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Co/C-catalyzed tandem carbocyclization reaction of 1,6-diynes

Sang Ick Lee,[a] Seung Uk Son,[a] Mi Ra Choi,[a] Young Keun Chung[a,*] and Sueg-Geun Lee[b]

[a]*School of Chemistry and Center for Molecular Catalysis, Seoul National University, Seoul 151-747, Republic of Korea*
[b]*Korea Research Institute of Chemical Technology, PO Box 107, Yusong, Taejeon 305-600, Republic of Korea*

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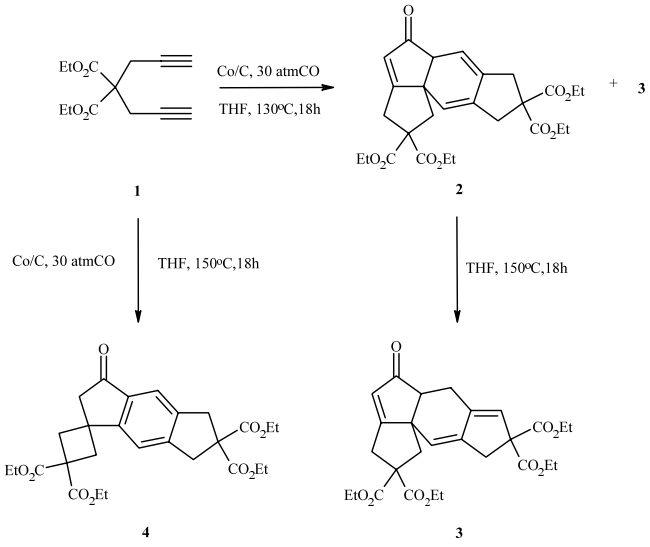
Abstract—Cobalt on charcoal (Co/C) can be used as a catalyst in the tandem carbocycloaddition reaction of 1,6-diyne and carbon monoxide. The reaction product is dependent upon the reaction temperature, the position of the functional group, and the substrate itself. © 2003 Elsevier Science Ltd. All rights reserved.

The use of transition metals including cobalt-mediated [2+2+1] cycloaddition reactions[1] of two alkynes and carbon monoxide in the synthesis of cyclopetadienone derivatives, which are very useful building blocks[2] for organic synthesis, has been extensively studied.[3] However, their practical catalytic version was recently reported.[4] We recently showed that the $Co_2(CO)_8$-catalyzed [2+2+1] cycloaddition reaction of two alkynes and carbon monoxide can be used to synthesize multi-ring skeletons such as angular triquinanes and fenestranes.[5] Although some useful homogeneous catalytic systems are known, a heterogeneous system has not been reported yet. We recently showed that heterogeneous cobalt on charcoal (Co/C) can be used as a catalyst for many carbocylization reactions including the Pauson–Khand reaction,[6] and carboamidation.[7] The heterogeneous Co/C catalytic system has many advantages over the homogeneous $Co_2(CO)_8$ system, including facile separation and reusability. We are continuing our efforts to enlarge the range of reaction which can be catalyzed by Co/C. We report herein the heterogeneous Co/C-catalyzed tandem cycloaddition to give multi-ring skeleton compounds.



Scheme 1.

Recently, we reported the $Co_2(CO)_8$-catalyzed tandem [2+2+1]/[2+2+2] of 1,6-diyne to give novel tetra-cyclic ring compounds.[5a] The reaction conditions were 100°C, 20 atm of CO, and duration 2 days. When we first attempted to use Co/C as a catalyst instead of $Co_2(CO)_8$, there was no conversion. However, a mixture of **2** (36%) and **3** (36%) was obtained at a higher temperature (130°C) (Scheme 1).[8,9] Previously, **2** was obtained in the $Co_2(CO)_8$-catalyzed reaction. Compound **3** was fully characterized.

When the reaction was performed in the presence of phenyl acetylene, phenyl acetylene did not participate in the reaction. Interestingly, a new compound **4** was obtained in 87% yield as the sole product at 150°C by Co/C. In case of $Co_2(CO)_8$, **4** was obtained in 85% yield. Compound **4** was fully characterized.[9] The structure of **4** was confirmed by a single-crystal X-ray diffraction study (Fig. 1).[10] The compound is a tetracyclic compound having a spiro ring.

