# A Radical and An Electron Transfer Process Are Compared in Their Regioselectivities Towards A Molecule with Two Different C-I Bonds: Effect of Steric Congestion

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Steric compression in 1,4-diiodo-2,6-dimethylbenzene (**2a**) makes the C–I bond flanked by methyls substantially weaker (a buttressing effect) than the unhindered C–I bond. Calculations also confirm the weaker bonding interaction of the hindered C–I bond of **2a**. This causes a remarkable regiose-lectivity toward the weaker bond in dehalogenation by stannyl radicals. Conversely, a much lower regioselectivity is found for a process –a photostimulated  $S_{RN}$ 1 reaction with

### Introduction

The goal of a recent investigation by this group<sup>[1]</sup> was to verify experimentally the reasonable expectation that, in the homolytic C-X bond cleavage induced by  $Bu_3Sn$  in a series of organic halides (RX) (Scheme 1), there should be a linear relationship between the ease of dehalogenation and the energy of the C-X bond of the precursors.

Scheme 1

In keeping with the Evans-Polanyi relationship  $(E_a = \alpha D(R-X) + \text{cost})$ ,<sup>[2]</sup> evidence was indeed found for linear relationships between the energy of activation  $(E_a)$  of the dehalogenation process of Scheme 1 vs. the dissociation energy, D(R-X), of the C-X bond undergoing homolysis. This was verified for series of aryl, alkyl, and benzyl iodides, bromides and chlorides.<sup>[1]</sup>

While this finding confirmed that, the weaker the C-X bond, the more easily the halogen is abstracted by tin radical, evidence was also acquired for a peculiar structural effect. Namely, 3-iododurene (i.e., 3-iodo-1,2,4,5-tetramethylbenzene **1a**) was clearly an anomaly with respect to the behaviour of the other iodo derivatives.<sup>[1]</sup> In contrast,



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the enolate ion of a ketone – which requires the conversion of 2a into a radical anion. A calculation of the BDE of the C–I bond for aa ArI<sup>•-</sup> system is offered. Finally, the hindered aryl radical intermediate resulting from cleavage of the weaker C–I bond of  $2a^{•-}$  shows a modest but detectable discrimination between reduction or substitution, this once again being due to the steric congestion.

no deviation was evident for 3-chlorodurene (**1b**) among the chloro derivatives, while the case of 3-bromodurene was somewhat intermediate.<sup>[1]</sup>

We interpreted this deviant behaviour of **1a**, proving more reactive than expected in the dehalogenation reaction of Scheme 1, as being due to a steric compression exerted by the two methyl groups flanking the C–I bond. This sort of buttressing effect<sup>[3]</sup> had to weaken the bond between carbon and iodine, and therefore enhance the ease of abstraction of iodine. In contrast, chlorine being smaller than iodine, the steric compression exerted by the methyls would be much less severe in 3-chlorodurene, and practically imperceptible.<sup>[1]</sup> Independent evidence for steric acceleration in the abstraction of bromine by stannyl radical from an aryl bromide bearing bulky *ortho* substituents, has also been reported.<sup>[4]</sup>

Our rationalisation of this finding also contained the seeds of a new experiment. According to this, a precursor such as 1,4-diiodo-2,6-dimethylbenzene (2a) might be viewed as a significant elaboration of the structure of 1a, in that it presents two kinds of C-I bonds: one normal and the other flanked by methyls, and therefore weaker. For this precursor, a substantial regioselectivity towards dehalogenation by a radical agent such as  $Bu_3Sn$  could be expected, the weaker C-I bond having to cleave more easily than the stronger one.



## **Results and Discussion**

### **Homolytic Process**

We extrapolated the representative point of substrate 1a to the linear reactivity trend of the other iodo derivatives,<sup>[1]</sup> thereby obtaining a D(C-I) of ca. 49 kcal/mol, about one third less than the D(C-I) of the parent compound PhI (67 kcal/mol), which obviously lacks the above-mentioned steric features of 1a. It is therefore reasonable that the buttressing effect of the *ortho*-methyls causes a substantial contribution to the reactivity of 1a. Investigating the behaviour of test substrate 2a therefore appeared worthwhile, in view of the fact that the buttressing effect represents a novel finding in radical processes.

Precursor 2a was synthesised from commercial 2,6-dimethylaniline (see experimental section), and subjected to a photochemically induced (with AIBN) hydrodehalogenation reaction in benzene at room temperature, using an insufficiency of Bu<sub>3</sub>SnH. Only one product, 3, was obtained, in which the hydrogen had uniquely replaced the iodine flanked by the methyls (Scheme 2). We have synthesised 3 independently, in order to confirm this assignment, but have also prepared the 'product that does not form', i.e., 4, to make sure that, had it been produced even in traces ( $\leq$ 0.2%), we could have detected it, either by GC or GC-MS. On the assumption that the 'normal' C-I bond of 2a has a BDE of 67 kcal/mol, while the one between methyls is worth about 49 kcal/mol, the exclusive formation of 3 represents a remarkable example of regioselectivity in a radical process, being simply based on bond energy values. In fact, we draw attention to the point that the site undergoing reaction in the molecule of 2a is the more hindered one, with respect to the approach first of the sterically demanding tributyltin radical, and later of tributyltin hydride.<sup>[5]</sup>



