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Unusual oxidative cleavage of the aryl—ethynyl bonds in (arylethynyl)polymethylbenzenes with iodine in dimethyl sulfoxide

M. S. Yusubov,[a] G. A. Zholobova,[a] I. L. Filimonova,[a] V. P. Vasil'eva,[b] V. D. Filimonov,[b] and Ki-Whan Chi[c]

[a]Siberian State Medical University,
2 Moskovskii Trakt, 634050 Tomsk, Russian Federation.
E-mail: yusubov@mail.ru
[b]Tomsk Polytechnic University,
30 prosp. Lenina, 634004 Tomsk, Russian Federation.
E-mail: filim@org.chtd.tpu.edu.ru
[c]University of Ulsan,
680-749, Ulsan, Republic of Korea

While heating 1,2,4,5-tetramethyl-3,6-bis(phenylethynyl)benzene, 1,3,5-trimethyl-2,4-bis(phenylethynyl)benzene, and 1,2,4,5-tetramethyl-3-(phenylethynyl)benzene with iodine in DMSO in the absence of oxygen, the triple bonds are oxidized to give the corresponding 1,2-diketones. In the presence of oxygen, the previously unknown competitive oxidative process causes the cleavage of the aryl—ethynyl bonds so that duroquinone and the corresponding 4-hydroxybenzils are formed. This cleavage is produced by oxygen only in the presence of iodine and DMSO. It was shown that the key stage of the process is the formation of intermediate charge-transfer complexes between polymethylbenzene rings and iodine.

Key words: alkynes, oxidation, iodine, dimethyl sulfoxide, 1,2-diketones.

Iodine and $PdCl_2$ in DMSO are among the mildest and most selective oxidants of internal alkynes to 1,2-diketones.[1—3] A fundamental advantage of these reagents is that they cause no cleavage of the carbon—carbon bonds in substrates or reaction products. However, we reported previously[4] that the reaction of I_2 with 1,2,4,5-tetramethyl-3,6-bis(phenylethynyl)benzene (**1**) in DMSO mainly gives duroquinone (**2**) and 1-(4-hydroxy-2,3,5,6-tetramethylphenyl)-2-phenylethanedione (**3**). In the present work, we extensively studied the influence of the reaction conditions on this new oxidative transformation of alkyne **1** and illustrated the general character of this process with other polymethylated diarylacetylenes.

It was shown that heating of alkyne **1** with iodine in DMSO initiates two competing reactions, which dominate each other depending on the reaction conditions (Scheme 1, Table 1):

(1) oxidation in an atmosphere of oxygen or in air to duroquinone **2** and 4-hydroxyphenyldiketone **3** and

(2) oxidation in an atmosphere of argon to diketone (**4**) and predominantly to tetraketone (**5**).

The yields of products **2**—**5** depend on the amount of iodine and the temperature. Thus, the yield of duroquinone **2** at 110 °C was higher than at 145 °C under the conditions of oxygen bubbling, probably, because of a decreased solubility of the latter in DMSO. At 145 °C, the yield of duroquinone **2** is independent of the

Table 1. Oxidation of 1,2,4,5-tetramethyl-3,6-bis(phenylethynyl)benzene (**1**) (1 mmol) with I_2 in DMSO

I_2 /mmol	*T* /°C	*t* /h	Yield (%)				Conditions
			2	**3**	**4**	**5**	
1.0	145	3.5	32	21	Trace amounts	7	Contact with air
1.0	145	5.5	Trace amounts	14	7	77	In an atmosphere of argon
1.0	145	5.5	Trace amounts	26	6.5	66	Argon bubbling
1.0	145	2.0	43	20	3	10	Oxygen bubbling
1.0	110	42.0	60	13	10	16	Oxygen bubbling
0.25	145	7.0	44	18	3	10	Oxygen bubbling
0.25	110	42.0	70	18	7	4	Oxygen bubbling
1.0	135	18.0	Trace amounts	14	Trace amounts	55	Sealed tube with air
—*	110	50.0	—	—	—	—	Oxygen bubbling

* The starting alkyne **1** was recovered.