A similar spiro compound was reported by Chiusoli and his co-workers several years ago.[11c] They prepared the spiro compound by the reaction of 1,6-diyne with

* Corresponding author. Tel.: +82-2-880-6662; fax: +82-2-889-0310; e-mail: ykchung@plaza.snu.ac.kr

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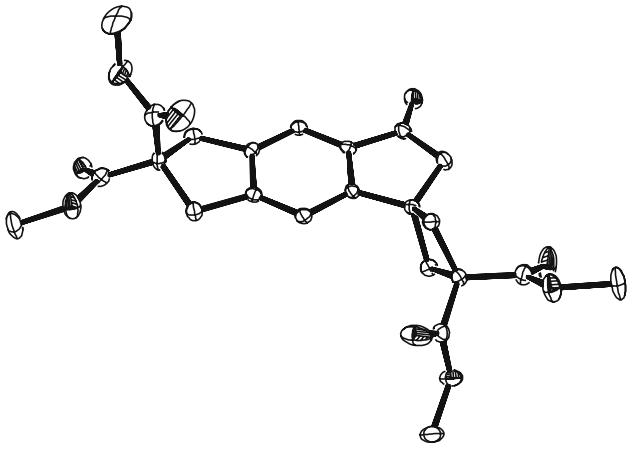
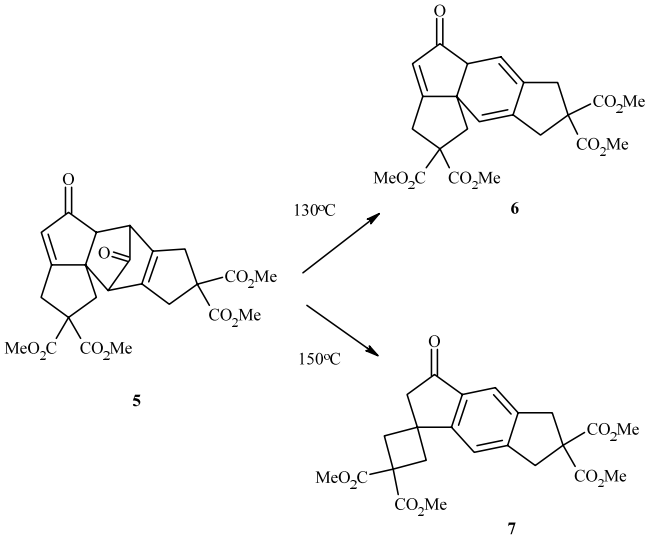


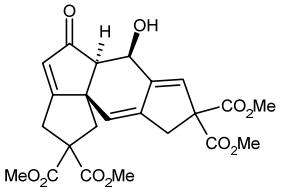
Figure 1. X-Ray structure of **4** (thermal eclipsoid 30%).



Scheme 2.

CO in the presence of Pd/C followed by treatment with sodium phenoxide or potassium *t*-butoxide in dimethoxyethane. Compound **5** was isolated at the first step of their reaction.[9] While we were studying the reactions, we were curious about the reaction pathways. The first question we asked was whether **2** could be transformed to **4** via aromatization by heat or catalysis of Co/C. The answer was negative. When **2** was heated under CO pressure, **3** formed by migration of one of the double bonds was obtained instead of **4**. The second question was whether **2** and **4** came from the same intermediate such as **5**.

Compound **5** was heated at 130 and 150°C, respectively. Surprisingly, at 130°C, **6** was obtained from **5** in 75% yield (Scheme 2).[9] This result gave also some hint to mechanism of formation of **2** in our previous report. As expected, at 150°C, **7** was obtained in 64% yield.[9] Thus, **2** and **4** can come from the same intermediate, which is similar to **5**. Due to the better crystallinity of product, we used a methyl ester substituted-substrate instead of **1**. Depending upon the reaction temperature, the reaction follows different reaction pathways to **2** and **4**, respectively. Interestingly, treatment of **5** in a wet solvent with heat led to the isolation of **8** in 87% yield.[9] We used a few other substrates for this tandem reaction at 150°C. As expected, substrates having acetonide or tertiary amine were good substrates (Table 1).



