JOC*Note*

Flexible Synthesis of Phenanthrenes by a $PtCl_2$-Catalyzed Cycloisomerization Reaction

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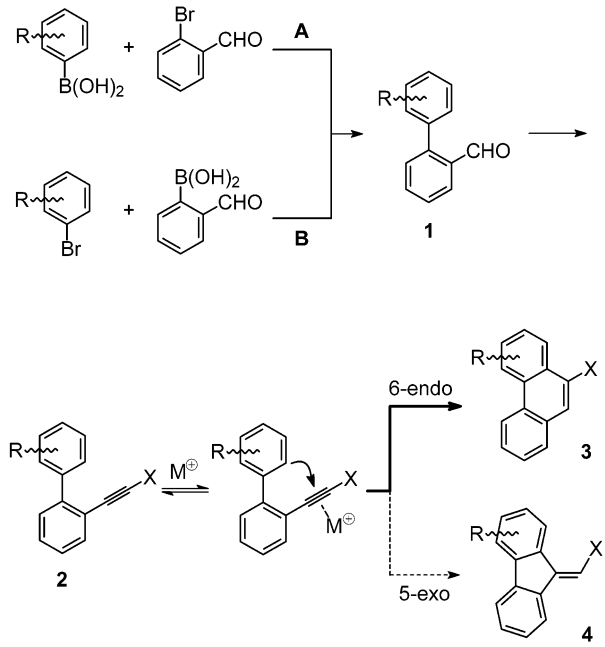
Abstract: Readily available biphenyl derivatives containing an alkyne unit at one of their ortho positions are converted into substituted phenanthrenes upon exposure to catalytic amounts of either $PtCl_2$, $AuCl_3$, $GaCl_3$, or $InCl_3$ in toluene. This 6-endo-dig cyclization likely proceeds through initial π-coordination of the alkyne unit followed by interception of the resulting η^2-metal complex by the adjacent arene ring. The reaction is inherently modular, allowing for substantial structural variations and for the incorporation of substituents at any site of the phenanthrene product except C-9. Moreover, the reaction is readily applied to the heterocyclic series as exemplified by the preparation of benzoindoles, naphthothiophenes as well as bridgehead nitrogen heterocycles.

Since the pioneering studies of Murai et al.,[1] $PtCl_2$ is rapidly gaining importance as a convenient catalyst for a host of skeletal rearrangements of enynes and related substrates.[1−8] Although the transformations are seemingly quite diverse in nature, substantial evidence has accumulated that they are invariably triggered by π-complexation of the alkyne to the transition metal, rendering the alkyne susceptible to attack by an external or a tethered nucleophile.[9] In pursuit of our previous investigations in this field,[3,10] we now report a flexible synthesis of phenanthrenes based on a $PtCl_2$-catalyzed carbocyclization reaction of alkynylated biphenyl derivatives.[11−13]

SCHEME 1



The required substrates **2** are prepared in two steps as shown in Scheme 1.[14] Standard Suzuki cross-coupling reactions[15] employing either 2-bromobenzaldehyde (path A) or 2-formyl-benzeneboronic acid (path B) afford sub-

(1) (a) Chatani, N.; Furukawa, N.; Sakurai, H.; Murai, S. *Organometallics* **1996**, *15*, 901−903. (b) Chatani, N.; Kataoka, K.; Murai, S.; Furukawa, N.; Seki, Y. *J. Am. Chem. Soc.* **1998**, *120*, 9104−9105.

(2) (a) Méndez, M.; Muñoz, M. P.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *J. Am. Chem. Soc.* **2001**, *123*, 10511−10520. (b) Fernández-Rivas, C.; Méndez, M.; Echavarren, A. M. *J. Am. Chem. Soc.* **2000**, *122*, 1221−1222. (c) Méndez, M.; Muñoz, M. P.; Echavarren, A. M. *J. Am. Chem. Soc.* **2000**, *122*, 11549−11550. (d) Martín-Matute, B.; Cárdenas, D. J.; Echavarren, A. M. *Angew. Chem.* **2001**, *113*, 4890−4893; *Angew. Chem., Int. Ed.* **2001**, *40*, 4754−4757.

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(4) Oi, S.; Tsukamoto, I.; Miyano, S.; Inoue, Y. *Organometallics* **2001**, *20*, 3704−3709.