As a further elaboration of the structure of **2a**, we have also synthesised precursor **2b**. This substrate features a C-Cl bond flanked by methyls, in addition to the unhindered C-I bond. The former bond, which should not be appreciably weakened,<sup>[1]</sup> is likely to have the 'normal' BDE of Ph-Cl, i.e., 98 kcal/mol, while the C-I bond of **2b** ought to have the 'normal' D(C-I) of 67 kcal/mol. In this case, bond energy considerations indicate that only the C-I bond will be cleaved homolytically by an insufficiency of the tin radical. In full agreement with this expectation, only the chloro derivative **5** was obtained (Scheme 3), and no traces of **3** could be detected. Once again, there is a remarkable correspondence between reactivity and bond energy in the homolytic process.



Scheme 3

#### **An Electron Transfer Process**

Precursor **2a** was then employed for an aromatic substitution of the  $S_{RN}1$  kind.<sup>[6]</sup> In this reaction, a nucleophile (Y<sup>-</sup>) behaves as a reductant under suitable photostimulation conditions and transfers one electron to the substrate (ArX), thereby converting it into the radical anion ArX<sup>•</sup> <sup>-</sup> (Scheme 4). The latter cleaves the C-X bond, giving an aryl radical plus halide ion. Combination of the nucleophile with the aryl radical then gives rise to the  $S_{RN}1$  substitution product through the fleeting intermediacy of the radical anion ArY<sup>•-</sup>.

$$\begin{array}{cccc} \operatorname{ArX} & \xrightarrow{\operatorname{Y}^{-}/\operatorname{hv}} & \operatorname{ArX}^{-} & + & \operatorname{Y} \\ \operatorname{ArX}^{+} & \longrightarrow & \operatorname{ArX}^{+} & + & \operatorname{X}^{-} \\ \operatorname{ArX}^{+} & \xrightarrow{\operatorname{Y}^{-}} & \operatorname{ArY}^{+} & \operatorname{ArY}^{+} \\ \operatorname{Ar} & \xrightarrow{\operatorname{SH}} & \operatorname{ArH} \\ \operatorname{ArY}^{+} & \xrightarrow{\operatorname{ArX}} & \operatorname{ArY} & + & \operatorname{ArX}^{+} \end{array}$$

Scheme 4. Propagation cycle of the  $S_{RN}$  reaction

Under these circumstances, which one of the two C–I bonds of  $2a^{\bullet-}$  would be cleaved? It must be pointed out that addition of one electron to an aryl halide may be viewed as a sort of activation of the molecule, in that the carbon-halogen bond is significantly weakened in the radical anion. For example, from a thermochemical cycle we have found that the energy of the C–Br bond of PhBr<sup>•-</sup> becomes one quarter (i.e., 20 kcal/mol) that of PhBr (82.6 kcal/mol).<sup>[1]</sup> Consistently, available gas-phase data<sup>[7]</sup> allow us to set out another thermochemical cycle (Scheme 5), in which the energy of the C–I bond of PhI<sup>•-</sup> even becomes one sixth (i.e., 10.3 kcal/mol) that of PhI.

Converting 2a into the radical anion should therefore reduce the difference in BDEs between the two C–I bonds of  $2a^{-}$ , to such an extent that it is reasonable to expect the regioselectivity of the  $S_{RN}1$  process to be *less pronounced* than that of the homolytic process of 2a seen above.

In order to test this hypothesis, substrate 2a was subjected to a photostimulated reaction in DMSO with the enolate ion of pinacolone (Me<sub>3</sub>CCOCH<sub>2</sub><sup>-</sup>) (Scheme 6), a "well-behaved" nucleophile in S<sub>RN</sub>1 processes.<sup>[6,8]</sup>

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Scheme 5. Evaluation of the BDE(C-I) of PhI• -; the heats of formation of the species are reported in brackets, while the gasphase electron affinities (EA) are given on the vertical arrows. All data are in kcal/mol



Scheme 6

After a short reaction time, irradiation was stopped and a small sample of the reaction mixture withdrawn; irradiation was then restarted for an additional period and another sample taken as above. This was repeated until the point when, after a longer irradiation time, all of the remaining reaction mixture was analysed. Analysis of the various samples was by GC and GC-MS; formation of several products was observed, and the results are reported in Table 1. The structure of these products was confirmed by comparison with authentic specimens synthesised independently, and by NMR spectroscopy. Incidentally, while attempting the synthesis of one of these products, we have once again found evidence for the adverse effect of the  $NH_2$ -substituent on the aryl halide  $S_{RN}1$  process (see experimental section).<sup>[9]</sup>

Table 1. Yield (%) of products for the reaction of Scheme 6, at various sampling times. The reaction was run in DMSO at room temp. under photostimulation at 350 nm. The experiments were run in duplicate (errors  $\pm 4\%$ )

