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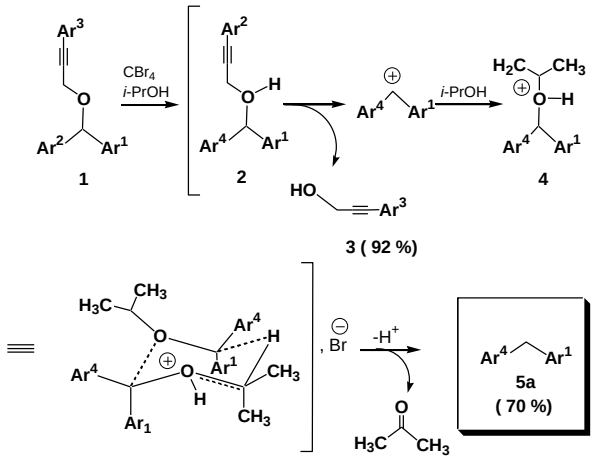
Abstract— An efficient synthesis of diarylmethanes under classical thermal conditions and under microwave heating has been established from diarylcarbinols via a new disproportionation reaction. The key step involve a selective hydride transfert of *iso*-propylic ethers intermediates. Soft experimental procedure using catalytic CBr_4 or TfOH in *i*-PrOH and good yields render this method useful and competitive to the conventional approaches relying on application of external reducing agents.

During our research on the synthesis of low generation poly(arylpropargylether) dendrimers,[1] we hoped to cleave a methoxyethoxymethyl (MEM) protected phenol under mild conditions as previously described by Lee.[2] However, when ether **1** was reacted with CBr_4 in *i*-PrOH at 80°C, the triarylether **2** was not detected. The only products isolated were the propargylic alcohol **3** (92%) and the diarylmethane **5** (70%). This latter derived from a selective disproportionation reaction of the unsymetrical intermediate ether **4** along with a loss of acetone (scheme 1).

To explain this unexpected reaction, we suggest the following mechanism. When **1** was treated with CBr_4 (20 mol%) at 80°C for 24 h, the unsymetrical ether **4** was formed *in situ* after the MEM deprotection and etherification of the biarylcarbonium ion (or its benzilic bromide equivalent) with *i*-PrOH. Then the resulting unsymetrical ether **4** evolved *via* a concerted selective hydride transfert as in Meerwein-Ponndorf-Verley-Oppenauer interconversion, according to a chair like tran-



Ar^1= 4-$OMeC_6H_4$; Ar^2= 4-$OMEMC_6H_4$; Ar^3= 4-$CO_2EtC_6H_4$; Ar^4= 4-OHC_6H_4

Scheme 1. Plausible mechanism for the disproportionation of arylether **1** with CBr_4 in *i*-PrOH.

-sition state including propably 2 molecules of **4** (scheme 1). We believe that the high selectivity of this dismutation could be explain by a preferable hydride transfert to the more electrophilic *bis*-benzilic species. In order to trap and identify the *bis*-arylmethyl ether intermediate **4**, the reaction was carry out at a lower temperature (55°C for 24 h). In these conditions, we isolated the unsymetrical ether

Keywords: disproportionation; diarylcarbinols, diarylmethanes; *i*-PrOH, CBr_4, TfOH, microwave heating.

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4 in a good yield (90 %) beside the propargylic alcohol **3**. Finally by increasing gradually the reactional temperature, we observed that the hydrogen transfert occured at higher temperatures. For that purpose, **4** was heated with catalytic CBr_4 at 80°C for 24 h in boiling *i*-PrOH and afforded cleanly the disproportionation diarylmethane product **5a** (99 %).

Diarylmethane derivatives are of considerable interest as biological and medicinal substrates,[3] models for analogous thermally robust linkages present in fuel resources such as coal,[4] components in acidic or alkaline treated lignins.[5] Beside this, some diarylmethanes are frequently used as subunits in the design of supramolecular structures.[6] A number of methods have been proposed including: transition metal-catalyzed cross coupling between either aryl nucleophiles and benzilic halides,[3b,3d,7] or aryl halides and benzylic nucleophiles;[8] reduction of diaryl ketones[9] involving the use of Clemmensen, Wolff-Kischner, polymethylhydrosiloxane-$B(C_6F_5)_3$, H_3PO_2/I_2, H_2/HCl/Pd or Pt, Cu/SiO_2, $AlCl_3/LiAlH_4$, supercritical alcohols combinations. The reduction of benzydrols[10] using TFA/HSi or $H^+/NaBH_4$, AcOH/Zn, Ra/Ni, $Mo(CO)_6$/Lawesson's reagent, $HSiEt_3/InCl_3$ or BF_3-Et_2O is well-documented too.