(5) Trost, B. M.; Doherty, G. A. *J. Am. Chem. Soc.* **2000**, *122*, 3801−3810.

(6) Blum, J.; Beer-Kraft, H.; Badrieh, Y. *J. Org. Chem.* **1995**, *60*, 5567−5569.

(7) For similar rearrangement reactions catalyzed by metals other than platinum, see: (a) Chatani, N.; Morimoto, T.; Muto, T.; Murai, S. *J. Am. Chem. Soc.* **1994**, *116*, 6049−6050. (b) Chatani, N.; Inoue, H.; Morimoto, T.; Muto, T.; Murai, S. *J. Org. Chem.* **2001**, *66*, 4433−4436. (c) Trost, B. M.; Trost, M. K. *J. Am. Chem. Soc.* **1991**, *113*, 1850−1852. (d) Trost, B. M.; Yanai, M.; Hoogsteen, K. *J. Am. Chem. Soc.* **1993**, *115*, 5294−5295. (e) Trost, B. M.; Chang, V. K. *Synthesis* **1993**, 824−832.

(8) For a general review, see: Aubert, C.; Buisine, O.; Malacria, M. *Chem. Rev.* **2002**, *102*, 813−834.

(9) In some cases, however, the formation of vinyl cationic complexes or metal carbenes may follow the initial π-complexation of the alkyne along the reaction coordinate; cf. refs 1−7.

(10) (a) Fürstner, A.; Voigtländer, D.; Schrader, W.; Giebel, D.; Reetz, M. T. *Org. Lett.* **2001**, *3*, 417−420. (b) Fürstner, A.; Voigtländer, D. *Synthesis* **2000**, 959−969.

(11) For related reactions of ω-aryl-1-alkynes catalyzed by Pt(II) or other metal species leading to (dihydro)naphthalenes, see: (a) Chatani, N.; Inoue, H.; Ikeda, T.; Murai, S. *J. Org. Chem.* **2000**, *65*, 4913−4918. (b) Inoue, H.; Chatani, N.; Murai, S. *J. Org. Chem.* **2002**, *67*, 1414−1417. (c) Dankwardt, J. W. *Tetrahedron Lett.* **2001**, *42*, 5809−5812. (d) Herndon, J. W.; Zhang, Y.; Wang, K. *J. Organomet. Chem.* **2001**, *634*, 1−4.

(12) For general reviews on the synthesis of phenanthrenes, see: (a) Floyd, A. J.; Dyke, S. F.; Ward, S. E. *Chem. Rev.* **1976**, *76*, 509−562. (b) Mallory, F. B.; Mallory, C. W. *Org. React.* **1984**, *30*, 1−456. See the following for leading references on generally applicable phenanthrene syntheses not yet covered by these reviews: (c) Hanson, P.; Lövenich, P. W.; Rowell, S. C.; Walton, P. H.; Timms, A. W. *J. Chem. Soc., Perkin Trans. 2* **1999**, 49−63. (d) Harrowven, D. C.; Nunn, M. I. T.; Fenwick, D. R. *Tetrahedron Lett.* **2002**, *43*, 3185−3187. (e) Ramana, M. M. V.; Potnis, P. V. *Synthesis* **1996**, 1090−1092. (f) Morrow, G. W.; Marks, T. M.; Sear, D. L. *Tetrahedron* **1995**, *51*, 10115−10124. (g) Bao, J.; Wulff, W. D.; Dominy, J. B.; Fumo, M. J.; Grant, E. B.; Rob, A. C.; Whitcomb, M. C.; Yeung, S.-M.; Ostrander, R. L.; Rheingold, A. L. *J. Am. Chem. Soc.* **1996**, *118*, 3392−3405. (h) Jung, K.; Koreeda, M. *J. Org. Chem.* **1989**, *54*, 5667−5675. (i) Mallory, F. B.; Rudolph, M. J.; Oh, S. M. *J. Org. Chem.* **1989**, *54*, 4619−4626. (j) Brown, C.; Sikkel, B. J.; Carvalho, C. F.; Sargent, M. V. *J. Chem. Soc., Perkin Trans. 1* **1982**, 3007−3010. (k) Liu, L.; Yang, B.; Katz, T. J.; Poindexter, M. K. *J. Org. Chem.* **1991**, *56*, 3769−3775. (l) Meier, H.; Fetten, M.; Schnorpfeil, C. *Eur. J. Org. Chem.* **2001**, 779−786. (m) Fu, J.; Snieckus, V. *Can. J. Chem.* **2000**, *78*, 905−919. (n) de Koning, C. B.; Michael, J. P.; Rousseau, A. L. *J. Chem. Soc., Perkin Trans. 1* **2000**, 787−797. (o) Hoarau, C.; Couture, A.; Deniau, E.; Grandclaudon, P. *Synthesis* **2001**, 1462−1470. (p) Kraus, G. A.; Zhang, N.; Melekhov, A.; Jensen, J. H. *Synlett* **2001**, 521−522 and literature cited therein.

