Pergamon

Tetrahedron 55 (1999) 7907–7914

TETRAHEDRON

Synthesis of New Enantiomerically Pure Monoketals of *p*-Benzoquinone with *C*2-Symmetry

Pedro de March,* Marta Figueredo,* Josep Font, and Jordi Medrano

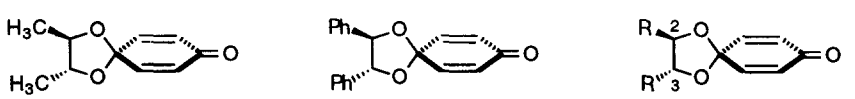
Departament de Química. Universitat Autònoma de Barcelona. 08193 Bellaterra. Spain.

Received 24 February 1999; revised 14 April 1999; accepted 29 April 1999

Abstract.- Several new monoketals of *p*-benzoquinone with the structure of 1,3-dioxaspiro[4.5]deca-6,9-dien-8-one have been synthesised in enantiopure form by the straightforward reaction of the quinone with secondary C_2-symmetric 1,2-diols. The preparation of two new enantiopure C_2-1,2-glycols is also reported.

Introduction

p-Benzoquinone derivatives have been widely considered as interesting target molecules in organic chemistry.[1] Since quinones are very reactive substrates, for synthetic purposes the use of their monoketals may be convenient to overcome reactivity and/or selectivity problems presented by the quinones themselves. On the other hand, the formation of a chiral ketal may influence the stereoselectivity of chemical transformations not only in the acetal function itself, but also in the prochiral vicinal olefins. The advantages of C_2-symmetric molecules as chiral directors has stimulated the synthesis of a large number of such molecules, in particular of 1,2-diols.[2] Recently, we have conveniently prepared two enantiopure *p*-benzoquinone monoketals **1** and **2**[3] (Figure 1), derived from (+)-butane-2,3-diol and (+)-1,2-diphenylethyleneglycol, respectively, and we intended to use these compounds as a source of chirality in the development of enantioselective processes. In these compounds the two faces of each double bond are diastereotopic, but both olefins are equivalent, due to the C_2-symmetry of the diols. We have already studied the efficiency of the chiral auxiliaries incorporated into ketals **1** and **2** in two reactions: the conjugate addition of several aromatic thiols, in which a thermodynamic control operated,[4] and the kinetically controlled 1,3-dipolar cycloaddition to cyclic nitrones.[5] Unfortunately, a lack of facial selectivity was always found. In the search for a good asymmetric induction in chemical transformations of the 1,3-dioxaspiro[4.5]deca-6,9-dien-8-one system, we decided to synthesise new enantiopure *p*-benzoquinone monoketals derived from differently substituted 1,2-diols with C_2-symmetry. Their preparation is described in this paper.



1 **2** **3**

Figure 1

0040-4020/99/$ - see front matter
PII: S0040-4020(99)00400-7

Results and Discussion

According to previous results,[3] the direct monoketalization of *p*-benzoquinone was only efficient with secondary 1,2-diols, and therefore we focused our attention on the preparation of ketals with the heterocyclic structure of 1,3-dioxaspiro[4.5]decane, **3**, as in **1** and **2**, and we were limited to introduce different substituents at positions 2 and 3 of this skeleton. Two possibilities were envisioned for a better differentiation between both faces of each double bond: the first one was to increase the steric demand of the substituent in relation to the methyl or phenyl groups, and the second to induce a π-stacking interaction[6] between the olefinic systems of the cyclohexadienone and an aromatic ring linked to the dioxolane moiety. Figure 2 shows the C_2-diols that we chose for these purposes. (1*R*,2*R*)-1,2-Dicyclohexylethyleneglycol, (*R*,*R*)-**4**, incorporates tertiary carbon atoms, enlarging substantially the size of the substituents, and it is easily accessible by hydrogenation of hydrobenzoin.[7] The rest of 1,2-glycols **5**-**9** were selected considering that a good diastereofacial differentiation on the monoketal substrates could be reached if each aromatic ring linked to the dioxolane were able to establish a benefitial π-stacking interaction only with one face of a single olefin. Molecular models show that this requirement can only be fulfilled if the aromatic ring is tethered to the dioxolane through a maximum of three consecutive bonds. A longer chain, allowing it to establish interactions with both faces of the olefin, could presumably be detrimental to the desired facial selectivity.