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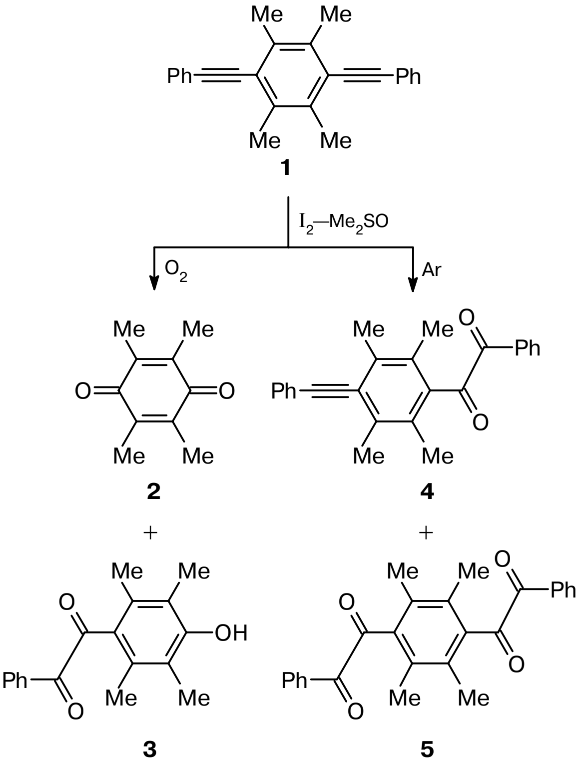
Scheme 1



amount of iodine, whereas its yield at 110 °C increases from 60 to 70% with a fourfold reduction in the iodine amount (see Table 1). Thus, the results in Table 1 indicate the dominant role of oxygen in the formation of quinone **2** and hydroxyphenyldiketone **3** and the dominant role of iodine in the formation of diketone **4** and tetraketone **5**. It was also found experimentally that alkyne **1** in an iodine-free atmosphere of oxygen in DMSO remains unchanged at 110 °C for 50 h. Thus, both the components (iodine and oxygen) are necessary to form quinone **2**. The formation of compounds **2** and **3** is also accompanied by the generation of benzoic acid from the eliminated phenylethynyl group.

It was found that hydroxyphenyldiketone **3** and tetraketone **5** remain inert to I_2 in DMSO. By contrast, diketone **4** at 110 °C in the presence of oxygen gives hydroxyphenyldiketone **3** (40%) and tetraketone **5** (28%). Because of these circumstances, the yields of diketone **4** are low (3—10%) in all the cases studied (see Table 1), indicating that hydroxyphenyldiketone **3** and quinone **2** result from the cleavage of the aryl—alkynyl rather than aryl—CO bonds in products **3**—**5**.

Table 2. Oxidation of 1,3,5-trimethyl-2,4-bis(phenylethynyl)benzene (**6**) (1.0 mmol) with I_2 in DMSO

I_2 /mmol	*T* /°C	*t* /h	Yield (%)		
			7	**8**	**9**
0.25*	105	40	11	<1	21
0.5*	105	41	<1	9	21
1.0**	130	4	26	<1	20

* In an atmosphere of oxygen.

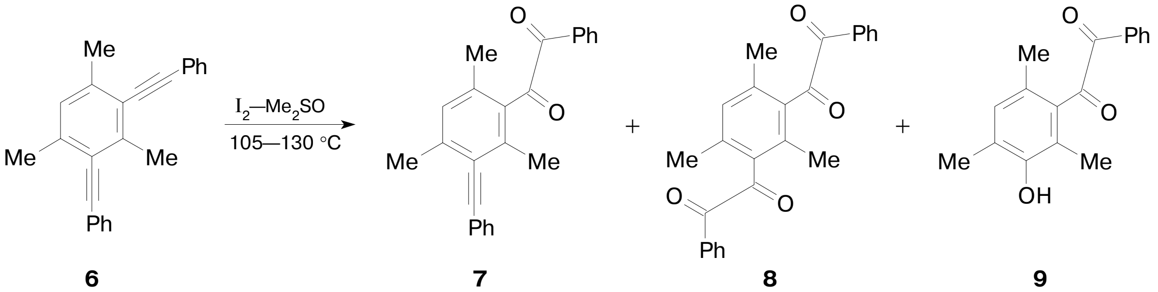
** In an atmosphere of argon.