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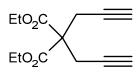
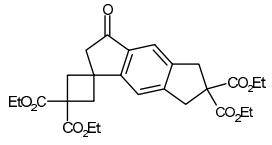
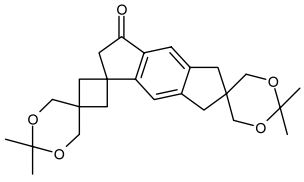
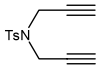
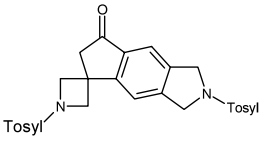
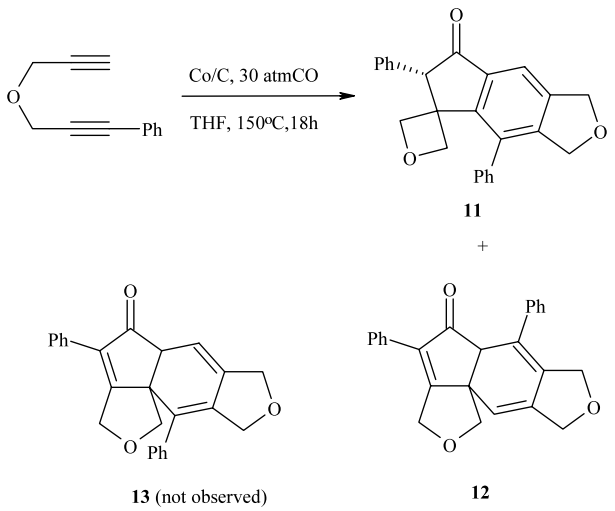
When we used an internal alkyne as a substrate, two products were obtained (Scheme 3).

At first we thought that the formation of two products might be due to the regioselectivity problem of the terminal group. However, interestingly, it was a problem of chemoselectivity. When the reaction was conducted with $Co_2(CO)_8$ as a catalyst, a mixture of **12** and **13** in the ratio 1:4.2 was obtained. Compounds **12** and **13** could not be separated by column chromatography. In the case of the use of Co/C as a catalyst, **13** was not found and **11** (67%) and **12** (12%) were isolated as pure forms. The structure of **11** was characterized by single crystal X-ray diffraction analysis (Fig. 2).[12] Two different reactions can occur in a regioselective manner. The reason why the high regioselectivity was observed was unclear.

Table 1. Tandem cycloaddition reaction catalyzed by Co/C[a]

Entry	Diyne	Product	Yield(%)
1		 **4**	87
2		 **9**	68
3		 **10**	79

[a] Reaction condition ; 150°C, 30 atm CO, 18h in THF. [b]Isolated yield



Scheme 3.

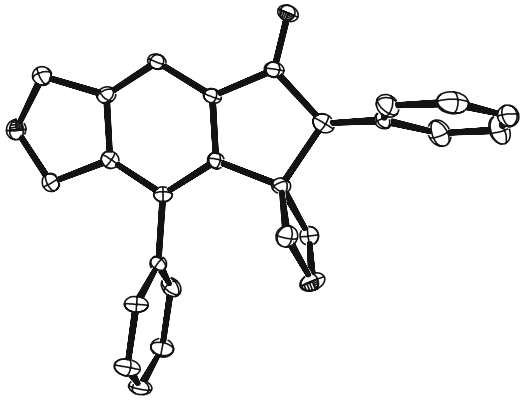
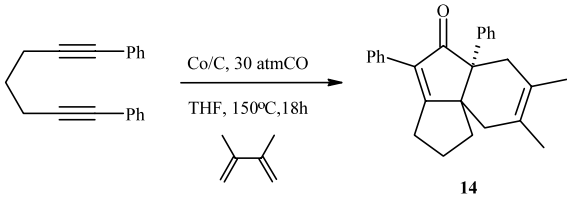


Figure 2. X-Ray structure of **11** (thermal eclipsoid 30%).

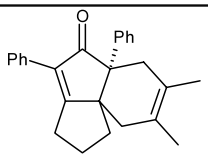
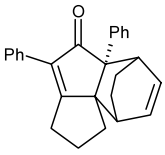
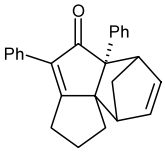


Scheme 4.

Next we explored a tandem [2+2+1]/[2+2+2] cycloaddition of 1,6-diyne having two internal alkynes (Scheme 4).