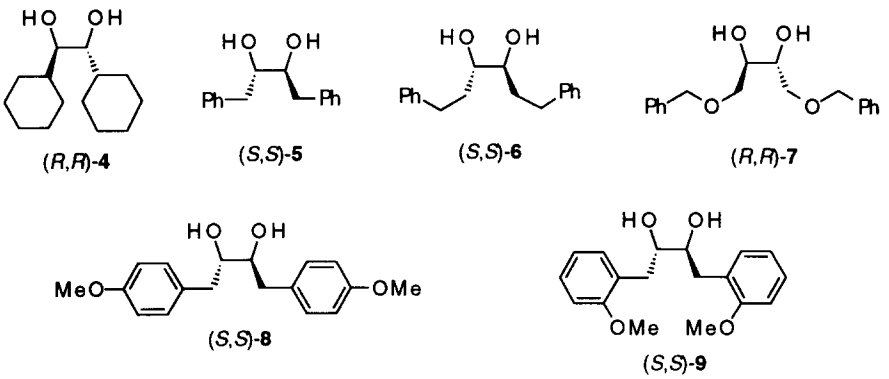
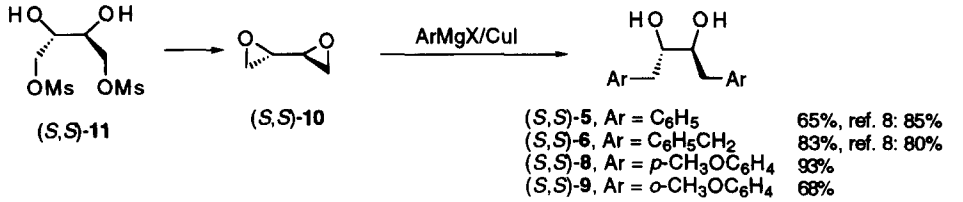


Figure 2

Preparations of (*S*,*S*)-**5**,[8] (*S*,*S*)-**6**,[8] and (*R*,*R*)-**7**[9] had been previously described and the *meso* and racemic forms of diol **8**[10] were also known. Following the same methodology previously described for the synthesis of (*S*,*S*)-**5** and (*S*,*S*)-**6**,[8] we prepared the enantiopure diols (*S*,*S*)-**8** and (*S*,*S*)-**9** by the nucleophilic opening of (2*S*,3*S*)-1,2:3,4-diepoxybutane, (*S*,*S*)-**10**, prepared *in situ* from dimesylate **11**,[11] with the appropriate Grignard reagent in the presence of CuI (Scheme 1). Thus, the addition of 4-anisylmagnesium bromide[12] to a freshly prepared solution of diepoxide (*S*,*S*)-**10** yielded (2*S*,3*S*)-1,4-bis(4-methoxyphenyl)-2,3-butanediol, (*S*,*S*)-**8**, as a solid in 93% overall yield although, according to literature data,[8,11] diepoxide **10** can be isolated only in 75% yield from **11**. Treatment of diepoxide (*S*,*S*)-**10** with 2-anisylmagnesium bromide[13] afforded diol (*S*,*S*)-**9**, also as a solid, in 68% overall yield.



Scheme 1

With the series of diols in hand, we proceeded to run the ketalization reactions, which were performed with $BF_3{\cdot}Et_2O$ as Lewis acid in DME at room temperature,[3] but using variable proportions of *p*-benzoquinone and diol. The reaction between *p*-benzoquinone and 0.5 equivalents of diol (*R,R*)-**4** was completed after 3 days giving rise to the monoketal (*R,R*)-**12** and the bisketal **13** in 75% and 19% yield, respectively (Figure 3). The partial hydrolysis of **13** allowed isolation of an additional amount of the monoketal, the overall yield for the conversion of (*R,R*)-**4** into (*R,R*)-**12** reaching about 90%.