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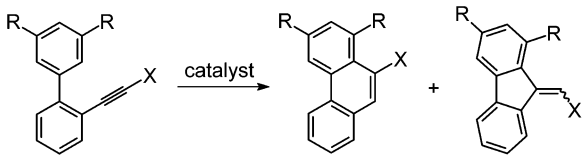
TABLE 1. Screening of the Activity and Selectivity of Different Catalysts in the Cycloisomerization of the Ortho-alkynylated Biphenyl Derivatives 2a−e



2 **3** **4**

substrate	R	X	catalyst[a]	conditions	GC %	**3**:**4**	yield[b] (%)
2a	OMe	H		toluene, 80 °C, 22 h	0		
			$GaCl_3$	toluene, 80 °C, 22 h	100	96:4	53
			$InCl_3$	toluene, 80 °C, 22 h	100	44:56	44
			$AuCl_3$	toluene, 80 °C, 22 h	100	97:3	95
			$PtCl_2$	toluene, 80 °C, 16 h	100	95:5	76
			$PtCl_2(PhCN)_2/2AgSbF_6$	CH_2Cl_2, rt, 4 h	100	87:13	56
			$PtCl_2(PhCN)_2/2AgBF_4$	CH_2Cl_2, rt, 4 h	100	92:8	82
			$PtCl_2(PhCN)_2/2NH_4PF_6$	CH_2Cl_2, rt, 16 h	62	90:10	
			$[RuCl_2(CO)_3]_2$	toluene, 80 °C, 21 h	52	67:33	
			$[(cymene)(PCy_3)RuCl_2]/2\ AgBF_4$	CH_2Cl_2, 50 °C, 20 h	100	30:70	17
			$[Cp^*Ru(MeCN)_3]PF_6$	toluene, 80 °C, 22 h	0		
			$RuCl_3$	toluene, 80 °C, 22 h	0		
			$RhCl_3$	toluene, 80 °C, 22 h	0		
2b	Me	H	$PtCl_2$	toluene, 80 °C, 20 h	100	97:3	64
2c	Me	Me	$PtCl_2$	toluene, 80 °C, 20 h	100	100:0	89
2d	Me	COOMe	$PtCl_2$	toluene, 80 °C, 40 h	73	5:95	
2e	Me	C_6H_4OMe	$PtCl_2$	toluene, 100 °C, 24 h	100	60:40	87[c]

[a] Using 5 mol % monomeric complexes or 2.5 mol % dimeric complexes, respectively. [b] Refers to the isolated yield of the major compound. [c] Inseparable mixture of **3e** and **4e**.

stituted biphenyl aldehyde derivatives **1**, which are converted into the required alkynes **2** according to the Corey−Fuchs protocol[16] or in one step by reaction with lithio trimethylsilyl diazomethane.[17] Addition of an electrophilic metal salt or metal complex leads to an equilibrium between the alkyne **2** and the corresponding η^2-complex; if the latter is intercepted by the adjacent aromatic ring, a C−C bond formation with concomitant release of the catalyst will ensue.

Screening of a set of different metal species has shown that either $PtCl_2$ or $AuCl_3$[18] in toluene at 80 °C not only result in good conversions but also are the most convenient from a practical point of view (Table 1).[19] Cationic platinum complexes formed in situ from $PtCl_2(PhCN)_2$ and a suitable halide sequestering agent ($AgBF_4$, $AgSbF_6$, NH_4PF_6) as well as $GaCl_3$[11b] also gave appreciable results, whereas $RhCl_3$, $RuCl_3$, or cationic ruthenium species resulted in low conversions and/or poor selectivities. Importantly, heating of the substrate in toluene at 80 °C for 22 h in the absence of any catalyst does not result in ring closure (Table 1, entry 1); this control experiment makes it clear that the observed reactions are not just thermal electrocyclization processes but definitely require assistance by the metal cation.