However, it seemed to be difficult to produce the second [2+2+2] cycloaddition due to the steric hindrance. Thus, the reactant was recovered. In order to carry out the tandem reaction in a catalytic manner, an additional substrate, 1,3-diene, would be needed. Reaction of 1,7-diphenyl-1,6-diyne with 1,3-diene in the presence of Co/C at 130°C under 30 atm CO for 18 h was tested. Besides the expected tricyclic product **14**, cyclopentadienone was obtained. When the reaction temperature was raised to 150°C, **14** was obtained as the sole product in 87% yield. We screened various 1,3-dienes (Table 2).

Table 2. Tandem cycloaddition reaction catalyzed by Co/C[a]

Entry	Diyne	Product	Yield(%)
1			87
2			62
3			77

[a]Reaction condition; 150°C, 30 atm CO, 18 h in THF. [b]Isolated yield

With 2,3-dimethyl-1,3-butadiene, 1,3-cyclohexadiene, or 1,3-cyclopentadiene, the expected product was obtained in good to high yields.

In conclusion, we have demonstrated that heterogeneous Co/C can be used as a catalyst in the tandem carbocycloaddition reaction of 1,6-diyne and carbon monoxide. The reaction product was dependent upon the reaction temperature, the position of the functional group, and the substrate itself. The experimental simplicity and the high conversion rate of the cycloaddition are noteworthy. Further studies on the application of the reaction are in progress.

Acknowledgements

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Chem. Commun. **1992**, 325; (d) Knölker, H.-J.; Baum, E.; Heber, J. *Tetrahedron Lett.* **1995**, *36*, 7647; (e) Jikyo, T.; Eto, M.; Harano, K. *Bull. Chem. Soc. Jpn.* **1997**, *45*, 1961; (f) Rainier, J. D.; Imbriglio, J. E. *Org. Lett.* **1999**, *1*, 2037.

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8. General procedure: Co/C-catalyzed tandem carbocyclization reaction of 1,6-diyne under carbon monoxide. Co/C (0.10 g, 12.2 wt% Co), diyne (1 mmol) and THF (10 mL) were put into a high pressure reactor (50 mL). The reactor was flushed with nitrogen for 5 min and pressurized with 30 atm CO. The reactor was heated at 150°C for 18 h. After the reactor was cooled to rt and the excess gas was released, the reaction mixture was transferred into a one-neck flask. Removal of the solvent followed by chromatography on a silica gel eluting with hexane and diethyl ether (v/v, 1:2) gave the product.
9. Spectral data:

Compound **3**: IR νC=O 1729, 1705 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.27 (t, 7.1 Hz, 6H), 1.32 (t, 7.1 Hz, 6H), 2.56 (m, 4H), 2.91 (d, 17.0 Hz, 1H), 3.06 (d, 1H, 17.0 Hz), 3.17 (s, 1H), 3.23 (s, 1H), 3.59 (d, 24.5 Hz, 1H), 4.20 (m, 6H), 4.29 (m, 2H), 5.34 (s, 1H), 5.74 (s, 1H), 5.80 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 14.3, 14.4, 20.9, 35.2, 36.4, 43.9, 55.1, 55.6, 60.7, 62.0, 62.6, 62.7, 64.6, 119.9, 122.3, 128.1, 140.8, 141.7, 170.4, 171.4, 171.5, 171.8, 185.2, 209.1; HRMS, M$^+$ ($C_{27}H_{32}O_9$): calcd 500.2046, obsd 500.2042.

Compound **4**: IR νC=O 1732, 1718 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.27 (t, 7.1 Hz, 6H), 1.32 (t, 7.1 Hz, 6H), 2.86 (d, 14.0 Hz, 2H), 2.93 (s, 2H), 3.08 (d, 14.0 Hz, 2H), 3.59 (s, 2H), 3.66 (s, 2H), 4.22 (q, 6.8 Hz, 4H), 4.29 (q, 6.8 Hz, 4H), 7.46 (s, 1H), 7.58 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 14.4, 38.86, 39.9, 40.9, 43.1, 47.6, 53.3, 60.9, 62.2, 118.8, 120.4, 141.4, 149.7, 160.3, 171.5, 171.8, 204; HRMS, M$^+$ ($C_{27}H_{32}O_9$): calcd 500.2046, obsd 500.2042.