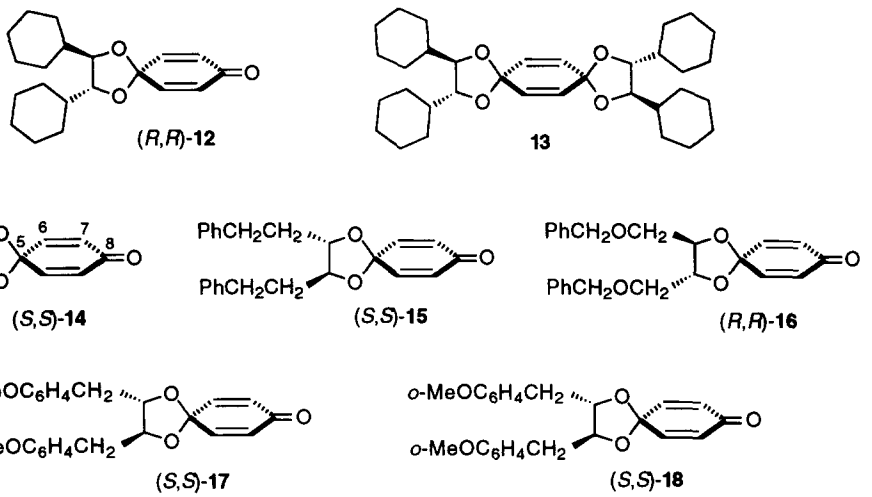


Figure 3

The formation of ketal (*S,S*)-**14** was achieved in 69% yield by the reaction between *p*-benzoquinone and a slight deficiency of diol (*S,S*)-**5**. In the ^{1}H-NMR spectrum of this ketal the olefinic proton H_6 presents its signal at δ 6.43, with a remarkable high field shifting in relation to the corresponding proton in ketal **2**, that absorbs at δ 6.94[3] (Table 1). Proton H_7 shows a similar trend, although less pronounced. The shielding of the olefinic protons in compound (*S,S*)-**14**, which incorporates a methylene group between the phenyl rings and the dioxolane, suggests the existence of the pursued π-stacking interaction.

Next, we prepared 2,3-diphenethyl-1,4-dioxaspiro[4.5]deca-6,9-dien-8-one, (*S,S*)-**15**, a compound in which the tether is extended by one additional methylene group. Again, a small excess of quinone was used, requiring five days to complete the reaction. This ketal was isolated as an oil in 43% yield and in its ^{1}H-NMR spectrum protons H_6 and H_7 absorb at δ 6.59 and 6.12, respectively. These chemical shift values are slightly higher than those of compound **14**, but still much lower than those of ketal **2**.

Table 1. Chemical shifts of the olefinic protons of ketals **2** and **14-18**.

Ketal	**2**	**14**	**15**	**16**	**17**	**18**
δH_6	6.94	6.43	6.59	6.69	6.45	6.49
δH_7	6.27	6.06	6.12	6.10	6.07	6.05

In order to complete the study of the tether prolongation, the reaction between *p*-benzoquinone and 0.66 equivalents of diol (*R,R*)-**7** was performed. This reaction was faster and treatment of the crude material after 40 hours afforded 90% yield of ketal (*R,R*)-**16** as an oil. Proton H_6 is shifted down field (δ 6.69) compared to ketals **15** and **14**, while H_7 presents approximately the same chemical shift ($\delta \approx 6.10$).

The results so far obtained seemed to indicate that the most effective interaction between the phenyl group and the olefin takes place when the aromatic ring is linked to the dioxolane through a single methylene group, according to the highest upfield absorption of H_6 presented by ketal **14** in the series **14-16**. For this reason, we decided to also prepare the ketals derived from diols (*S,S*)-**8** and (*S,S*)-**9** which have the same distance between the double bond and the aromatic ring, but incorporate a methoxy group. In principle, the increased electronic density of the phenyl ring should enhance its interaction with the electron deficient olefin, resulting in a more effective shielding of one of its faces. Both ketals **17** and **18** were isolated in 79% and 67% yields, respectively. Unexpectedly, the chemical shifts of H_6 and H_7 in these compounds are very similar to those of ketal **14** and therefore we assume that the introduction of an electron releasing group does not modify substantially the π-interaction between the aromatic ring and the carbon-carbon double bond.