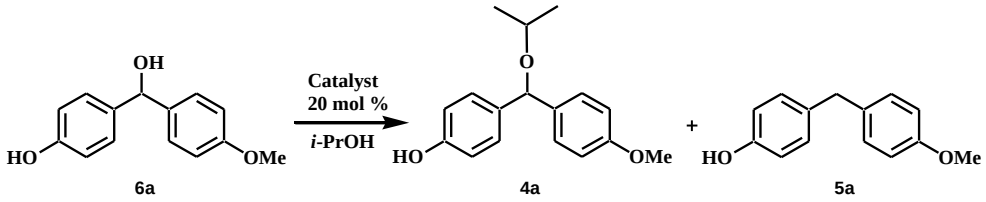


Table 1. Disproportionation of **6** in *i*-PrOH

Entry	Catalyst	Temperature (°C)	Conditions[a]	Time (h)	4 / 5[b]	5 Yield[c] (%)
1	CBr_4	80	A	24	0 / 100	83
2	APTS	80	A	24	0 / 100	74
3	TFA	80	A	24	100 / 0	-
4	TfOH	80	A	24	0 / 100	70
5	HCO_2H	80	A	24	100 / 0	-
6	Amberlyst	80	A	24	30 / 70	-
7	Aqueous HBr	80	A	24	0 / 100	57
8	CBr_4	100	B	0,25	0 / 100[d]	40
9	CBr_4	140	B	0.25	0 / 100	78
10	APTS	140	B	0.25	0 / 100	80
11	TFA	140	B	0.25	22 / 78	-
12	TfOH	140	B	0.25	0 / 100	81
13	HCO_2H	140	B	0.25	50 / 50	-
14	Amberlyst	140	B	0.25	0 / 100	60
15	CBr_4[e]	140	B	0.25	0 / 100	70
16	APTS[e]	140	B	0.25	0 / 100	65
17	CBr_4	140	C	0.25	0 / 100	49

[a] Method: **A**: Classical thermal conditions[11]; **B**: Microwave irradiation; **C**: Scelled tube

[b] Ratio determinated by ^{1}H NMR analysis ($CDCl_3$) of the crude reaction mixtures

[c] Yield of isolated product after column chromatography

[d] The ^{1}H NMR spectrum of the crude mixture revealed the presence of an unidentified byproduct

[e] The reaction was carry out using 5 mol% of CBr_4.

However, in the large majory of cases, these methods are incompatible with a variety of sensitive functional groups. Some examples of disproportionation reactions giving access to diarylmethane derivatives[12] were mentioned in the Literature. All of these methods, while offering some advantages, also suffer from disadvantages. Most of them are sometimes harsh, need strong acidic activations and are often associated with low yields (<50 %) due to the dismutation of symetrically intermediate ethers. In this letter, we report a simple and convenient procedure for the synthesis of a range of substituted diarylmethane derivatives catalyzed with CBr_4 or TfOH in *i*-PrOH.

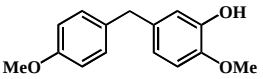
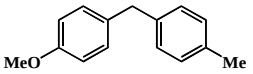
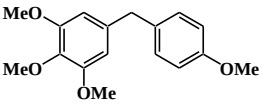
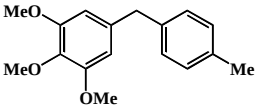
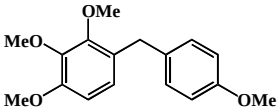
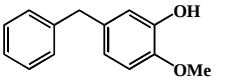
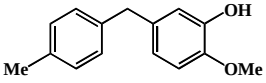
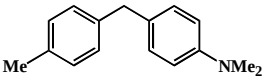
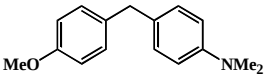
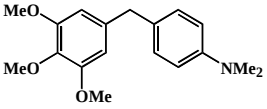
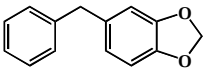
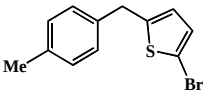
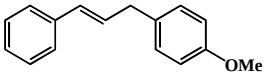
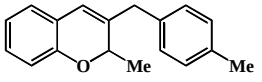
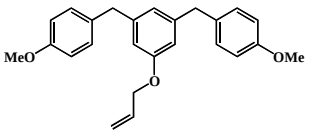
At the set out of this work, we began our approach by screening a variety of catalysts, using the diaryl carbinol **6a** as model substrate. Table 1 summarizes the results of

our investigations into the disproportionation reaction of **6a**.

