Control over [2+2+2] and Carbonylative [4+2] Cycloaddition by CO Pressure in Co-Catalyzed Cycloaddition between Internal Diynes and Cyclopentadiene

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The reaction of internal diynes and cyclopentadiene in the presence of 5 mol % of cobalt catalysts proceeded under 5 atm of carbon monoxide pressure to give a high yield of the corresponding [2+2+2] cycloaddition product. By lowering carbon monoxide pressure from 30 atm to 5atm, cyclopentadiene can be used as a dienophile in the cobalt carbonyl-catalyzed [2+2+2] cycloaddition reaction between internal diynes and cyclopentadiene.

Key Words : [2+2+2] Cycloaddition, Diyne, Cobalt catalyst

Introduction

Cobalt-catalyzed or -mediated [2+2+2] cycloaddition has been an important step in the preparation of useful organic molecules.[1,2] The cobalt-catalyzed cycloaddition of three unsaturated C-C bonds with a high degree of chemo-, regio-, and stereoselectivity led to the synthesis of several natural and unnatural products.[3] A number of acetylenes and heterocyclic olefins have been utilized as cyclization partners,[4] whereas the use of simple alkenes is uncommon in these cycloaddition reactions.[5] In particular, use of conjugated dienes as a dienophile in the [2+2+2] cycloaddition has not been reported yet, as far as we are aware.

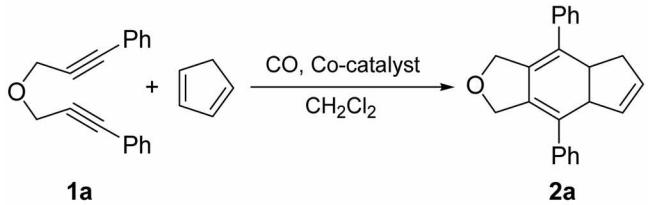
On our continuous efforts for synthesis of polycyclic compounds utilizing the Pauson-Khand reaction,[6] we found that reaction pathways could be changed simply by varying CO pressure in the cobalt-catalyzed cycloaddition reaction of diynes in the presence of cyclopentadiene. Recently, we reported that Co-catalyzed tandem carbonylative cyclization of internal diynes in the presence of cyclopentadiene under 30 atm of CO pressure afforded tetracyclic enone compounds, in which reaction carbon monoxide took a part at the first step of the tandem reaction.[6a] On the other hand, we also found that only simple [2+2+2] cycloadducts of an internal diyne and cyclopentadiene in a similar reaction condition under 5 atm of CO pressure were obtained (Figure 1).[7]

We decided to examine the reaction carefully focusing on the pressure of carbon monoxide and found that cyclopentadiene could be used as a dienophile in cobalt-catalyzed [2+2+2] cycloaddition under a low pressure of CO. Herein, we report the $Co_2(CO)_8$-catalyzed intermolecular [2+2+2] cycloaddition of internal diynes and cyclopentadiene under a low pressure of carbon monoxide.

Results and Discussion

In order to investigate the influence of CO pressure and to optimize reaction conditions, the CO pressure, the cobalt-catalysts, and the reaction temperature were screened for cobalt-catalyzed [2+2+2] cycloaddition of bis(1-phenyl-1-propynyl) ether (**1a**) and cyclopentadiene (Scheme 1 and Table 1).

As expected, no reaction was observed without any cobalt-catalysts (entry 1 in Table 1). The [2+2+2] cycloadduct **2a** was not obtained in the presence of the well-known catalyst,[2] $CpCo(CO)_2$, either, whereas **2a** was obtained in 75% yield without any other product in the presence of



Scheme 1. [2+2+2] cycloaddition of internal diyne **1a** and cyclopentadiene.