A notable feature observed for the whole set of substrates investigated (Tables 1 and 2) is the pronounced preference for the 6-endo-dig cyclization to give phenanthrenes over the conceivable 5-exo mode.[20] The only exception is compound **2d** in which the strongly electron-withdrawing ester group on the alkyne not only diminishes the reaction rate but also overturns this inherent bias by enforcing a 1,4-addition process formally corresponding to the 5-exo pathway (**3d**:**4d** = 5:95). The tolane derivative **2e** gives a mixture of both possible isomers, i.e., the phenanthrene **3e** and the corresponding 9-alkylidene fluorene derivative **4e**, in a ∼3:2 ratio.

In a formal sense, this new phenanthrene synthesis is reminiscent of the endo-selective cyclizations of dienyl-

(13) See the following for leading references on phenanthrene syntheses by palladium-catalyzed annulations: (a) Wu, G.; Rheingold, A. L.; Geib, S. J.; Heck, R. F. *Organometallics* **1987**, *6*, 1941−1946. (b) Larock, R. C.; Doty, M. J.; Tian, Q.; Zenner, J. M. *J. Org. Chem*. **1997**, *62*, 7536−7537. (c) Larock, R. C.; Tian, Q. *J. Org. Chem*. **1998**, *63*, 2002−2009. (d) Dyker, G.; Kellner, A. *Tetrahedron Lett*. **1994**, *35*, 7633−7636. (e) Mandal, A. B.; Lee, G.-H.; Liu, Y.-H.; Peng, S.-M.; Leung, M. *J. Org. Chem*. **2000**, *65*, 332−336. (f) Yoshikawa, E.; Radhakrishnan, K. V.; Yamamoto, Y. *J. Am. Chem. Soc*. **2000**, *122*, 7280−7286.

(14) Some substrates have been prepared via Sonogashira coupling. For details concerning the synthesis of all starting materials, see Supporting Information.

(15) (a) Suzuki, A. *J. Organomet. Chem*. **1999**, *576*, 147−168. (b) Miyaura, N.; Suzuki, A. *Chem. Rev*. **1995**, *95*, 2457−2483.

(16) Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett*. **1972**, 3769−3772.

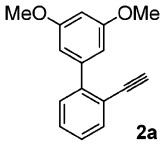
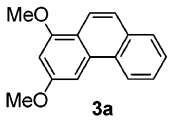
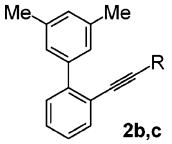
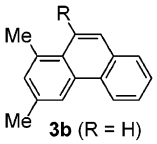
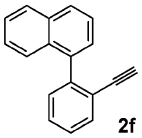
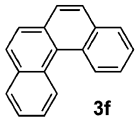
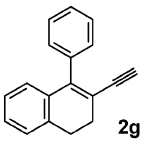
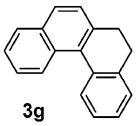
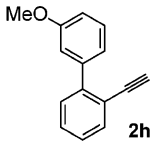
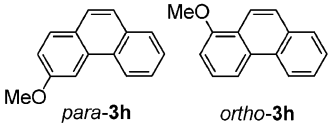
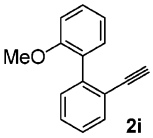
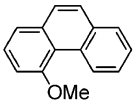
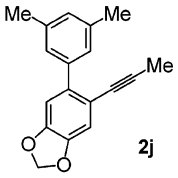
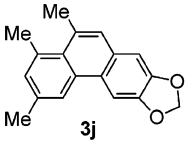
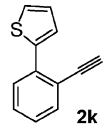
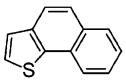
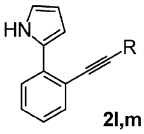
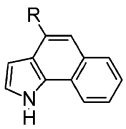
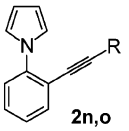
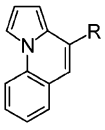
(17) Miwa, K.; Aoyama, T.; Shioiri, T. *Synlett* **1994**, 107−108.