In summary, the synthesis in enantiopure form of two new 1,2-diols and six new monoketals of *p*-benzoquinone all of them presenting C_2-symmetry has been described. All these ketals have been prepared by direct reaction between the quinone and the corresponding diols, demonstrating the general applicability of this simple method for secondary 1,2-diols. The differently substituted 1,3-dioxaspiro[4.5]deca-6,9-dien-8-ones will be tested as a source of chirality in further transformations of the olefins and the carbonyl group. The results of these investigations will be reported in due time.

Experimental Section

The following diols were prepared according to previously described methods: **4**,[7] **5**,[8] (*S,S*)-**6**,[8] **7**.[9] Reaction mixtures were stirred magnetically. The organic extracts were dried over anhydrous sodium sulfate. Reaction solutions were concentrated using a rotary evaporator at 15-20 Torr. Flash column chromatography was performed using Merck silica gel (230-400 mesh). Infrared spectra were recorded on a Nicolet 5 ZDX spectrophotometer. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on Bruker AC-250-WB or AM-400-WB instruments in $CDCl_3$ solutions. Mass spectra were performed on a Hewlett-Packard 5985B instrument at 70 eV; only peaks with higher intensity than 20% are reported, unless they belong to molecular ions or to significant fragments.

(2S,3S)-1,4-Bis(4-methoxyphenyl)-2,3-butanediol, **8**

The general procedure described by Devine and Oh[8] was used. To a magnetically stirred suspension of CuI (557 mg, 2.93 mmol) in anhydrous THF (40 mL) at -40 °C under nitrogen atmosphere, a solution of 27.49 mmol of 4-anisylmagnesium bromide[12] (prepared from 3.45 mL, 27.49 mmol, of 4-anisyl bromide and 781

mg, 32.15 mmol, of magnesium) in anhydrous THF (7.5 mL) was added. The mixture was stirred for 5 min and a solution of (*S,S*)-1,2:3,4-diepoxybutane[11] (prepared from 2.53 g, 9.10 mmol, of 2,3-*O*-isopropylidene-L-threitol 1,4-bismethanesulphonate[9,11]) in ether (8 mL) was added. The flask was allowed to warm up to 0 °C and stirred for 2 h. Cold water was added to the reaction mixture and the organic phase was extracted with ether (2x15 mL). Purification of the crude material (2.82 g) by recrystallization from toluene gave 2.56 g (8.47 mmol, 93% yield from **11**) of **8** as a white solid: mp 129-130 °C; IR (KBr): 3390, 2926, 1514, 1253, 1071, 1027 (i), 805 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ 7.11 (d, J=8.4 Hz, 4 H), 6.82 (d, J=8.4 Hz, 4 H), 3.76 (s, 6 H), 3.75-3.60 (m, 2 H: H_2), 2.83 (dd, J=13.9 Hz, J'=4.7 Hz, 2 H: H_1), 2.73 (dd, J=13.9 Hz, J'=7.7 Hz, 2 H: H_1), 2.25 (s, 2 H: OH); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 158.2/130.3/130.0/114.0 (C_{Ar}), 74.0 (C_2), 55.2 (CH_3O), 39.3 (C_1); MS (*m/z*): 302 (M^+, 3), 163 (45), 151 (49), 122 (100), 121 (80), 91 (61); $[\alpha]_D^{20}$=+16.0 (*c*=2.5, $CHCl_3$). Anal. Calcd for $C_{18}H_{22}O_4$: C, 71.50; H, 7.33. Found: C, 71.45; H, 7.25.

(2S,3S)-1,4-Bis(2-methoxyphenyl)-2,3-butanediol, **9**

The same procedure described for the synthesis of **8** was used, but employing 2-anisylmagnesium bromide[13] as Grignard reagent. Purification of the crude material by flash chromatography using hexane-ethyl acetate (2:1) as eluent afforded diol **7** (68% yield from **11**) as a pale pink solid: mp 65-66 °C (toluene); IR (KBr): 3475, 3320, 1493, 1239, 1095, 1035, 747 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ 7.25-7.10 (m, 4 H), 6.86 (t, J=7.3 Hz, 2 H), 6.81 (d, J=7.7 Hz, 2 H), 3.75 (s, 6 H), 3.80-3.65 (m, 2 H: H_2), 3.00-2.80 (m, 4 H: H_1), 2.65 (s, 2H: OH); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 157.4/131.3/127.6/126.9/120.7/110.3 (C_{Ar}), 73.2 (C_2), 55.2 (CH_3O), 34.8 (C_1); MS (*m/z*) 302 (M^+, 1), 163 (51), 151 (44), 122 (100), 121 (98), 107 (20), 91 (91), 77 (24), 65 (22); $[\alpha]_D^{20}$=-16.8 (*c*=3.1, $CHCl_3$). Anal. Calcd. for $C_{18}H_{22}O_4$: C, 71.50; H, 7.33. Found: C, 71.56; H, 7.45.