After screening a series of Lewis acids, we were delighted to find that the use of CBr_4, APTS, TfOH and aqueous HBr (entries 1, 2, 4, 7), instead of TFA, HCO_2H and Amberlyst (entries 3, 5, 6) virtually completely suppressed the formation of unsymetrical diaryl-isopropyl ether **4a**. After stirring for 24 h, no by-products under these reaction conditions were observed and the yields were satisfactory. Next, in the continuation of our work to develop rapid and efficent methodologies, we choose to promote and accelerate the synthesis of **5a** using microwaves-assisted irradiation.[13] Because the heating was not foreseen to cause any serious decomposition problems, we gradually increased the temperature. We were pleased to observe that, in the presence of CBr_4 (20 mol %) and using microwave irradiation at 140°C (entry 9), **6a** was totally transformed into **5a** in only 15 minutes with a good yield (78%). Under these conditions, **6a** was reacted with the others previously tested catalysts. One can also note that under microwaves irradiation at 140°C, the disappearance of the intermediate ether **4a** occured in favour of the diarylmethane **5a** (compare entries 3 and 11, 5 and 13, 6 and 14). Moreover, for complete transformations using CBr_4, APTS, TfOH under microwaves heating, the yields obtained at 140°C were similar or better to those observed under classical thermal conditions (compare entries 1 and 9, 2 and 10, 4 and 12). Finally, the amount of catalyst was then studied. With 5 mol % of either CBr_4 or APTS, the conversion was also efficient and no starting material or intermediate ether **4a** were detected (entries 15, 16). Finally, as control experiment, **6a** was heated with CBr_4 (5 mol %) in *i*-PrOH maintained at 140°C for 15 minutes in a sealed tube. Comparison of the results obtained using convection or microwaves heating indicated clairly the efficiency of the latter method (entry 15, 75% vs entry 17, 49%).

Having optimized the reaction parameters, we then examinated the reaction with a wide of benzhydrols **6**, prepared from Grignard reagents and aromatic aldehydes. All benzhydrols subjected to the CBr_4/*i*-PrOH system produced the corresponding diarylmethane derivatives in good yield but with variable amounts of the diaryl-*i*-propyl ethers intermediates, except **5b** (entry 1). As exam-

Table 2. Disproportionation of **6** under microwaves irradiation giving diarylmethanes **5**.

Entry	Diarylmethanes 5	Cpnd[14]	Catalyst (20 mol %)	Yield[a] (%)
1		5b	CBr_4	70
2		5c	CBr_4	61[b]
			TfOH	85
3		5d	CBr_4	62[b]
			TfOH	70
4		5e	TfOH	72
5		5f	TfOH	80
6		5g	TfOH	64
7		5h	TfOH	78
8		5i	TfOH	87
9		5j	TfOH	64
10		5k	TfOH	86
11		5l	TfOH[c]	75
12		5m	TfOH	86
13		5n	TfOH	80[d]
14		5o	TfOH	51[d]
15		5p	TfOH	67

[a] Yield of isolated product after column chromatography

[b] 15-20 % of unsymetrical diaryl-isopropyl ethers were also isolated.

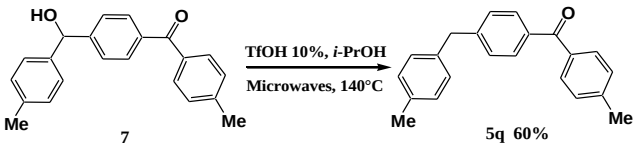
[c] reaction time: 1 h.

[d] obtained with the double bond transposed isomer.