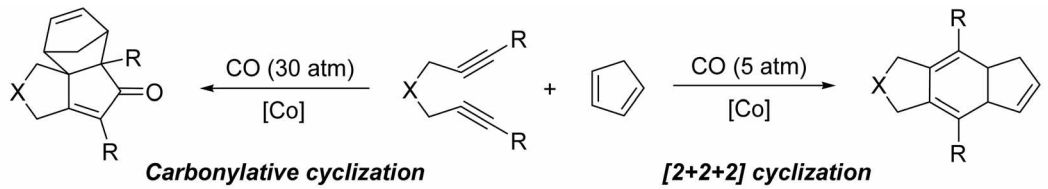


Figure 1. Different reaction pathways attained by varying CO pressure in the Co-catalyzed cyclization of internal diynes in the presence of cyclopentadiene.

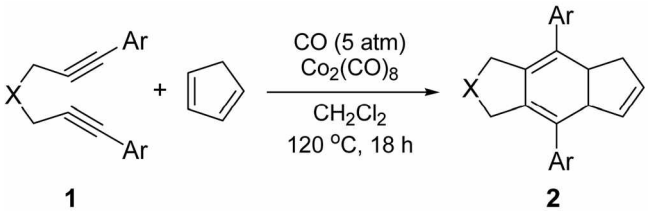
Table 1. [2+2+2] Cycloaddition of internal diyne **1a** and cyclopentadiene[a]

Entry	Catalyst	CO (atm)	Temp (°C)	Yield (%)[b]
1	–	5	120	–[c]
2	$CpCo(CO)_2$	5	120	–[c]
3	$Co_2(CO)_8$	5	120	75
4	$Co_2(CO)_8$	–[d]	120	2
5	$Co_2(CO)_8$	–[e]	120	35
6	$Co_2(CO)_8$	2	120	49
7	$Co_2(CO)_8$	10	120	38[f]
8	$Co_2(CO)_8$	5	80	19

[a]Reactions were carried out with **1a** (0.8 mmol), CpH (4.0 mmol), and appropriate CO pressure with 5 mol % of Co-catalyst in CH_2Cl_2 (30 mL) for 18 h. [b]Isolated yield. [c]No reaction. [d]Under 1 atm of N_2. [e]Under 5 atm of N_2. [f]Tandem carbonylative cyclization product was obtained additionally in 19% yield.

$Co_2(CO)_8$ under 5 atm of CO (entries 2 and 3 in Table 1). Because carbon monoxide did not participate in the cycloaddition reaction as a cyclization partner, it was necessary to determine the importance of CO in the reaction. Thus, reactions were carried out under nitrogen pressure instead of CO pressure (entries 4 and 5 in Table 1). Under 1 atm of N_2 pressure, a stoichiometric reaction occurred to give 2% yield based on the diyne used or 40% yield based on the cobalt carbonyl used. Interestingly, the reaction under 5 atm of N_2 pressure was revealed to be a catalytic reaction giving an improved yield of 35%. These results indicate that the increased nitrogen pressure may help regeneration and/or stability of catalytic species. The optimum pressure of CO was found to be 5 atm for this [2+2+2] cycloaddition (entries 3, 6, and 7 in Table 1). As CO pressure increased from 2 atm to 5 atm, the yield increased from 49% to 75%. The role of CO pressure in the reaction would also be related to regeneration and/or stability of the catalyst. However, a CO pressure higher than 5 atm was not beneficial to the [2+2+2] cycloaddition. Under 10 atm of CO pressure, a carbonylative cycloaddition product in 19% yield was obtained additionally in company with **2a** in 38% yield. The carbonylative cycloaddition product was characterized as the same product synthesized by the Pauson-Khand reaction and subsequent [4+2] cycloaddition of **1a** and cyclopentadiene in a tandem fashion.[6a] As previously reported, the tandem carbonylative cycloaddition was the main reaction pathway under CO pressure higher than 10 atm.[6] Catalytic activity was also decreased by lowering the reaction temperature from 120 °C to 80 °C (entry 8 in Table 1).

These results in Table 1 show that reaction pathways can be changed simply by varying CO pressure in the cobalt carbonyl-catalyzed cycloaddition reaction of internal diyne **1a** in the presence of cyclopentadiene. By lowering CO pressure to 5 atm, carbon monoxide did not take part in the reaction to give the [2+2+2] cycloadduct without producing the carbonylative cycloadduct of which CO was one of the components. It is intriguing that the pressure of CO in such a narrow range can be used to control the cycloaddition outcome.