The oxidation of 1,3,5-trimethyl-2,4-bis(phenylethynyl)benzene (**6**) in air is accompanied by resinification, yielding several products. The major products were diketone **7** (1—11%), tetraketone **8** (1—9%) as products of normal oxidation of the triple bonds and diketone **9** (21%) as a product of oxidative cleavage of the aryl—ethynyl bond (Table 2). Under argon, the major oxidation products were diketones **7** (26%) and **9** (20%) (Scheme 2). In this case, no quinones are formed in an atmosphere of oxygen or in air, as distinct from the oxidation of alkyne **1**. Apart from the aforementioned products, the reaction mixture also contains benzoic acid (up to 16%).

At the same time, the oxidation of 1,4-bis(phenylethynyl)benzene (**10**) (a methyl-free structural analog of compound **1**) with I_2—DMSO under the conditions of oxygen bubbling involves only the triple bonds to give 1,4-bis(1,2-dioxo-2-phenylethyl)benzene (**11**) (yield 88%), *i.e.*, the reaction outcome only slightly differ from that in the oxidation with the same system simply in the air[2] (yield 90%).

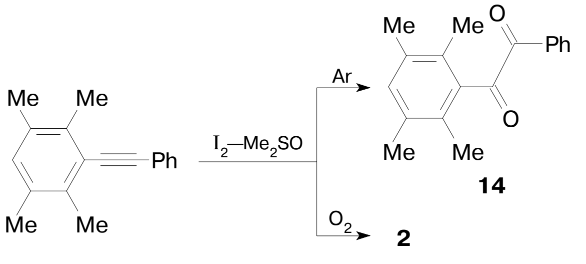
The study of the oxidation of tolan derivatives **12** and **13** with I_2/DMSO gave the following results. In the case of 1,2,4,5-tetramethyl-3-(phenylethynyl)benzene (**12**), oxygen bubbling through the reaction mixture

Scheme 2



affords duroquinone **2** (66%) and benzoic acid (54%), while the reaction in an atmosphere of oxygen-free argon yields diketone **14** (77%). It should be noted that the use of commercial, oxygen-containing argon results not only in diketone **14** but also in noticeable amounts of duroquinone **2** (5—6%). Diketone **14** does not further oxidize to duroquinone **2** or hydroxyphenyldiketone **3** (Scheme 3).

Scheme 3



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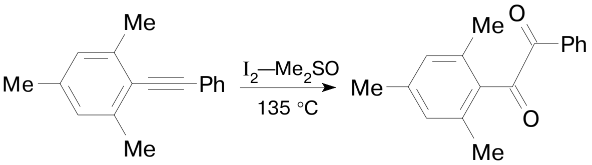
Previously,[5] it was also shown that the action of iodine on 2,4,6-trimethyltolan **13** in DMSO with access for atmospheric oxygen at a low conversion of the substrate causes the oxidation of only the triple bond to give diketone **15** in 33% yield (Scheme 4). No carboxylic acids were detected in the reaction mixture.

Scheme 4



13 **15**

To sum up the results obtained, one can conclude that quinone **2** and hydroxyphenyldiketones **3** and **9** result from the elimination of the phenylethynyl rather than COCOPh fragment and that duroquinone **2** is formed in noticeable amounts only upon oxidation in an atmosphere of oxygen. Under argon, the triple bonds of the substrates are normally oxidized with I_2 and DMSO to give 1,2-diketones.

We found no reported analogs of oxidative cleavage of the aryl—phenylethynyl bonds under the action of either DMSO or other reagents, which were discovered for compounds **1**, **4**, **6**, and **12**. As far as we know, DMSO neither alone nor in combination with oxygen or halogens was referred to as an oxidant of arenes to quinones. Among a number of methods for the synthesis of quinones from arenes, oxygen is used in the presence of catalytic amounts of nitrogen-containing oxidants.[6,7] A certain specific effect of oxygen and DMSO as oxidants was noted earlier[8] for the oxidation of 3-bromocamphor into camphorquinone when air is passed through a solution of a substrate and NaI in DMSO. The most essential statement[8] says that DMSO does not oxidize bromocamphor according to the Kornblum reaction mechanism (as could be expected), but the process involving oxygen and DMSO proceeds through intermediate free radicals of unidentified structures.

