 & 3.10 & 1.22 & 2.51 & 2.63 & 3.91 & 7.10 & 7.11 & 7.13 & 7.14 & 7.34 & 7.34 & 7.37
\end{align*}
\]

\[
\begin{align*}
1^\text{H NMR}
\end{align*}
\]
3-(Dichloroacetyloxy)-2-phenyl-5,5-dimethyl-2-cyclohexen-1-one (S10)

\[
\text{C}_{16}\text{H}_{16}\text{Cl}_{2}\text{O}_{3}
\]

**IR**

![IR spectrum of the compound]

**\(^1\)H NMR**

![\(^1\)H NMR spectrum of the compound]
3-(Phenoxyacetyloxy)-2-phenyl-2-cyclohexen-1-one (S11)

C_{20}H_{18}O_{4}

IR

Transmittance [%]

Wavenumber cm⁻¹

\[ \text{\textsuperscript{1}H NMR} \]

[Diagram of IR spectrum and \textsuperscript{1}H NMR spectrum]
$^{13}$C NMR

HRMS
3-(Phenoxyacetyloxy)-2-phenyl-5-methyl-2-cyclohexen-1-one (S12)

\[ \text{C}_{21}\text{H}_{20}\text{O}_{4} \]

**IR**

![Infrared spectrum image]

**\(^1\)H NMR**
$^{13}$C NMR

HRMS
3-(Phenoxyacetyloxy)-2-phenyl-5,5-dimethyl-2-cyclohexen-1-one (S13)

\[
\text{C}_{22}\text{H}_{22}\text{O}_4
\]

**IR**

**\(^1\)H NMR**
3-(3-Acetylpropionoxy)-2-phenyl-2-cyclohexen-1-one (S14)

C_{16}H_{16}O_{5}

IR

\begin{center}
\begin{figure}
\includegraphics[width=\textwidth]{IR_spectrum.png}
\end{figure}
\end{center}

\begin{center}
\begin{figure}
\includegraphics[width=\textwidth]{1H_NMR.png}
\end{figure}
\end{center}
3-(3-Acetylpropionoxy)-2-phenyl-5-methyl-2-cyclohexen-1-one (S15)

C_{17}H_{18}O_{5}

IR

Wavenumber cm\(^{-1}\)

\begin{align*}
3034.22 & \quad 3002.55 \\
2935.26 & \quad 2903.81 \\
2851.57 & \quad 1742.65 \\
1667.58 & \quad 1637.15 \\
1484.09 & \quad 1447.44 \\
1433.98 & \quad 1408.19 \\
1359.52 & \quad 1314.79 \\
1225.46 & \quad 1143.50 \\
1072.45 & \quad 996.69 \\
953.76 & \quad 901.77 \\
834.18 & \quad 759.26 \\
695.99 & \quad 600.35 \\
555.36 & \quad 537.78 \\
510.21 & \quad 471.09 \\
430.69 & \quad 500
\end{align*}

Transmittance [%]

\begin{align*}
100 & \quad 80 \\
60 & \quad 40 \\
20 & \quad 10 \\
0
\end{align*}

\begin{align*}
\text{\textsuperscript{1}H NMR}
\end{align*}
3-(3-Acetylpropionoxy)-2-phenyl-5,5-dimethyl-2-cyclohexen-1-one (S16)

C\textsubscript{18}H\textsubscript{20}O\textsubscript{5}

**IR**

**\textsuperscript{1}H NMR**
**13C NMR**

![NMR Spectrum](image)

**HRMS**

![HRMS Graph](image)
3-[1-(2,4-Dichlorophenyl)-5-(trichloromethyl)-1H-1,2,4-triazol-3-yl]carbonyloxy-2-phenyl-2-cyclohexen-1-one (S17)

\[
\text{C}_{22}\text{H}_{14}\text{Cl}_{5}\text{N}_{3}\text{O}_{3}
\]

**IR**

![IR spectrum](image)

**\(^1\)H NMR**

![\(^1\)H NMR spectrum](image)
3-[1-(2,4-Dichlorophenyl)-5-(trichloromethyl)-1H,1,2,4-triazol-3-yl]carbonyloxy-2-phenyl-5-methyl-2-cyclohexen-1-one (S18)

\[ \text{C}_{23}\text{H}_{16}\text{Cl}_5\text{N}_3\text{O}_3 \]