-ples, when using CBr_4 (10 mol%) in *i*-PrOH for 15 min under microwave irradiation at 140°C, **5c** and **5d** have

been obtained but accompanied by the ethers intermediates. On the contrary, replacing CBr_4 by TfOH resulted in a complete disproportionation reaction with higher yields and easier purifications (entries 2 and 3). In this way, reduced phenstatin[15] analogs **5e** and **5f** have been prepared with 72% and 80% good isolated yields (entries 4 and 5). As firstly showed with the model **5a** (table 1), phenolic benzhydrols compounds and anilino derivatives afforded the expected diarylmethanes **5g-k** within good yields (entries 6-10). We have noticed that the disproportionation was efficient with methylenedioxyaryl compound, but required a prolongated reaction time (1 h, entry 11). Because various functional groups survived the reaction conditions, we have applied this process to a weak brominated thiophene and we were pleased to observe its total transformation affording the reduced compound **5m** with a satisfactory result (86%). The protocol was also applicable to allylic aryl alcohols. The expected diarylmethane derivatives **5n, o** were then obtained with fair to good yields accompanied by isomers resulting in the double bond migration (entries 13, 14). Disproportionation was also successful (67% with a symetrical triaryl compound containing two bis-benzylic alcohols under this protocol affording **5p** with a good 67% isolated yield. In that case, we were delighted to find that this process took place with only 5% of TfOH per hydroxyle and preserve and allylic alcohol function (entry 15).

Finally, we have tested this microwave protocol (catalytic TfOH in *i*-PrOH) with the hydroxyketone **7**.[16] After stirring for 2 h at 170°C[17] using microwave heating, we were pleased to observe that the disproportionation process occured (60%). Examination of the crude by ^{1}H NMR did not reveale the presence of reduced by-products (alcohols or diarylmethanes), demonstrating in this manner the selectivity of the present reductive method (scheme 2).



Scheme 2 Disproportionation of **7** preserving a ketone function

To confirm the selectivity of this process, wa have carry out the following experiments. When the model **6a** and benzophenone (as external carbonyl compound) were reacted together for 30 min at 140°C using microwave heating, we were pleased to observe that the disproportionation of **6a** occured without affecting the benzophenone which was recovered totally unchanged. However, we have noticed that under these conditions (TfOH 10%, *i*-Propanol, microwaves, 140°C) several benzaldehydes were partially reduced under these conditions even in the absence of **6a**.

In conclusion, we describe herein a fast and efficient systhesis of functionalized diarylmethane derivatives under classical thermal conditions and in a faster way under microwave irradiation.[18] This process is chemoselective since several functional groups are tolerated (hydroxy, allyle, ketones) on the contrary of some of previously reported methods.[9, 10] The key step involve a selective disproportionation reaction of diaryl-isopropyl ethers intermediates implying probably two molecules of ethers even if an intramolecular hydrogen transfert[11g] could not be excluded. Further developments will be disclosed in due course.

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11 *Typical procedure for the disproportionation of carbinols under thermal conditions:* To a flask containing **6a** (1 mmol) was added CBr_4 (66 mg, 0.2 mmol) in *i*-PrOH (8 mL). The mixture was then stirred at 80°C for 24 h. After cooling to room temperature, the crude mixture was hydrolyzed with H_2O (5 mL) and extracted with CH_2Cl_2 (3 x 5 mL). The combined organic layers were then dried with $MgSO_4$ and evaporated to dryness. Purification by flash chromatography afforded the diarylmethane derivative **5a**.

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14 *Typical procedure for the disproportionation of carbinols under microwave irradiation*: To an Emrys Optimizer 2-5 mL pyrex reaction vessel were added 0.2 mL of a 1M solution of TfOH in *i*-PrOH, 1 mmol of diarylcarbinol (prepared from arylaldehyde and aryl Grignard), and *i*-PrOH (3 mL). The reaction vessel was then placed in the Emrys Optimizer and exposed to microwave irradiation according to the following specifications: temperature: 140°C, time 900 s, fixed hold time: on, sample absorption: high, pre-stirring: 60 s. After cooling to room temperature, the crude mixture was treated as in ref. 11.

All diarylmethane compounds **5** gave satisfactory NMR, IR spectral data and elemental analyses. Selected spectral data for new compounds is reported below.