General procedure for the synthesis of the acetals **12-18**

To a vigorously stirred solution of the diol and *p*-benzoquinone in anhydrous DME (2.2 mL/mmol of quinone) at room temperature under nitrogen atmosphere, $BF_3{\cdot}Et_2O$ was added dropwise. The mixture was stirred until the reaction went to completion as monitored by thin layer chromatography and was then neutralized with aqueous saturated $NaHCO_3$ solution. The organic phase was separated and the aqueous layer was extracted twice with methylene chloride. The crude material was purified by flash chromatography.

(2R,3R)-2,3-Dicyclohexyl-1,4-dioxaspiro[4.5]deca-6,9-dien-8-one, **12**

The reaction was performed with 1.50 g (6.6 mmol) of diol **4** using a molar ratio of diol:*p*-benzoquinone:$BF_3{\cdot}Et_2O$ of 1:2:1, and the reaction was completed after 3 d. Flash chromatography of the crude product using hexane-ethyl acetate (50:1) as eluent afforded the following fractions: i) 350 mg of impure (2*R*,3*R*,10*R*,11*R*)-2,3,10,11-tetracyclohexyl-1,4,9,12-tetraoxadispiro[4.2.4.2]tetradeca-6,13-diene, **13**; ii) 1.35 g (4.3 mmol) of ketal **12** as a white solid crystallized from chloroform/pentane; and iii) starting diol (15%). The yield of **12** considering the recovered diol is 75%. Repeated chromatography of the first eluted fraction allowed the isolation of pure **13** (278 mg, 0.53 mmol, 19% yield) as a white solid. **12**: mp 84-86 °C ($CHCl_3$/pentane); IR (KBr): 2924, 2847, 1673, 1644, 1441, 1391, 1293, 1173, 991 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ 6.56 (d, $J_{6,7}$=9.9 Hz, 2 H: H_6), 6.08 (d, $J_{7,6}$=9.9 Hz, 2 H :H_7), 3.79 (d, J=5.1 Hz, 2 H: H_2), 1.90-1.10 (m, 22 H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 185.4 (C_8), 145.1 (C_6), 128.3 (C_7), 97.7 (C_5),

84.3 (C_2), 41.0, 30.3, 27.7, 26.2, 26.1, 25.8; MS (*m/z*): 316 (M^+, 2), 234 (11), 205 (27), 110 (61), 109 (25), 96 (100), 95 (41), 81 (65), 67 (35), 55 (49), 41 (26); $[\alpha]_D^{20}$=+22.3 (*c*=2.6, $CHCl_3$). Anal. Calcd for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92. Found: C, 75.92; H, 9.00. **13**: mp 169-170 °C ($CHCl_3$/pentane); IR (KBr): 2926, 2852, 1448, 1412, 1122, 992 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ 5.78 (s, 4 H: H_6), 3.68 (br d, J≈3.6 Hz, 4 H: H_2), 1.90-1.10 (m, 44 H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 131.4 (C_6), 98.0 (C_5), 83.7 (C_2), 41.3, 30.2, 27.8, 26.3, 26.2, 25.9; MS (*m/z*): 524 (M^+, 6), 441 (26), 217 (23), 209 (22), 191 (20), 189 (21), 110 (27), 109 (84), 96 (44), 95 (100), 83 (36), 81 (52), 67 (58), 55 (90), 41 (31); $[\alpha]_D^{20}$=+24.0 (*c*=3.0, $CHCl_3$). Anal. Calcd for $C_{34}H_{52}O_4$: C, 77.82; H, 9.99. Found: C, 77.67; H, 9.97.