Scheme 2. $Co_2(CO)_8$-catalyzed [2+2+2] cycloaddition of internal diynes **1** and CpH.

Table 2. $Co_2(CO)_8$-catalyzed [2+2+2] cycloaddition of internal diynes **1** and CpH[a]

Entry	X	Ar	Diyne	Cycloadduct	Yield (%)[b]
1	O	Ph	**1a**	**2a**	75
2	O	4-MeC_6H_4	**1b**	**2b**	72
3	O	4-FC_6H_4	**1c**	**2c**	58
4	TsN	Ph	**1d**	**2d**	89
5	H_2C	Ph	**1e**	**2e**	18
6	$(MeO_2C)_2C$	Ph	**1f**	**2f**	89

[a]Reactions were carried out with **1** (0.8 mmol), CpH (4.0 mmol), and 5 atm of CO pressure with 5 mol % of $Co_2(CO)_8$ in CH_2Cl_2 (30 mL) for 18 h. [b]Isolated yield.

Cobalt carbonyl-catalyzed [2+2+2] cycloaddition between cyclopentadiene and internal diynes having various tether groups and aryl substituents at both alkyne termini were examined under the optimized reaction conditions for **1a** (Scheme 2 and Table 2).[7]

Cobalt carbonyl-catalyzed [2+2+2] cycloaddition reactions of propargyl ether derivatives having aryl groups with either electron-donating or electron-withdrawing substituents at both of alkyne termini afforded the desired product in good yields (entries 1-3 in Table 2). For these oxygen-tethered internal diynes, the diyne with electron-withdrawing aryl substituents showed a lower catalytic reactivity than that with electron-donating aryl substituents. For a nitrogen-tethered internal diyne (**1d**) and a quaternary carbon-tethered diyne (**1f**) with phenyl substituents, the reactions proceeded well to give the corresponding cycloadduct in good yields (entry 4 and 6 in Table 2). However, the [2+2+2] cycloaddition between 1,7-diphenyl-1,6-heptadiyne (**1e**) and cyclopentadiene showed a significantly decreased catalytic reactivity (entry 5 in Table 2). The reaction gave only 18% of the cycloadduct **2e** and the starting diyne **1e** was recovered intact.

Although the precise reaction mechanism of Co-catalyzed [2+2+2] cycloaddition and carbonylative [4+2] cycloaddition between internal diynes and cyclopentadiene under CO pressure has not been revealed yet, an explanation for variability in the reaction pathways according to CO pressure may be provided from the results investigated here (Figure 2).

It is assumed that the effect of CO pressure on the transformation of a cobaltacyclopentadiene intermediate **I** into each of the cycloadducts will play a major role in determining the reaction routes. If the CO pressure is not high enough

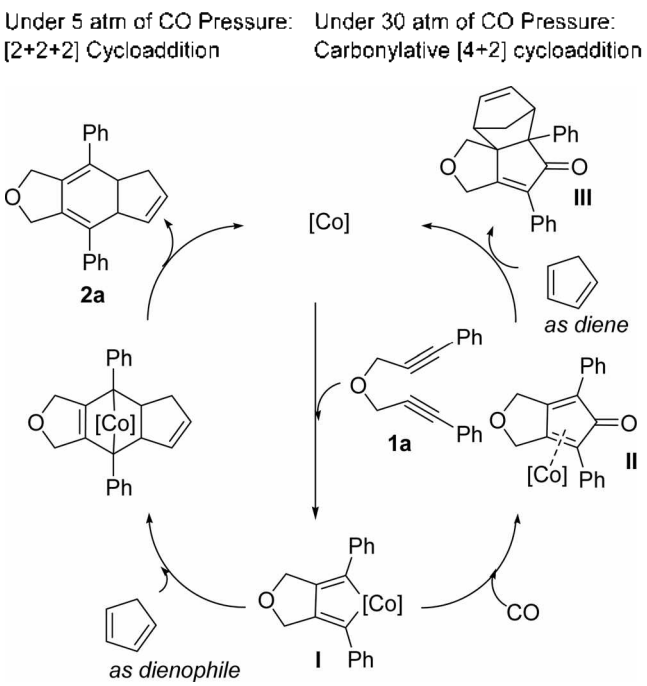
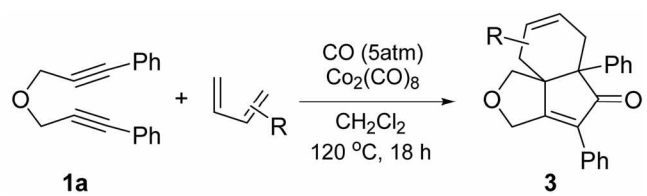