5b: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.78 (s, 3H), 3.83 (s, 2H), 3.85 (s, 3H), 5.56 (s, 1H, OH), 6.66 (dd, 1H, *J* = 8.2 Hz, *J* = 1.8 Hz), 6.76 (d, 1H, *J* = 1.8 Hz), 6.77 (d, 1H, *J* = 8.2 Hz), 6.82 (d, 2H, *J* = 8.4 Hz), 7.10 (d, 2H, *J* = 8.4 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ 40.4, 55.2, 56.0, 110.6, 113.8 (2), 115.1, 120.0, 129.7 (2), 133.5, 135.0, 144.9, 145.5, 157.9. IR (cm^{-1}) 3467, 1609, 1586, 1508, 1463, 1444, 1271, 1223, 1202, 1178, 1130, 1020. Anal. calcd for **5b** ($C_{15}H_{16}O_3$): C, 73.75; H, 6.60. Found: C, 73.71; H, 6.67. **5e**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.34 (s, 3H), 3.82 (s, 6H), 3.84 (s, 3H), 3.90 (s, 2H), 6.42 (s, 2H), 7.12 (s, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.9, 41.7, 56.0, 60.8, 105.8 (2), 128.6 (2), 129.1 (2), 135.6, 136.2, 136.9, 137.8, 153.1. IR (cm^{-1}) 1588, 1506, 1465, 1421, 1324, 1240, 1120, 1001. Anal. calcd for **5e** ($C_{17}H_{20}O_3$): C, 74.97; H, 7.40. Found: C, 74.99; H, 7.54. **5h**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.32 (s, 3H), 3.86 (s, 5H), 5.56 (s, 1H, OH), 6.67 (dd, 1H, *J* = 10.0 Hz, *J* = 2.1 Hz), 6.76-6.80 (m, 2H), 7.09 (s, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.0, 40.9, 56.0, 110.6, 115.1, 120.1, 128.7 (2), 129.1 (2), 134.8, 135.4, 138.3, 144.9, 145.5. IR (cm^{-1}) 3435, 1587, 1502, 1468, 1446, 1351, 1302, 1238, 1127, 1020. Anal. calcd for **5h** ($C_{15}H_{16}O_2$): C, 78.92; H, 7.06. Found: C, 78.87; H, 7.05. **5k**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.93 (s, 6H), 3.82 (s, 9H), 3.84 (s, 2H), 6.41 (s, 2H), 6.73 (d, 2H, *J* = 8.7 Hz), 7.08 (d, 2H, *J* = 8.7 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ 40.8 (2), 41.2, 56.0 (2), 60.8, 105.7 (2), 113.0 (2), 129.3 (2), 136.1, 137.7 (2), 149.1, 153.1 (2). IR (cm^{-1}) 1614, 1588, 1521, 1505, 1461, 1421, 1237, 1123, 1006. Anal. calcd for **5k** ($C_{18}H_{23}NO_3$): C, 71.73; H, 7.69; N, 4.65. Found: C, 71.55; H, 7.95; N, 4.50. **5m**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.78 (s, 3H), 3.99 (s, 2H), 6.52 (d, 1H, *J* = 4.0 Hz), 6.82-6.85 (m, 3H), 7.13 (d, 2H, *J* = 8.4 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ 35.6, 55.2, 109.9, 114.0 (2), 125.1, 129.5, 129.6, 130.9, 131.6, 146.6, 158.4. IR (cm^{-1}) 1614, 1588, 1521, 1505, 1461, 1421, 1237, 1123, 1006. Anal. calcd for **5m** ($C_{12}H_{11}BrSO$): C, 50.40; H, 3.92; S, 11.32. Found: C, 50.20; H, 3.78; S, 11.08. **5o**: (obtained as an inseparable mixture (4/1) with its minor double bond transposed isomer) ^{1}H NMR (300 MHz, $CDCl_3$) (*major isomer*) δ 1.33 (d, 3H, *J* = 6.6 Hz), 2.35 (s, 3H), 3.36 (d, 1H, *J* = 15.9 Hz), 3.46 (d, 1H, *J* = 15.9 Hz), 4.79 (q, 1H, *J* = 6.6 Hz), 6.07 (s, 1H), 6.78 (d, 2H, *J* = 8.1 Hz), 6.84 (t, 1H, *J* = 16.0 Hz), 6.93 (dd, 1H, *J* = 6.0 Hz, *J* = 1.3 Hz), 7.05-7.13 (m, 5H). ^{1}H NMR (300 MHz, $CDCl_3$) (*minor isomer*: only the most significant resonances are listed) δ 1.50 (d, 3H, *J* = 6.6 Hz), 2.36 (s, 3H), 3.38 (d, 1H, *J* = 19.0 Hz), 3.87 (d, 1H, *J* = 19.0 Hz) 5.37 (d, 1H, *J* = 6.6 Hz), 6.56 (s, 1H), 6.89 (d, 2H, *J* = 7.2 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) (*major isomer*) δ 18.9, 29.9, 39.3, 73.7, 115.9, 119.6, 120.9, 122.5, 125.9, 128.4, 129.0 (2), 129.2 (2), 134.8, 136.0, 138.5, 151.5. ^{13}C NMR (75 MHz, $CDCl_3$) (*minor isomer*: only the most significant resonances are listed) δ 21.1, 19.6, 31.6, 70.1, 117.1, 120.3, 125.4, 127.4, 128.5, 153.0. IR (cm^{-1}) (mixture of isomers) 2922, 1766, 1657, 1607, 1578, 1514, 1487, 1456, 1370, 1236, 1207, 1108, 1039. **5p**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.80 (s, 6H), 3.86 (s, 4H), 5.44 (td, 2H, *J* = 5.7 Hz, *J* = 1.5 Hz), 5.28 (dq, 1H, *J* = 10.5 Hz, *J* = 1.5 Hz), 5.36 (dq, 1H, *J* = 17.4 Hz, *J* = 1.5 Hz), 5.95-6.08 (m, 1H), 6.56 (s, 2H), 6.65 (s, 1H), 6.83 (d, 4H, *J* = 8.7 Hz), 7.10 (d, 4H, *J* = 8.7 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ 41.0 (2), 55.2 (2), 68.6, 112.9 (2), 113.8 (4), 117.6 (2), 122.1, 129.8 (4), 133.0 (2), 133.3, 143.0 (2), 157.9 (2), 158.9. IR (cm^{-1}) 1592, 1509, 1453, 1241, 1175, 1107, 1034. Anal. calcd for **5p** ($C_{25}H_{26}O_3$): C, 80.18; H, 7.00. Found: C, 80.11; H, 7.05. **5q**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.43 (s, 3H), 2.53 (s, 3H), 4.11 (s, 2H), 7.21 (s, 4H), 7.35-7.40 (m, 4H), 7.79-7.83 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.0, 21.6, 41.5, 120.1 (2), 129.3 (4), 130.1 (2), 130.2 (2), 130.3 (2), 135.1, 135.7, 135.8, 137.1, 143.0, 146.1, 196.1. IR (cm^{-1}) 1652, 1605, 1312, 1276, 1177, 1114.. Anal. calcd for **5q** ($C_{22}H_{20}O$): C, 87.96; H, 6.71. Found: C, 87.94; H, 6.66.