IR

\[ \text{IR} \]

\[ \text{Wavenumber cm}^{-1} \]

\[ \text{Transmittance} \% \]

\[ \text{1H NMR} \]
3-[1-(2,4-Dichlorophenyl)-5-(trichloromethyl)-1H-1,2,4-triazol-3-yl]carbonyloxy-2-phenyl-5,5-dimethyl-2-cyclohexen-1-one (S19)

C$_{24}$H$_{18}$N$_3$O$_3$Cl$_5$

IR

$^{1}$H NMR
$^{13}$C NMR

HRMS
3-[5-Methyl-3-phenylisoxazole-4-carbonyloxy]-2-phenyl-2-cyclohexen-1-one (S20)

\[
\text{C}_{23}\text{H}_{19}\text{NO}_{4}
\]

IR

\[
\begin{array}{c}
\text{Wavenumber cm}^{-1} \\
3500 & 3000 & 2500 & 2000 & 1500 & 1000 & 500 \\
\text{Transmittance [%]} \\
100 & 90 & 80 & 70 & 60 & 50 & 40 & 30 & 20 & 10 & 0
\end{array}
\]

\[\text{1H NMR}\]
**13C NMR**

None

**HRMS**

\[
\begin{array}{c|c}
\text{m/z} & \text{Relative Abundance} \\
374.1392 & \text{NL: 3.63E6} \\
396.1210 & \text{fuying-9_161110152428} \\
412.0950 & \text{RT: 0.00 AV: 1 T:} \text{FTMS + p ESI Full} \\
375.1424 & \text{ms [100.00-2000.00]} \\
397.1243 & \text{C 23 H19 N1 O4 +H:} \\
426.0908 & \text{C 23 H20 N1 O4} \\
448.0728 & \text{pa Chrg 1} \\
464.0466 & \text{330} \\
413.0983 & \text{428.0877} \\
374.1387 & \text{450.0699} \\
375.1420 & \text{466.0440} \\
376.1454 & \text{414.0932} \\
\end{array}
\]
3-[5-Methyl-3-phenylisoxazole-4-carbonyloxy]-2-phenyl-5-methyl-2-cyclohexen-1-one (S21)

\[
\text{C}_{24}\text{H}_{21}\text{NO}_4
\]

**IR**

![IR spectrum](image)

**\(^1\)H NMR**

![NMR spectrum](image)
$^{13}$C NMR

**HRMS**

```
N: 1.59E+06
Error=1.3 ppm

340 350 360 370 380 390 400 410 420 430 440 450 460 470 480 490
m/z
```

```
Relative Abundance
410.1367 388.1548 426.1106 411.1400 389.1581 427.1139 405.1815 412.1435 428.1086 390.1615 437.1937 381.2982 448.0723 360.3240 424.1523 338.3423 464.0467
```

```
NL: 7.60E5
```

```
C 24 H21 N1 O4 +H: C 24 H22 N1 O4
```
3-[5-Methyl-3-phenylisoxazole-4-carbonyloxy]-2-phenyl-5,5-dimethyl-2-cyclohexen-1-one (S22)

C_{25}H_{23}NO_{4}

IR

\text{\textsuperscript{1}H NMR}
$^{13}$C NMR

HRMS
3-[5-Methyl-3-(2-fluoro-6-chlorophenyl)isoxazole-4-carbonyloxy]-2-phenyl-2-cyclohexen-1-one (S23)

C_{23}H_{17}ClFNO_{4}

IR

\begin{figure}
\centering
\includegraphics[width=\textwidth]{ir_spectrum.png}
\caption{IR spectrum of the compound.}
\end{figure}

^1H NMR

\begin{figure}
\centering
\includegraphics[width=\textwidth]{nmr_spectrum.png}
\caption{^1H NMR spectrum of the compound.}
\end{figure}
3-[5-Methyl-3-(2-fluoro-6-chlorophenyl)isoxazole-4-carbonyloxy]-2-phenyl-5-methyl-2-cyclohexen-1-one (S24)