(18) For recent applications of gold catalysts in organic synthesis, see: (a) Hashmi, A. S. K.; Schwarz, L.; Choi, J.-H.; Frost, T. M. *Angew. Chem*. **2000**, *112*, 2382−2385; *Angew. Chem., Int. Ed*. **2000**, *39*, 2285−2288. (b) Hashmi, A. S. K.; Frost, T. M.; Bats, J. W. *J. Am. Chem. Soc*. **2000**, *122*, 11553−11554. (c) Fukuda, Y.; Utimoto, K. *J. Org. Chem*. **1991**, *56*, 3729−3731. (d) Teles, J. H.; Brode, S., Chabanas, M. *Angew. Chem*. **1998**, *110*, 1475−1478; *Angew. Chem., Int. Ed*. **1998**, *37*, 1415−1418. (e) Ito, Y.; Sawamura, M.; Hayashi, T. *J. Am. Chem. Soc*. **1986**, *108*, 6405−6406. (f) Togni, A.; Pastor, S. D. *J. Org. Chem*. **1990**, *55*, 1649−1664. (g) Arcadi, A.; Di Guiseppe, S.; Marinelli, F.; Rossi, E. *Adv. Synth. Catal*. **2001**, *343*, 443−446. (h) Hoffmann-Röder, A.; Krause, N. *Org. Lett*. **2001**, *3*, 2537−2538. (i) Shul'pin, G. B.; Shilov, A. E.; Suss-Fink, G. *Tetrahedron Lett*. **2001**, *42*, 7253−7256. (j) Hashmi, A. S. K.; Frost, T. M.; Bats, J. W. *Org. Lett*. **2001**, *3*, 3769−3771. (k) Shi, F.; Deng, Y. Q.; Yang, H. Z.; SiMa, T. *Chem. Commun*. **2001**, 345−346. (l) Short review: Dyker, G. *Angew. Chem., Int. Ed*. **2000**, *39*, 4237−4239.

(19) For a discussion see: Fürstner, A. *Synlett* **1999**, 1523−1533.

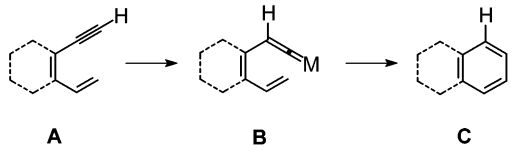
(20) Note that this pattern is distinctly different from the one described in Murai's reports on seemingly related $PtCl_2$-catalyzed dihydronaphthalene syntheses, which occur via an 6-exo-dig cyclization followed by an isomerization of the *exo*-methylene product initially formed; cf. ref 11a.

TABLE 2. Formation of Phenanthrenes and Heterocyclic Congeners by Cyclization of Ortho-alkynylated Biaryls; All Reactions Were Carried out with 5 Mol % $PtCl_2$ in Toluene at 80 °C unless Stated Otherwise

Entry	Substrate	t (h)	Products	Yield
1	 **2a**	16	 **3a**	76% / 95%[a]
2	 **2b,c**	20	 **3b** (R = H) **3c** (R = Me)	73% (R = H)
3		20		89% (R = Me)
4	 **2f**	20	 **3f**	65%
5	 **2g**	21	 **3g**	75%
6	 **2h**	17	 *para*-**3h** *ortho*-**3h**	70% (4:1)
7	 **2i**	20	 **3i**	55%
8	 **2j**	24	 **3j**	94%
9	 **2k**	20	 **3k**	54%
10	 **2l,m**	14	 **3l** (R = H)	63% (R = H)
11		20	**3m** (R = Me)	76% (R = Me)
12	 **2n,o**	30	 **3n** (R = H)	56% (R = H)
13		13	**3o** (R = C_6H_{13})	80% (R = C_6H_{13})[b]
14		20		91% (R = C_6H_{13})[c]

[a] Using $AuCl_3$ (5 mol %) as the catalyst. [b] Using $GaCl_3$ (10 mol %) as the catalyst; in this case, the use of either $PtCl_2$ or $AuCl_3$ led to <40% conversion. [c] Using $InCl_3$ (5 mol %) in toluene at 100 °C as the catalyst.