Compound **5**: IR νC=O 1732, 1699 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.54 (d, 14.1 Hz, 1H), 2.69 (d, 14.1 Hz, 1H), 2.76 (d, 5.0 Hz, 1H), 2.91 (d, 17.4 Hz, 1H), 3.02 (d, 18.0 Hz, 1H), 3.05 (s, 2H), 3.27 (d, 15.2 Hz, 1H), 3.30 (s, 1H), 3.34 (d, 14.5 Hz, 1H), 3.46 (d, 5.1 Hz, 1H), 3.71 (s, 3H), 3.72 (s, 3H), 3.75 (s, 3H), 3.85 (s, 3H), 6.00 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 35.6, 39.4, 39.9, 49.8, 52.6, 52.9, 53.0, 53.3, 53.6, 55.8, 57.4, 59.6, 59.9, 130.2, 137.8, 139.6, 170.9, 171.3, 171.5, 171.7, 181.1, 194.4, 205.5; HRMS, M$^+$ ($C_{24}H_{24}O_{10}$): calcd 472.1369, obsd 472.1363.

Compound **6**: IR νC=O 1718, 1635, 1425 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.21 (d, 14.1 Hz, 1H), 2.62 (d, 14.1 Hz, 1H), 2.91 (s, 2H), 2.95 (d, 13.0 Hz, 1H), 3.07 (d, 13.0 Hz, 1H), 3.10 (s, 1H), 3.27 (d, 17.2 Hz, 1H), 3.59 (d, 17.2 Hz, 1H), 3.70 (s, 3H), 3.73 (s, 3H), 3.74 (s, 3H), 3.83 (s, 3H), 3.84 (s, 3H), 5.38 (s, 1H), 5.84 (dd, 2.3 Hz, 1H), 6.01 (d, 1.3 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 33.3, 38.8, 39.1, 47.6, 53.3, 53.7, 53.8, 55.2, 56.9, 59.0, 59.4, 116.5, 119.8, 134.7, 136.1, 171.7, 171.9, 172.4, 186.3, 210.6; HRMS, M$^+$ ($C_{23}H_{24}O_9$): calcd 444.1420, obsd 444.1418.

Compound **7**: IR νC=O 1728, 1700 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): 2.88 (d, 13.3 Hz, 2H), 2.93 (s, 2H), 3.10 (d, 13.1 Hz, 2H), 3.67 (s, 2H), 3.60 (s, 2H), 3.77 (s, 6H), 3.85 (s, 6H), 7.46 (s, 1H), 7.57 (s, 1H); anal. calcd for $C_{23}H_{24}O_9$: C, 62.16; H, 5.44. Found: C, 62.49; H, 5.42.

Compound **8**: IR νC=O 1730, 1718, 1704 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.60 (d, 14.2 Hz, 1H), 2.67 (d, 14.2 Hz, 1H), 2.86 (d, 1.8 Hz, 1H), 2.96 (d, 17.2 Hz, 1H), 3.13 (d, 17.2 Hz, 1H), 3.22 (d, 18.0 Hz, 1H), 3.54 (d, 18.0 Hz, 1H), 3.67 (s, 3H), 3.71 (s, 3H), 3.72 (s, 3H), 3.79 (s, 3H), 5.04 (d, 1.8 Hz, 1H), 5.40 (d, 1.5 Hz, 1H), 5.73 (d, 1.5 Hz, 1H), 6.06 (d, 2.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 29.6, 34.7, 36.1, 43.6, 53.1, 53.3, 53.4, 54.5, 60.5, 62.1, 62.8, 64.2, 120.0, 122.6, 130.7, 137.4, 143.5, 169.8, 171.0, 171.5, 172.0, 185.0, 206.2; HRMS, M$^+$ ($C_{23}H_{24}O_{10}$): calcd 460.1369, obsd 460.1367.