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16 **7** has been obtained as a by product (22%) of the reaction between *p*-tolyl magnesium bromide (1 eq) and terephthaldicarboxaldehyde (2eq) as follow: To a solution of terephthaldicarboxaldehyde (2.68 g, 22 mmol) in 40 mL of THF was added dropwise at -40°C under argon, 11 mL (11 mmol) of a 1M solution *p*-tolyl magnesium bromide. After stirring for a night at RT, the mixture was treated with H_2O (30 mL) and extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layers were then dried with $MgSO_4$ and evaporated to dryness. Purification by flash chromatography afforded **7** as a white solid (22%). **7**: F: 108°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.75 (s, 3H), 1.84 (s, 3H), 2.40 (s, 1H, OH), 5.25 (s, 1H), 6.56 (d, 2H, *J* = 7.8 Hz), 6.67 (d, 4H, *J* = 7.8 Hz), 6.88 (d, 2H, *J* = 8.4 Hz), 7.10 (d, 2H, *J* = 7.8 Hz), 7.13 (d, 2H, *J* = 8.4 Hz). ^{13}C NMR (75 MHz) δ 21.1, 21.6, 60.4, 126.6 (2), 127.2 (2), 128.9 (2), 129.8

(2), 130.1 (2), 130.2 (2), 134.8, 136.7, 137.5, 140.5, 143.1, 148.3, 196.2. IR (cm^{-1}) 3483, 2918, 1637, 1604, 1569, 1413, 1316, 1279, 1177, 1043, 1017. Anal. calcd for **7** ($C_{20}H_{20}O_2$): C, 83.51; H, 6.37. Found: C, 83.29; H, 6.22.

17 At 140°C, the disproportionation was incomplete (30% of isopropyl ether intermediate were observed in the crude mixture).

18 The experimental microwaves experiments described in this letter are well established and controlled and can be safely and beneficially reproduced.