Semiempirical PM3 optimization of the geometry of alkyne **12** and tolan shows that the triple bond lengths are nearly equal in both acetylene derivatives (1.196 and 1.195 Å, respectively) and that the duryl—alkynyl bond is slightly longer (1.418 Å) than the phenyl—alkynyl bond in tolan (1.415 Å). Therefore, the quantum-chemical calculations of the ground state of the sterically hindered alkyne do not predict easy or, moreover, spontaneous cleavage of the aryl—phenylethynyl bond in any way.

At the same time, we can advance the following hypothesis that does not contradict the experimental data. It is well known that iodine as an electron acceptor can form charge-transfer complexes with arenes; the latter, in the case of complete electron transfer, decompose into the corresponding radical cations and anions.[9]

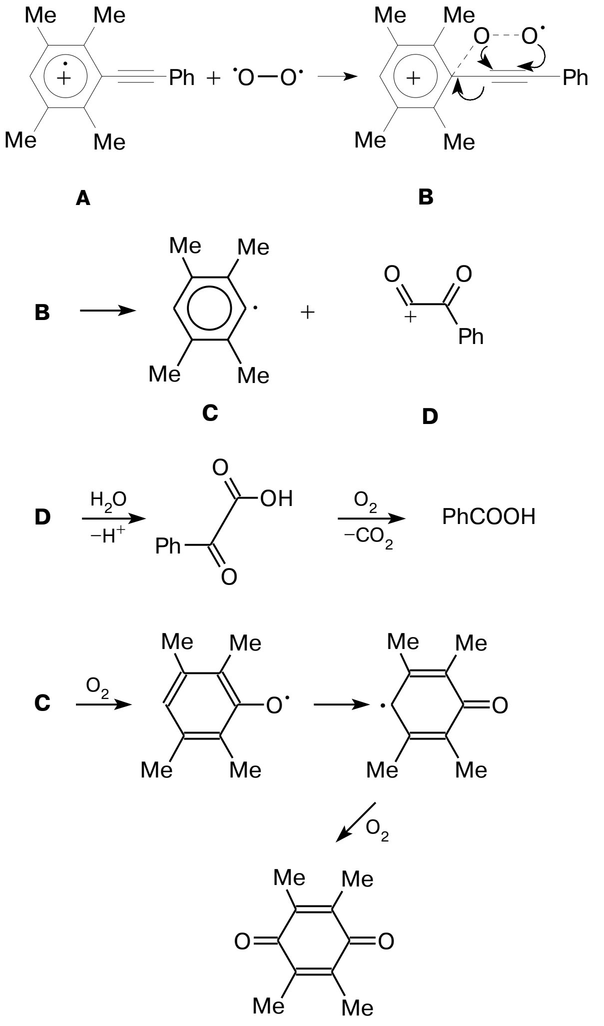
The stability of charge-transfer complexes increases with an increase in the electron-donating properties of arenes.[9] From this point of view, polymethylbenzene rings in compounds **1**, **4**, **6**, and **12** should be a preferred site for the formation of charge-transfer complexes with iodine. Indeed, the PM3 calculations show that both highest-energy occupied molecular orbitals (HOMO) of compound **12** ($7B_1$, 8.73 and $4A_2$, 9.05 eV) has a lower energy than the HOMO of tolan ($3B_{3u}$, 8.89 and $1A_2$, 9.88 eV), which makes it a stronger electron donor. The electron for the lowest-energy unoccupied orbital of iodine has to be delivered from HOMO2 of compound **12** (9.05 eV), which is localized on the durene ring and has the fit type of symmetry.

After the radical cation of compound **12** is formed (**A**), it can be attacked by oxygen according to the radical ion mechanism to follow the transformations presented in Scheme 5.