Figure 2. Reaction pathways according to CO pressure in Co-catalyzed cycloaddition between internal diynes and cyclopentadiene.

to insert carbon monoxide into the Co-C bond of the intermediate **I**, then cobaltacyclopentadiene will act as a diene[8] and participate in the cyclization with a double bond of cyclopentadiene producing the [2+2+2] cycloadduct **2a**. On the contrary, the cobaltacyclopentadiene intermediate **I** will be transformed into a cyclopentadienone intermediate **II** under a high pressure of CO, and then the intermediate **II** acts as a dienophile[9] to react with cyclopentadiene in a tandem fashion producing the carbonylative [4+2] cycloadduct **III**.

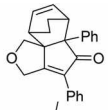
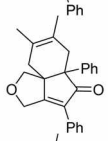
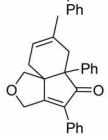
According to the explanation of reaction pathways, cyclopentadiene acted as a dienophile[10] during the [2+2+2] cycloaddition reaction under 5 atm of CO pressure. At this stage, it is somewhat strange that cyclopentadiene participated as a dienophile, not as a diene, in the reaction conditions under 5 atm of CO pressure. In order to confirm whether the reaction proceeded due to a special property of cyclopentadiene was also examined reactions involving other conjugated dienes (Scheme 3 and Table 3).

Surprisingly, the [2+2+2] cycloaddition was not observed at all with the 1,3-dienes tested. Instead, the tandem carbonylative [4+2] cyclization products were obtained in moderate yields. It is envisioned that CO insertion into the cobaltacyclopentadiene intermediate **I** in Figure 2, which would lead to the tandem carbonylative [4+2] cyclization, could not happen easily under a low CO pressure. The intermediate **I**, which did not react as a diene either with the dienes other than cyclopentadiene in the [2+2+2] cycloaddition pathway, existed for long enough to react with CO and was finally transformed into the carbonylated [4+2] product. In other words, cyclopentadiene seems to have a better dienophilicity than the dienes tested in the present cyclization reaction conditions.



Scheme 3. $Co_2(CO)_8$-catalyzed tandem carbonylative [4+2] cycloaddition of the internal diyne **1a** and conjugated dienes other than CpH.

Table 3. $Co_2(CO)_8$-catalyzed tandem carbonylative [4+2] cycloaddition of **1a** and dienes[a]

Entry	Diene	Cycloaddition	Product	Yield (%)[b]
1			**3a**	61
2			**3b**	35
3			**3c**	40[c]

[a]Reactions were carried out with **1a** (0.8 mmol), diene (4.0 mmol), and 5 atm of CO pressure with 5 mol % of $Co_2(CO)_8$ in CH_2Cl_2 (30 mL) for 18 h. [b]Isolated yield. [c]Combined yield of two regioisomers with ratio of 1:1. The ratio was determined by a crude ^1H NMR spectrum.

In summary, we have demonstrated that varying carbon monoxide pressure enables the use of cyclopentadiene as a dienophile, instead of as a diene, in the cobalt carbonyl-catalyzed [2+2+2] cycloaddition reaction and that the selection of the reaction route between the [2+2+2] cycloaddition and the tandem carbonylative [4+2] cycloaddition can be achieved by varying pressure of carbon monoxide. Synthesis of polycyclic compounds containing 5- and 6-membered rings has been achieved by the method disclosed in this study.