C_{24}H_{19}ClFNO_{4}

IR

Wavenumber cm\(^{-1}\)

Transmittance [%]

1H NMR

f (ppm)
3-[5-Methyl-3-(2-fluoro-6-chlorophenyl)isoxazole-4-carbonyloxy]-2-phenyl-5,5-dimethyl-2-cyclohexen-1-one (S25)

C_{25}H_{21}ClFNO_{4}

IR

\begin{align*}
\text{Wavenumber cm}^{-1} & \quad \text{Transmittance [%]} \\
3000 & \quad 5000 \\
2500 & \quad 4000 \\
2000 & \quad 3500 \\
1500 & \quad 3000 \\
1000 & \quad 2500 \\
500 & \quad 2000 \\
& \quad 1500 \\
& \quad 1000 \\
& \quad 500 \\
& \quad 100 \\
\end{align*}

\begin{align*}
\text{Transmittance [%]} & \quad f_1 (\text{ppm}) \\
0 & \quad 0 \\
20 & \quad 20 \\
40 & \quad 40 \\
60 & \quad 60 \\
80 & \quad 80 \\
100 & \quad 100 \\
200 & \quad 200 \\
300 & \quad 300 \\
400 & \quad 400 \\
500 & \quad 500 \\
& \quad 1000 \\
& \quad 2000 \\
& \quad 3000 \\
& \quad 4000 \\
& \quad 5000 \\
\end{align*}

^1H NMR

\begin{align*}
\text{δ (ppm)} & \quad \text{Integration} \\
8.5 & \quad 1 \\
8.0 & \quad 1 \\
7.5 & \quad 1 \\
7.0 & \quad 1 \\
6.5 & \quad 1 \\
6.0 & \quad 1 \\
5.5 & \quad 1 \\
5.0 & \quad 1 \\
4.5 & \quad 1 \\
4.0 & \quad 1 \\
3.5 & \quad 1 \\
3.0 & \quad 1 \\
2.5 & \quad 1 \\
2.0 & \quad 1 \\
1.5 & \quad 1 \\
1.0 & \quad 1 \\
0.5 & \quad 1 \\
0.0 & \quad 1 \\
\end{align*}
3-[(2-Trifluoromethyl-4-methyl)pyrazoloyloxy]-2-phenyl-2-cyclohexen-1-one (S26)

C_{18}H_{15}F_{3}N_{2}O_{3}

**IR**

**\(^1\)H NMR**
$^{13}$C NMR

None

HRMS
3-[(2-Trifluoromethyl-4-methyl)pyrazoloyloxy]-2-phenyl-5-methyl-2-cyclohexen-1-one (S27)

![Chemical Structure](image)

**C_{19}H_{17}F_{3}N_{2}O_{3}**

**IR**

![Infrared Spectrogram](image)

**{H NMR**

![NMR Spectrum](image)
3-[(2-Trifluoromethyl-4-methyl)pyrazoloyloxy]-2-phenyl-5,5-dimethyl-2-cyclohexen-1-one (S28)

\[
\text{C}_{20}\text{H}_{19}\text{F}_{3}\text{N}_{2}\text{O}_{3}
\]

**IR**

![IR spectrum](image)

**\(^1\)H NMR**

![\(^1\)H NMR spectrum](image)
**13C NMR**

| ppm | 100.00 | 101.00 | 102.00 | 103.00 | 104.00 | 105.00 | 106.00 | 107.00 | 108.00 | 109.00 | 110.00 |
|-----|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| peak | 102.24 | 102.63 | 108.80 | 109.48 | 110.21 | 110.61 | 110.93 | 112.94 | 113.04 | 113.45 | 113.64 |

**HRMS**

| m/z | 340.1243 | 351.0982 | 393.1425 | 415.1276 | 432.1016 | 433.0964 | 453.2100 | 466.2317 | 481.2618 |
|-----|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| Relative Abundance | 415.1243 | 431.0982 | 393.1425 | 416.1276 | 387.0932 | 432.1016 | 394.1458 | 365.1110 | 381.1104 |

NL: 2.24E6

F:\Users\...\fuying-5_161110152428

Error=1.0 ppm