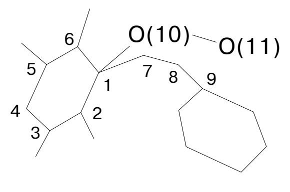
This scheme can also be valid for the stepwise cleavage of the aryl—ethynyl bonds in compounds **1**, **4**, **6**, and **7**. The advanced hypothesis also correlates with the fact that, if the *para*-position in intermediate **C** is occupied by the noneliminable group, the reaction stops at the stage of formation of the corresponding phenol (compounds **3** and **9**).

To estimate the probability of forming the hypothetical radical cation **B** and determine its spatial and electronic structure, the potential energy surface for a system composed of intermediate **A** and the oxygen molecule was calculated by the PM3 method. The minimum found corresponds to structure **B**; its enthalpy of formation is lower by $\Delta\Delta H = 120.6$ kcal mol^{-1} than that of the isolated oxygen molecules and species **A**. Structure **B** is schematically displayed in Fig. 1 (its selected geometrical parameters and effective charges are given in Table 3).

Scheme 5



Analysis of the calculated geometrical and charge parameters leads one to the conclusion that there is a strong bonding between the C(7)—O(10) and C(8)—O(11) atoms in intermediate **B**, and the C(7)—C(8) bond is no longer a triple one. The length of this bond (1.543 Å) and the C(7)—O(10) and C(8)—O(11) interatomic distances are very close to the normal CO—CO and C=O bond lengths in dicarbonyl compounds. It should be specially stressed that the C(1)—C(7) bond becomes significantly longer, which can cause its cleavage. In addition, the total spin density in intermediate **A** is distributed over the whole aromatic system, including both rings and the triple bond, whereas in radical cation **B** it is localized only on the durene fragment and the O(11) atom. This fact is an additional piece of evidence in favor of the formation of radical **C** through the cleavage of the C(1)—C(7) bond.



Thus, the scheme proposed for oxidative cleavage of the bonds between the ethynyl groups and polymethylated aromatic rings upon the action of iodine and oxygen in DMSO correlates with the experimental facts and is not contradictory to our quantum-chemical results.

Experimental

IR spectra were recorded on a Mattson 5000 spectrophotometer (thin films or pellets with KBr). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX 500 spectrometer (500.13 and 125 MHz, respectively) in $CDCl_3$, acetone-d_6, or CCl_4 with Me_4Si as the internal standard. Elemental analysis was carried out on an E.A. 1106 Carlo Erba CHNS-O instrument. The melting point was measured on an Electrothermal-9100 instrument. Column chromatography used L 40/100 μm (Chemapol) and Silica gel 60 G (Merck) silica gels; TLC was carried out on Silufol UV-254 (Kavalier) and Silica gel 60 F_{254} (Merck) plates with hexane, hexane—benzene (3 : 1 and 3 : 2), or hexane—ethyl acetate (9 : 1) as eluents. The structures of the compounds described in the literature were confirmed by analytical and spectral data and compared with the characteristics of the authentic samples.

Oxidation of 1,2,4,5-tetramethyl-3,6-bis(phenylethynyl)benzene (1). Iodine (64 mg, 0.25 mmol) was added to a solution of compound **1** (334 mg, 1.0 mmol) in 10 mL of DMSO, and oxygen was bubbled through the reaction mixture stirred with a magnetic stirrer at 110 °C for 42 h. The resulting solution was poured into 30 mL of a 5% aqueous solution of $Na_2S_2O_3$, and the products were extracted with ether (3×30 mL). the extract was washed with water and brine and dried with Na_2SO_4. The ether was removed, and the residue was dissolved in 3.0 mL of benzene and chromatographed on silica gel. Elution with hexane gave **6-(1,2-dioxo-2-phenylethyl)-1,2,4,5-tetramethyl-**

Table 3. PM3-calculated effective charges (*q*), interatomic distances (*d*), and bond angles (ω) in radical cation **B**