Experimental Section

Solvents were dried and distilled according to standard methods before use. Dichloromethane was distilled from P_2O_5 under nitrogen. Reagents were purchased from Aldrich Chemical Co. and Strem Chemical Co. and were used as received. All yields are based upon isolated material. ^1H NMR and ^{13}C NMR spectra were obtained with a Bruker 300 MHz spectrometer. High Resolution Mass Spectra were obtained at Korea Basic Science Institute (Daegu, Korea).

Representative reaction procedures. To a 100 mL high-pressure reactor were added bis(1-phenyl-1-propynyl) ether (**1a**) (0.20 g, 0.81 mmol), cyclopentadiene (0.33 mL, 4.05 mmol), 30 mL of CH_2Cl_2, and $Co_2(CO)_8$ (14 mg, 41 μmol). After the solution was flushed with CO gas in several

seconds, the reactor was pressurized with 5 atm of CO. The reactor was heated at 120 °C for 18 h. After the reactor was cooled to room temperature and excess gas was vented, the solution was transferred into a flask and then evaporated to dryness. The residue was chromatographed on a silica gel column eluting with hexane and ethyl acetate (v/v, 10:1).

Compound 2a. Yield: 75%; ^{1}H NMR ($CDCl_3$): 7.49-7.36 (m, 4H), 7.34-7.27 (m, 6H), 5.80 (m, 1H), 5.67 (m, 1H), 4.75 (d, J = 12.7 Hz, 2H), 4.53 (t, J = 12.9, 2H), 4.40 (d, J = 11.6 Hz, 1H), 3.91 (q, J = 8.8 Hz, 1H), 2.80 (dd, J = 8.8, 16.7 Hz, 1H), 2.43 (dd, J = 5.6, 16.4 Hz, 1H); ^{13}C NMR ($CDCl_3$): 140.2, 139.7, 132.3, 132.2, 131.9, 130.2, 130.0, 129.1, 128.8, 128.6, 128.5, 128.4, 127.3, 127.1, 71.5, 48.4, 42.8, 41.3, 38.8; HRMS for $C_{23}H_{20}O_1$: calcd. 312.1514, obsd. 312.1513.

Compound 2b. Yield: 72%; ^{1}H NMR ($CDCl_3$): 7.18 (brs, 8H), 5.74 (br, 1H), 5.65 (br, 1H), 4.72 (d, J = 12.4 Hz, 2H), 4.46 (t, J = 12.6, 2H), 4.35 (d, J = 11.3 Hz, 1H), 3.87 (q, J = 8.6 Hz, 1H), 2.76 (dd, J = 8.6, 16.1 Hz, 1H), 2.41 (br, 1H), 2.36 (brs, 6H); ^{13}C NMR ($CDCl_3$): 137.1, 136.9, 136.6, 132.3, 131.6, 131.3, 130.0, 129.4, 129.2, 129.1, 127.0, 126.6, 71.5, 48.1, 42.8, 40.9, 21.3; HRMS for $C_{25}H_{24}O_1$: calcd. 340.1827, obsd. 340.1825.

Compound 2c. Yield: 58%; ^{1}H NMR ($CDCl_3$): 7.25 (dd, J = 4.8, 9.1 Hz, 4H), 7.10 (t, J = 8.6 Hz, 4H), 5.78 (dd, J = 2.4, 5.4 Hz, 1H), 5.60 (dd, J = 2.1, 5.6 Hz, 1H), 4.70-4.64 (m, 2H), 4.46 (t, J = 13.1, 2H), 4.31 (d, J = 11.5 Hz, 1H), 3.82 (m, 1H), 2.75 (dd, J = 8.7, 16.4 Hz, 1H), 2.37 (ddd, J = 2.2, 6.7, 16.4 Hz, 1H); ^{13}C NMR ($CDCl_3$): 131.9, 131.6, 130.2, 128.8, 128.7, 125.9, 115.6, 115.5, 115.3, 115.2, 71.3, 71.2, 48.3, 42.6, 41.2; HRMS for $C_{23}H_{18}O_1F_2$: calcd. 348.1326, obsd. 348.1327.