Compound **9**: IR νC=O 1702 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.43 (s, 6H), 1.47 (s, 6H), 2.23 (d, 13.4 Hz, 2H), 2.31 (d, 13.5 Hz, 2H), 2.86 (s, 2H), 2.90 (s, 2H), 3.01 (s, 2H), 3.71 (d, 11 Hz, 2H), 3.74 (d, 13 Hz, 2H), 3.87 (s, 2H), 3.92 (s, 2H), 7.40 (s, 1H), 7.45 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 23.5, 24.1, 24.9, 31.1, 38.5, 39.2, 40.7, 43.0, 43.4, 55.0, 68.8, 69.0, 69.8, 98.3, 98.5, 119.5, 120.8, 126.3, 135.2, 142.3, 151.3, 161.6, 204.7; HRMS, M$^+$ ($C_{25}H_{32}O_5$): calcd 412.2249, obsd 412.2250.

Compound **10**: IR νC=O 1714 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.41 (s, 3H), 2.53 (s, 3H), 2.77 (s, 2H), 4.00 (d, 8.1 Hz, 2H), 3.96 (d, 8.1 Hz, 2H), 4.59 (s, 4H), 7.16 (s, 1H), 7.34 (d, 8.0 Hz, 2H), 7.43 (d, 4.4 Hz, 2H), 7.46 (s, 1H), 7.78 (dd, 8.1 Hz, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.9, 22.0, 38.2, 49.7, 53.2, 63.2, 117.8, 118.7, 128.0, 129.0, 130.3, 130.4, 131.5, 136.5, 138.4, 144.4, 145.1, 145.6, 157.3, 201.8; HRMS, M$^+$ ($C_{27}H_{26}O_5N_2S_2$): calcd 522.1283, obsd 522.1286.

Compound **11**: IR νC=O 1734 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 4.14 (s, 1H), 4.17 (d, 6.7 Hz, 1H), 4.5 (d, 6.7 Hz, 1H), 4.77 (d, 5.8 Hz, 1H), 4.85 (s, 2H), 4.86 (d, 6.0 Hz, 1H), 5.21 (s, 2H), 6.99 (m, 2H), 7.29 (m, 3H), 7.48 (m, 5H), 7.64 (s, 1H); anal. calcd for $C_{25}H_{20}O_3$: C, 81.50; H, 5.47. Found: C, 81.34; H, 5.47.

Compound **12**: IR νC=O 1713 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.29 (d, 8.3 Hz, 1H), 3.73 (s, 1H), 4.27 (d, 8.3 Hz, 1H), 4.41 (d, 12.9 Hz, 1H), 4.52 (d, 12.9 Hz, 1H), 4.70 (d, 5.2 Hz, 2H), 4.78 (d, 16.4 Hz, 1H), 5.14 (d, 16.7 Hz, 1H), 5.81 (s, 1H), 7.38 (m, 5H), 7.33 (m, 3H), 7.51 (d, 6.9 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 56.2, 58.5, 66.6, 70.8, 71.2, 78.5, 116.4, 126.5, 127.7, 128.0, 128.4,

129.0, 129.3, 130.7, 134.0, 136.0, 137.2, 139.8, 176.9, 206.8; HRMS, M^+ ($C_{25}H_{20}O_3$): calcd 368.1412, obsd 368.1412.

10. Crystal system, triclinic, $P1$, unit cell dimensions, $a=7.9680(10)$, $b=11.2140(10)$, $c=25.6410(10)$ Å, $\alpha=91.1520(10)$, $\beta=91.8200(10)$, $\gamma=93.749(2)°$. Final R indices [$I>2\sigma(I)$], $R_1=0.0684$, $wR_2=0.1643$. CCDC reference number: 198522.
11. (a) Chiusoli, G. P.; Costa, M.; Gerbella, M.; Salerno, G. *Gazz. Chim. Ital.* **1985**, *115*, 697; (b) Chiusoli, G. P.; Costa, M.; Gerbella, M.; Reverberi, S.; Salerno, G.; Terenghi, M. G. *Gazz. Chim. Ital.* **1987**, *117*, 695; (c) Bocelli, G.; Chiusoli, P.; Costa, M.; Fambri, L. *J. Chem. Soc., Chem. Commun.* **1987**, 1182.
12. Crystal system, monoclinic, $P2_1/n$, unit cell dimensions, $a=13.0280(10)$, $b=9.1620(10)$, $c=16.5430(10)$ Å, $\beta=106.031(2)°$, final R indices [$I>2\sigma(I)$], $R_1=0.0649$, $wR_2=0.2008$. CCDC reference number: 195583.