Atom	*q*/au	Bond	*d*/Å	Angle	ω/deg
C(1)	−0.21	C(1)—C(7)	1.508	O(10)—C(1)—C(7)	25.6
C(7)	0.27	C(1)—O(10)	2.376	C(1)—C(7)—C(8)	115.6
C(8)	0.33	C(7)—C(8)	1.543	C(7)—C(8)—C(9)	119.8
O(10)	−0.22	C(8)—C(9)	1.474	C(1)—O(10)—O(11)	64.19
O(11)	−0.30	O(10)—O(11)	3.237		
		C(7)—O(10)	1.208		
		C(8)—O(11)	1.221		

3-(phenylethynyl)benzene (4) (26 mg, 7%), m.p. 154—156 °C (from ethanol) (*cf.* Ref. 10: 159—160 °C). Further elution with hexane—benzene (3 : 1) gave **3,6-bis(1,2-dioxo-2-phenylethynyl)-1,2,4,5-tetramethylbenzene (5)** (16 mg, 4%), m.p. 202—204 °C (from ethyl acetate) (*cf.* Ref. 10: 203—204 °C) and duroquinone **2** (115 mg, 70%) as yellow needles, m.p. 110—112 °C (from hexane) (*cf.* Ref. 11: 110—112 °C). The residue was eluted with hexane—benzene (3 : 2) to give **3-(1,2-dioxo-2-phenylethyl)-6-hydroxy-1,2,4,5-tetramethylbenzene (3)** (51 mg, 18%), m.p. 164—166 °C (from ethanol) (*cf.* Ref. 4: 164—166 °C). IR (KBr), ν/cm^{-1}: 3530 (O—H), 1680 (C=O), 1140 (C—O). ^{1}H NMR (acetone-d$_6$—CCl$_4$), δ: 2.10 (s, 6 H, 2 Me); 2.15 (s, 6 H, 2 Me); 7.58 (m, 2 H arom); 7.70 (m, 1 H arom); 8.10 (d, 2 H arom, *J* = 7.6 Hz); 8.60 (s, 1 H, OH). ^{13}C NMR (acetone-d$_6$—CCl$_4$), δ: 12.23 and 17.72 (Me), 121.41, 129.43, 130.86, 133.07, 133.57, 134.72, 155.34 (C arom), 191.48 and 199.12 (C=O). Final elution gave benzoic acid (60 mg, 25%), m.p. 122—123 °C (*cf.* Ref. 12: 122.5 °C).

Oxidation of 1,3,5-trimethyl-2,4-bis(phenylethynyl)benzene (6). Iodine (127 mg, 0.5 mmol) was added to a solution of compound **6** (162 mg, 0.5 mmol) in 5.0 mL of DMSO. The reaction mixture was stirred with access for atmospheric oxygen at 105 °C for 4 h and treated as described above. The product was chromatographed on silica gel. Elution with hexane recovered the starting alkyne **6** (30 mg). Further elution with hexane—ethyl acetate (9 : 1) gave **4-(1,2-dioxo-2-phenylethyl)-1,3,5-trimethyl-2-phenylethynylbenzene (7)** (46 mg, 26%), m.p. 90—92 °C (from propanol) (*cf.* Ref. 10: 91—92 °C); **2,4-bis(1,2-dioxo-2-phenylethyl)-1,3,5-trimethylbenzene (8)** (1.5 mg), m.p. 126—127 °C (from ethanol) (*cf.* Ref. 10); and **1-(3-hydroxy-2,4,6-trimethylphenyl)-2-phenylethanedione (9)** (27 mg, 20%), m.p. 132—133 °C (from hexane—benzene, 3 : 1). IR, ν/cm^{-1}: 3497 (O—H), 1670 (C=O), 1217 (C—O). ^{1}H NMR (CDCl$_3$), δ: 2.16 (s, 3 H, Me); 2.17 (s, 3 H, Me); 2.23 (s, 3 H, Me); 4.62 (s, 1 H, OH); 6.84 (s, 1 H arom); 7.51 (m, 2 H arom); 7.65 (m, 1 H arom); 8.13 (d, 2 H arom). ^{13}C NMR (acetone-d$_6$—CCl$_4$), δ: 13.35, 16.01 and 19.76 (Me), 122.13, 126.42, 128.20, 128.81, 130.42, 130.66, 132.00, 134.35, 135.04, 155.34 (C arom), 191.06 and 197.50 (C=O). Found (%): C, 75.74; H, 5.96. $C_{17}H_{16}O_3$. Calculated (%): C, 76.10; H, 6.01. Final elution gave benzoic acid (10 mg, 16%), m.p. 122—123 °C (*cf.* Ref. 12: 122.5 °C).