SCHEME 2



alkynes **A** and related substrates catalyzed by either [(η^6-cymene)(PPh_3)$RuCl_2$] or $W(CO)_5$·THF (Scheme 2).[21] These reactions likely involve vinylidene complexes **B**, which undergo a 6π-electrocyclization to form the new arene ring in product **C**. Since only terminal alkynes can afford such intermediates via complexation followed by a 1,2-hydride shift (cf. **A** → **B**),[22] however, the scope of this methodology is inherently limited. The platinum-catalyzed phenanthrene synthesis, in contrast, works equally well or even better with nonterminal alkynes as evident from entries 3, 8, and 11 in Table 2, suggesting that the activation of the π-system by coordination to Pt(II) rather than the formation of metal vinylidenes suffices to trigger the observed ring closure.

The examples compiled in Table 2 show the generality of this novel entry into phenanthrenes. In principle, this method allows the introduction of substituents at any position exept C-9. The ready reaction of compound **2g** (easily prepared from α-tetralone in three high-yielding operations)[14] illustrates that dihydrophenanthrenes are equally accessible via this route. Likewise, the phenyl rings can also be replaced by heteroarene units (entries 9−14). Although in the case of the N-unprotected pyrrole derivatives **2l**−**m** one might expect the nitrogen atom to act as the nucleophile, exclusive carbocyclization with formation of 1*H*-benzo[*g*]indoles is observed.[23] A simple change of the connectivity pattern in the substrate opens access to the pyrrolo[1,2-*a*]quinoline skeleton bearing the heteroatom in the bridgehead position; interestingly though, substrate **2o** (R = C_6H_{13}) required the use of $GaCl_3$ (entry 13) or $InCl_3$ (entry 14) for efficient cyclization, while $PtCl_2$ is the best catalyst for the terminal alkyne **2n** (entry 12). Further studies on the scope and mechanism of this and related platinum-catalyzed transformations are currently in progress.

(21) (a) Merlic, C. A.; Pauly, M. E. *J. Am. Chem. Soc.* **1996**, *118*, 11319−11320. (b) Maeyama, K.; Iwasawa, N. *J. Org. Chem.* **1999**, *64*, 1344−1346. (c) Maeyama, K.; Iwasawa, N. *J. Am. Chem. Soc.* **1998**, *120*, 1928−1929.

(22) For recent reviews on the preparation and application of vinylidene complexes, see: (a) Bruneau, C.; Dixneuf, P. H. *Acc. Chem. Res.* **1999**, *32*, 311−323. (b) McDonald, F. E. *Chem. Eur. J.* **1999**, *5*, 3103−3106. (c) Trost, B. M.; Toste, F. D.; Pinkerton, A. B. *Chem. Rev.* **2001**, *101*, 2067−2096. (d) Bruce, M. I. *Chem. Rev.* **1991**, *91*, 197−257.

(23) For a related example in which the nitrogen atom is blocked by a methyl group, see ref 11c.

Experimental Section

General. For details, see Supporting Information.

Representative Procedure. Preparation of 1,3,10-Trimethyl-6,7-methylenedioxy-phenanthrene (3j). A solution of alkyne **2j** (528 mg, 2.0 mmol) and $PtCl_2$ (26.6 mg, 0.1 mmol) in toluene (10 mL) was stirred for 24h at 80 °C under Ar until GC showed complete conversion of the substrate. The solvent was then evaporated, and the residue was purified by flash chromatography (silica gel, hexanes) to give phenanthrene **3j** as a white solid (495 mg, 94%): mp 126−127 °C; IR (KBr) 2965, 2931, 2904, 1614, 1596, 1504, 1490, 1460, 1438, 1233, 1039, 942, 876 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.44 (s, 3H), 2.82 (s, 3H), 2.83 (s, 3H), 5.98 (s, 2H), 6.98 (s, 1H), 7.09 (s, 1H), 7.24 (s, 1H), 7.87 (s, 1H), 8.08 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1, 25.7, 26.1, 100.7, 100.9, 104.0, 120.9, 125.4, 127.8, 129.0, 131.4, 131.6, 131.7, 134.4, 135.5, 147.0, 147.1; MS (EI) *m*/*z* 264 ([M^+], 100), 249 (18), 189 (11). Anal. Calcd for $C_{18}H_{16}O_2$ (264.33): C, 81.79; H, 6.10. Found: C, 81.75; H 6.13.

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Supporting Information Available: Full experimental details including procedures for the preparation of the starting materials as well as the analytical and spectroscopic data of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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