Compound 2d. Yield: 89%; ^{1}H NMR ($CDCl_3$): 7.59 (d, J = 8.1 Hz, 2H), 7.45-7.33 (m, 4H), 7.32-7.22 (m, 4 H), 7.20-7.15 (m, 4H), 5.70 (m, 1H), 5.49 (m, 1H), 4.10 (m, 1H), 4.07-4.02 (m, 4H), 3.61 (q, J = 8.8 Hz, 1H), 2.64 (dd, J = 8.8, 16.3 Hz, 1H), 2.45 (s, 3H), 2.27(m, 1H); ^{13}C NMR ($CDCl_3$): 144.1, 140.2, 139.6, 132.7, 132.1, 130.4, 130.1, 129.9, 129.5, 129.1, 128.5, 128.4, 128.1, 128.0, 127.8, 127.3, 127.1, 125.8, 52.8, 52.4, 49.0, 42.7, 41.8, 22.0; HRMS for $C_{30}H_{27}O_2N_1S_1$: calcd. 465.1763, obsd. 465.1762.

Compound 2e. Yield: 18%; ^{1}H NMR ($CDCl_3$): 7.43-7.15 (m, 10H), 5.71 (m, 1H), 5.58 (m, 1H), 4.29 (d, J = 11.0 Hz, 1H), 3.79 (q, J = 8.7 Hz, 1H), 2.70-2.49 (m, 4H), 2.48-2.31 (m, 2H), 1.84 (m, 1H), 1.37 (m, 1H); ^{13}C NMR ($CDCl_3$): 141.7, 141.2, 135.2, 132.9, 131.7, 130.6, 129.8, 128.4, 128.2, 128.1, 128.0, 127.8, 127.5, 126.5, 48.7, 42.8, 41.5, 32.6, 32.5, 25.4; HRMS for $C_{24}H_{22}$: calcd. 310.1722, obsd. 310.1725.

Compound 2f. Yield: 89%; ^{1}H NMR ($CDCl_3$): 7.42-7.30 (m, 10H), 5.72 (m, 1H), 5.53 (m, 1H), 4.24 (d, J = 11.2 Hz, 1H), 3.72 (m, 1H), 3.71 (s, 3H), 3.58 (s, 3H), 3.17 (dt, J = 3.3, 16.3 Hz, 2H), 3.13-3.00 (m, 2H), 2.66 (dd, J = 8.8, 16.3 Hz, 1H), 2.33 (m, 1H); ^{13}C NMR ($CDCl_3$): 172.2, 171.7, 141.0, 140.4, 132.6, 132.2, 131.2, 130.9, 129.9, 129.6, 129.2, 128.4, 128.3, 128.0, 127.9, 126.9, 58.8, 53.1, 53.0, 52.9, 48.9, 42.7, 41.8, 39.4; HRMS for $C_{28}H_{26}O_4$: calcd. 426.1831, obsd. 426.1832.

Compound 3a. Yield: 61%; ^{1}H NMR ($CDCl_3$): 7.43-7.25 (m, 10H), 6.30 (t, J = 7.5 Hz, 1H), 6.10 (t, J = 7.4 Hz, 1H), 4.94 (d, J = 16.1 Hz, 1H), 4.58 (d, J = 16.1 Hz, 1H), 4.22 (d, J = 8.5 Hz, 1H), 3.51 (d, J = 8.5 Hz, 1H), 3.22 (br s, 1H), 2.98 (br s, 1H), 2.07 (m, 2H), 1.52 (m, 1H), 1.29 (m, 1H); ^{13}C NMR ($CDCl_3$): 208.8, 177.9, 136.4, 136.3, 134.9, 131.6, 130.6, 128.7, 128.6, 128.5, 128.4, 128.2, 127.0, 70.7, 65.7, 63.0, 59.4, 39.8, 36.5, 22.4, 19.2; IR (C=O) 1700 cm^{-1}; HRMS for $C_{25}H_{22}O_2$: calcd. 354.1620, obsd. 354.1617.