Oxidation of 1,2,4,5-tetramethyl-3-(phenylethynyl)benzene (12). ***A.*** In an atmosphere of argon. Iodine (254 mg, 1.0 mmol) was added to a solution of compound **12** (234 mg, 1.0 mmol) in 5.0 mL of DMSO. Argon was bubbled through the reaction mixture stirred at 115 °C for 11 h. The resulting solution was treated as described above and chromatographed on silica gel. Elution with hexane gave **3-(1,2-dioxo-2-phenylethyl)-1,2,4,5-tetramethylbenzene (14)** (205 mg, 77%), m.p. 61.5—62.5 °C (from methanol). ^{1}H NMR (CDCl$_3$), δ: 2.11 (s, 6 H, 2 Me); 2.22 (s, 6 H, 2 Me); 7.05 (s, 1 H arom); 7.54 (m, 2 H arom); 7.65 (d, 1 H arom); 8.22 (d, 2 H arom, *J* = 7.5 Hz). ^{13}C NMR (CDCl$_3$), δ: 16.54 and 19.40 (Me), 128.75, 130.50, 131.14, 131.99, 133.58, 134.25, 134.29, 137.53 (C arom), 190.26 and 199.42 (C=O). Found (%): C, 81.28; H, 6.97. $C_{18}H_{18}O_2$. Calculated (%): C, 81.17; H, 6.81.

B. In an atmosphere of oxygen. Iodine (127 mg, 0.5 mmol) was added to a solution of compound **12** (117 mg, 0.5 mmol) in 3.0 mL of DMSO. Oxygen was bubbled through the reaction mixture stirred at 115 °C for 8 h. The resulting solution was treated as described above and chromatographed on silica gel. Elution with hexane recovered the starting alkyne **12** (22 mg). Further elution with hexane—benzene (3 : 1) gave duroquinone **2** (52 mg, 63%), m.p. 110—112 °C. Final elution with hexane—ethyl acetate (9 : 1) gave benzoic acid (23 mg, 48%), m.p. 122—123 °C (*cf.* Ref. 12: 122.5 °C).

Oxidation of 6-(1,2-dioxo-2-phenylethyl)-1,2,4,5-tetramethyl-3-(phenylethynyl)benzene (4). Iodine (38 mg, 0.15 mmol) was added to a solution of compound **4** (55 mg, 0.15 mmol) in 2.0 mL of DMSO. Oxygen was bubbled through the reaction mixture with stirring at 110 °C for 23 h. The resulting solution was treated as described above and chromatographed on silica gel. Elution with hexane—benzene (3 : 1) gave tetraketone **5** (15.5 mg, 26%), m.p. 202—204 °C (from ethyl acetate). Further elution with hexane—benzene (3 : 2) gave diketone **3** (17 mg, 40%), m.p. 164—166 °C (from ethanol). Final elution gave benzoic acid (5.0 mg, 25%), m.p. 122—123 °C (*cf.* Ref. 12: 122.5 °C).

Oxidation of 1,4-bis(phenylethynyl)benzene (10). Iodine (127 mg, 0.5 mmol) was added to a solution of compound **10** (140 mg, 0.5 mmol) in 4.0 mL of DMSO. Oxygen was bubbled through the reaction mixture stirred at 135 °C for 11 h. The resulting solution was poured into 15 mL of 5% $Na_2S_2O_3$. The yellow acicular crystals that formed were filtered off and recrystallized from ethanol to give 1,4-bis(1,2-dioxo-2-phenylethyl)benzene (**11**) (151 mg, 88%), m.p. 125—126 °C (from ethanol) (*cf.* Ref. 2: 124—125 °C).

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