Hydrolysis of **13**

A solution of bisketal **13** (405 mg, 0.77 mmol) in dioxane/acetonitrile/3% HCl (10/1/1 ml) was heated at reflux temperature for 1 h. After neutralization with saturated $NaHCO_3$ solution, extraction with methylene chloride (2x10 ml), drying, and removal of the solvent, 450 mg of crude material were obtained. Purification by flash chromatography (hexane-AcOEt 40:1) afforded monoketal **12** (191 mg, 0.60 mmol, 78% yield) and diol **4** (141 mg, 0.62 mmol).

(2S,3S)-2,3-Dibenzyl-1,4-dioxaspiro[4.5]deca-6,9-dien-8-one, **14**

The reaction was performed with 500 mg (2.6 mmol) of diol **5** using a molar ratio of diol:*p*-benzoquinone:BF_3·Et_2O of 1:1.1:1, and the reaction was completed after 3 d. Flash chromatography of the crude product using hexane-ethyl acetate (15:1) as eluent afforded the following fractions: i) ketal **14** (400 mg, 1.20 mmol) as a white solid; and ii) starting diol (15%). The yield of **14** considering the recovered diol is 69%. **14**: mp 87-88 °C (ethyl acetate/pentane); IR (KBr): 3029, 2880, 1674, 1632, 1095, 1024, 965, 703 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ 7.40-7.15 (m, 6 H), 7.15-7.05 (m, 4 H), 6.43 (d, $J_{6,7}$=10.2 Hz, 2 H: H_6), 6.06 (d, $J_{7,6}$=10.2 Hz, 2 H: H_7), 4.09 (m, 2 H: H_2), 2.84 (dd, J=13.9 Hz, J'=5.5 Hz, 2 H), 2.74 (dd, J=13.9 Hz, J'=4.4 Hz, 2 H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 185.3 (C_8), 144.3 (C_6), 136.2/129.6/128.5/126.9 (C_{Ar}+C_7), 97.7 (C_5), 81.6 (C_2), 38.5 (CH_2); MS (*m/z*): 332 (M^+, 1), 306 (5), 268 (12), 133 (40), 105 (53), 92 (28), 91 (100), 77 (22); $[\alpha]_D^{20}$=-55.6 (*c*=2.3, $CHCl_3$). Anal. Calcd for $C_{22}H_{20}O_3$: C, 79.50; H, 6.06. Found: C, 79.40; H, 6.09.

(2S,3S)-2,3-Diphenethyl-1,4-dioxaspiro[4.5]deca-6,9-dien-8-one, (*S,S*)-**15**

The reaction was performed with 1.20 g (4.4 mmol) of diol (*S,S*)-**6** using a molar ratio of diol:*p*-benzoquinone:BF_3·Et_2O of 1:1.1:1, and the reaction was completed after 5 d. Flash chromatography of the crude product using hexane-ethyl acetate (25:1 to 5:1) as eluent afforded the following fractions: i) ketal (*S,S*)-**15** as a pale yellow oil (650 mg, 1.81 mmol, 43% yield considering the recovered diol); and ii) starting diol (6%). (*S,S*)-**15**: IR (film): 3027, 2929, 1723, 1680, 1496, 1452, 1103, 750, 699 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ 7.40-7.00 (m, 10 H), 6.59 (d, $J_{6,7}$=10.2 Hz, 2 H: H_6), 6.12 (d, $J_{7,6}$=10.2 Hz, 2 H: H_7), 3.76 (m, 2 H: H_2), 2.80 (dt, J=13.9 Hz, J'=7.3 Hz, 2 H: CH_2Ph), 2.63 (dt, J=13.9 Hz, J'=8.4 Hz, 2 H: CH_2Ph), 2.00-1.70 (m, 4 H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 185.3 (C_8), 144.4 (C_6), 140.9 (C_{Ar}), 128.7-126.1 (C_{Ar}+C_7), 97.8 (C_5), 81.3 (C_2), 34.1/32.1 (CH_2CH_2Ph); MS (*m/z*): 360 (M^+, 0.4), 161 (28), 92 (30), 91 (100); $[\alpha]_D^{20}$=-86.7 (*c*=3.3, $CHCl_3$). Anal. Calcd for $C_{24}H_{24}O_3$: C, 79.97; H, 6.71. Found: C, 79.90; H, 6.72.