Compound 3b. Yield: 35%; ^{1}H NMR ($CDCl_3$): 7.41 (d, J = 7.2 Hz, 2H), 7.30-7.20 (m, 3H), 7.09-7.05 (m, 3H), 6.90 (d, J = 7.1 Hz, 2H), 4.81 (d, J = 17.0 Hz, 1H), 4.37 (d, J = 17.0 Hz, 1H), 3.51 (d, J = 8.4 Hz, 1H), 2.69 (d, J = 8.4 Hz, 1H), 2.51 (d, J = 15.0 Hz, 1H), 2.45 (d, J = 14.0 Hz, 1H), 2.41 (d, J = 13.0 Hz, 1H), 2.28 (d, J = 15.0 Hz, 1H), 1.50 (s, 3 H), 1.46 (s, 3 H); ^{13}C NMR ($CDCl_3$): 209.6, 177.3, 141.3, 134.7, 130.6, 129.7, 128.7, 128.6, 128.5, 128.1, 126.9, 126.7, 125.8, 74.8, 65.7, 62.5, 59.4, 40.3, 39.8, 19.4, 19.0; IR (C=O) 1702 cm^{-1}; HRMS for $C_{25}H_{24}O_2$: calcd. 356.1776, obsd. 356.1776.

Compound 3c. Two regioisomers having methyl group in different position were obtained.

3c-1: Yield: 28%; ^{1}H NMR ($CDCl_3$): 7.61 (d, J = 7.2 Hz, 2H), 7.43 (m, 3H), 7.26 (m, 3H), 7.10 (d, J = 7.0 Hz, 2H), 5.70 (br s, 1H), 5.00 (d, J = 16.7 Hz, 1H), 4.53 (d, J = 16.7 Hz, 1H), 3.69 (d, J = 9.0 Hz, 1H), 2.86 (d, J = 8.6 Hz, 1H), 2.83 (d, J = 8.6 Hz, 1H), 2.64 (d, J = 15.1 Hz, 1H), 2.55 (d, J = 14.7 Hz, 1H), 2.47 (d, J = 14.7, 1H), 1.70 (s, 3H); ^{13}C NMR ($CDCl_3$): 210.3, 177.6, 141.6, 139.6, 134.9, 130.6, 128.8, 128.7, 128.3, 128.2, 127.0, 126.8, 119.5, 75.0, 65.7, 62.2, 59.0, 38.3, 33.9, 23.6; IR (C=O) 1706 cm^{-1}; HRMS for $C_{24}H_{22}O_2$: calcd. 342.1620, obsd. 342.1617.

3c-2: Yield: 12%; ^{1}H NMR ($CDCl_3$): 7.60 (d, J = 7.2 Hz, 2H), 7.34 (m, 3H), 7.19 (m, 3H), 7.09 (d, J = 7.0 Hz, 2H), 5.45 (br s, 1H), 4.94 (d, J = 16.7 Hz, 1H), 4.53 (d, J = 16.7 Hz, 1H), 3.67 (d, J = 9.0 Hz, 1H), 2.84 (d, J = 8.5 Hz, 1H), 2.67 (d, J = 8.5 Hz, 1H), 2.60 (d, J = 14.9 Hz, 1H), 2.58 (d, J = 14.8 Hz, 1H), 2.43 (d, J = 14.8 Hz, 1H), 1.73 (s, 3H); ^{13}C NMR ($CDCl_3$): 209.5, 177.8, 141.4, 135.4, 134.5, 128.8, 128.7, 128.5, 128.2, 128.0, 126.9, 123.0, 75.2, 65.8, 62.5, 58.9, 38.4, 33.9, 23.2; IR (C=O) 1706 cm^{-1}; HRMS for $C_{24}H_{22}O_2$: calcd. 342.1620, obsd. 342.1618.

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