(2R,3R)-2,3-Bis(benzyloxymethyl)-1,4-dioxaspiro[4.5]deca-6,9-dien-8-one, **16**

The reaction was performed with 182 mg (0.60 mmol) of diol **7** using a molar ratio of diol:*p*-benzoquinone:BF_3·Et_2O of 1:1.5:1, and the reaction was completed after 40 h. Flash chromatography of the crude product using hexane-ethyl acetate (15:1) as eluent afforded the following fractions: i) ketal **16** (180 mg, 0.46 mmol) as a pale yellow oil; and ii) starting diol (15%). The yield of 16 considering the recovered diol is 90%. **16**: IR (film): 3032, 2921, 2863, 1678, 1637, 1453, 1385, 1307, 1189, 1106, 742, 699 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ 7.35-7.20 (m, 10 H), 6.69 (d, $J_{6,7}$=10.2 Hz, 2 H: H_6), 6.10 (d, $J_{7,6}$=10.2 Hz, 2 H: H_7), 4.56 (s, 4 H: CH_2Ph), 4.30 (s, 2 H: H_2), 3.68 (br d, J=10.6 Hz, 2 H: $CHCH_2O$), 3.61 (br d, J=10.6 Hz, 2 H: $CHCH_2O$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 185.3 (C_8), 144.1 (C_6), 137.6/128.6/128.4/127.8/127.6 (C_7+C_{Ar}), 98.9 (C_5), 78.4 (C_2), 73.7 (CH_2Ph), 69.3 ($CHCH_2O$); MS (*m/z*) (CI/NH_3): 410 (M^++18), 393 (M^++1); $[\alpha]_D^{20}$=-53.8 (*c*=2.8, $CHCl_3$). Anal. Calcd for $C_{24}H_{24}O_5$: C, 73.45; H, 6.16. Found: C, 73.20; H, 6.16.

(2S,3S)-2,3-Bis(4-methoxyphenylmethyl)-1,4-dioxaspiro[4.5]deca-6,9-dien-8-one, **17**

The reaction was performed with 3.16 g (10.4 mmol) of diol **8** using a molar ratio of diol:*p*-benzoquinone:BF_3·Et_2O of 1:1.2:1, and the reaction was completed after 6 d. Flash chromatography of the crude product using hexane-ethyl acetate (15:1) as eluent afforded the following fractions: i) ketal **17** (2.90 g, 7.39 mmol, 79% yield considering the recovered diol) as a pale yellow solid; and ii) starting diol (11%). **17**: mp 97-98 °C (ethyl acetate/pentane); IR (KBr): 2883, 2839, 1677, 1510, 1247, 1176, 1024, 843 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ 7.04 (d, J=8.7 Hz, 4 H), 6.83 (d, J=8.7 Hz, 4 H), 6.45 (d, $J_{6,7}$=10.2 Hz, 2 H: H_6), 6.07 (d, $J_{7,6}$=10.2 Hz, 2 H: H_7), 4.03 (m, 2 H: H_2), 3.77 (s, 6 H), 2.80 (dd, J=13.9 Hz, J'=5.1 Hz, 2 H), 2.72 (dd, J=13.9 Hz, J'=4.4 Hz, 2 H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 185.3 (C_8), 158.5 (C_{Ar}), 144.4 (C_6), 130.5/128.4/128.2/113.8 (C_7+C_{Ar}), 97.6 (C_5), 81.7 (C_2), 55.2 (CH_3O), 37.5 (CH_2); MS (*m/z*): 392 (M^+, 3), 163 (4), 135 (4), 121 (100); $[\alpha]_D^{20}$=-37.6 (*c*=2.5, $CHCl_3$). Anal. Calcd for $C_{24}H_{24}O_5$: C, 73.45; H, 6.16. Found: C, 73.39; H, 6.29.

(2S,3S)-2,3-Bis(2-methoxyphenylmethyl)-1,4-dioxaspiro[4.5]deca-6,9-dien-8-one, **18**

The reaction was performed with 350 mg (2.81 mmol) of diol **9** using a molar ratio of diol:*p*-benzoquinone:BF_3·Et_2O of 1:1.1:1, and the reaction was completed after 4 d. Flash chromatography of the crude product using hexane-ethyl acetate (12:1) as eluent afforded the following fractions: i) ketal **18** (680 mg, 1.73 mmol, 67% yield considering the recovered diol) as a pale yellow oil; and ii) starting diol (9%). **18**: IR (film): 2929, 1681, 1495, 1460, 1245, 1117, 1028, 754 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ 7.25-7.10 (m, 4 H), 6.84 (t, J=7.3 Hz, 2 H), 6.79 (d, J=8.0 Hz, 2 H), 6.49 (d, $J_{6,7}$=10.2 Hz, 2 H: H_6), 6.05 (d, $J_{7,6}$=10.2 Hz, 2 H: H_7), 4.19 (m, 2 H: H_2), 3.76 (s, 6 H), 2.95-2.85 (m, 4 H: CH_2); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 185.5 (C_8), 157.3 (C_{Ar}), 144.4 (C_6), 131.1/128.2/128.0/125.0/120.3/110.2 (C_7+C_{Ar}), 97.7 (C_5), 81.1 (C_2), 55.1 (CH_3O), 33.0 (CH_2); MS (*m/z*): 392 (M^+, 1), 163 (4), 135 (4), 121 (100); $[\alpha]_D^{20}$=-30.0 (*c*=1.6, $CHCl_3$). Anal. Calcd for $C_{24}H_{24}O_5$: C, 73.45; H, 6.16. Found: C, 73.33; H, 6.48.

Acknowledgements

We gratefully acknowledge financial support of *DGICYT* (project QFN95-4719) and *CIRIT* (QFN95-4719 and SGR95-00400). We also thank *DGU* for a grant to J. M.

References

1. Swenton, J. S. *The Chemistry of the Quinonoid Compounds;* Patai, S.; Rappoport, Z., Eds.; Wiley: Chichester, 1988, Vol. 2, pp 899-962.
2. a) Whitesell, J. K. *Chem. Rev.*, **1989**, *89*, 1581-1590; b) Wallace, R. H.; Lu, Y.; Liu, J.; Atwood, J. L. *Synlett*, **1992**, 992-994; c) Sakai, K.; Suemune, H. *Tetrahedron: Asymmetry* **1993**, *4*, 2109-2118; d) Yuan, T.-M.; Hsieh, Y.-T.; Yeh, S.-M.; Shyue, J.-J.; Luh, T.-Y. *Synlett*, **1966**, 53-54, e) Yamanoi, Y.; Imamoto, T. *J. Org. Chem.* **1997**, *62*, 8560-8564.
3. de March, P.; Escoda, M.; Figueredo, M.; Font, J.; Alvarez-Larena, A.; Piniella, J. F. *J. Org. Chem.*, **1995**, *60*, 3895-3897.
4. de March, P.; Escoda, M.; Figueredo, M.; Font, J.; Medrano, J. *An. Quím. Int. Ed.* **1997**, *93*, 81-87.
5. de March, P.; Escoda, M.; Figueredo, M.; Font, J.; Alvarez-Larena, A.; Piniella, J. F. *J. Org. Chem.* **1997**, *62*, 7781-7787.
6. Jones, G. B., Chapman, B. *Synthesis* **1995**, 475-497.
7. Hoffmann, R. W.; Ditrich, K.; Köster, G.; Stürmer, R. *Chem. Ber.* **1989**, *122*, 1783-1789.
8. Devine, P. N.; Oh, T. *Tetrahedron Lett.* **1991**, *32*, 883-886.
9. Mash, E. A.; Nelson, K. A.; Van Deusen, S.; Hemperly, S. B. *Org. Synth.* **1989**, *68*, 92-101.
10. Crotti, P.; Ferretti, M.; Macchia, F.; Stoppioni, A. *J. Org. Chem.* **1986**, *51*, 2759-2766.
11. Feit, P. W. *J. Med. Chem.* **1964**, *7*, 14-17.
12. Barfield, M.; Spear, R. J.; Sternhell, S. *Aust. J. Chem.* **1989**, *42*, 659-664.
13. Maffei, M.; Buono, G. *New J. Chem.* **1988**, *12*, 923-929.