Compound	Samp 0.5	ling time 1	(min) 2	10	20
6	1.4	7.4	12	31	20
7	3.7	7.8	8.9	7.1	0.7
8	2	3.5	6.1	21	20
9	5.7	9.1	14	42	37
10	_	4.5	5.5	15	10
3	2	4	6	< 0.5	_
4	1	2	3	_	_
11	_	_	< 0.5	1	3
2a (recovd.)	90	82	77	5	< 0.5

The most salient information deriving from the reaction outlined in Scheme 6 is that the cleavage of the two C-I bonds of 2a<sup>•-</sup> takes place with similar efficiency. Hence, the electron transfer induced process is no longer regioselective like the radical one (see previous section). Inspection of the

products formed indeed suggests that each of the aryl radical species (c and d, in Scheme 7) arising from cleavage of the two corresponding C-I bonds partitions between combination with the nucleophile or hydrogen atom abstraction. The former step results in the formation of the radical anion of the monoiodinated substitution products  $(6^{\bullet-} \text{ and } 7^{\bullet-})$ , while the latter gives rise to the monoiodinated reduction products (3 and 4).

The radical anions  $6^{\bullet-}$  and  $7^{\bullet-}$  can then transfer the extra electron to another molecule of substrate 2a, thus perpetuating the chain and affording 6 and 7. Alternatively, they can undergo cleavage of the residual C-I bond. The



C–I bond of  $7^{\bullet-}$  being *slightly* weaker than that of  $6^{\bullet-}$  (see above), fragmentation into radical f (plus I<sup>-</sup>) is expected to prevail slightly over fragmentation into radical e (plus I<sup>-</sup>). Then, partition of both radicals e and f between combination with the nucleophile or hydrogen atom abstraction (Scheme 8) is again possible. The monosubstituted reduction products (8 and 9) will thus result, along with the bissubstituted product 10.

Finally, even the previously formed monoiodinated reduction products (3 and 4) present in the medium can take part in further electron-induced steps; the latter will lead, via the corresponding radical anions, to additional quantities of the monosubstituted reduction products (8 and 9) and to the bis-reduced *m*-xylene product **11** (Scheme 9).

All products are obtained in varying amounts at the sampling times adopted. In particular, the first generation products 3, 4, 6 and 7 accumulate at early stages but tend to vanish at later stages (the fate of 7 is particularly interesting). This pattern is consistent with their being 'substrates' for the second-generation products 8, 9, 10 and 11. Similar cascade-like product patterns have typically been obtained in other  $S_{RN}$  reactions with bis-halogenobenzenes.<sup>[10]</sup>

Without overemphasising the yield figures of Table 1, some comments are possible. We repeat that product 7 (as we indicated for its radical anion) has a weak C-I bond and, therefore, is more prone to further electron-induced fragmentations: at longer reaction times in fact, it is more extensively consumed than product 6. Consistently, even 9 prevails slightly over 8, since the former originates from intermediate f, which in turn originates from the easier cleavage of the weaker C–I bond ( $7^{\bullet-} > 6^{\bullet-}$ , in Scheme 7). However, this prevalence is possibly also due to the steric hindrance from the two ortho-methyls of radical f, which affect its reactivity in the partitioning between reduction or substitution (see Scheme 8). In general, H atom abstraction

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Scheme 7. Distribution of the first generation products from the two intermediate radicals (c and d) deriving from the cleavage of  $2a^{-1}$ 



Scheme 8. Second generation products from radicals e and f

contrast, independent reaction of compound **4** with the enolate ion of pinacolone afforded reduction vs. substitution products in a ratio as high as 1:4 (Scheme 10).

This suggests that the approach of the sterically demanding enolate ion to a hindered radical such as f suffers more from the hindrance of the *ortho*-methyls than the approach of the solvent molecules delivering the H atoms. A final piece of evidence concerns the second generation bissubstituted product **10**, which is absent at the first sampling time, but later builds up, as is reasonable for a cascade series of events (Scheme 8).



Scheme 10



Scheme 9. Further evolution to further products

by the radical intermediate of a  $S_{RN}1$  process with simple halobenzenes (see Scheme 4) provides only a negligible contribution (less than 1%) to the overall mass balance;<sup>[6c]</sup> in

As for the relative ease of cleavage of the C–I bonds of **2a**, it is a common notion that single-electron donation to an aryl halide populates first the lower-energy  $\pi^*$  MO of

the molecule; intramolecular electron transfer to the higherenergy  $\sigma^*$  MO of the C–X bond then occurs, whereby cleavage takes place.<sup>[11]</sup> In aryl iodide derivatives, it often instead happens that the  $\sigma^*$  MO (C–X) is of energy comparable to that of the  $\pi^*$  MO, so that the  $\sigma^*$  is more easily populated than with the other aryl halides and cleavage occurs in a 'follow-up' fashion.<sup>[6][7d,12]</sup> In the particular case of precursor **2a**, it is likely that the energies of the  $\sigma^*$  MOs of the two C–I bonds of **2a**<sup>•–</sup> are very similar (see Scheme 5), so that the cleavage of the more hindered C–I bond is no longer as dominant over the other as it was in the radical process.

#### Ab Initio Calculation

We attempted to acquire some independent evidence for the weaker bonding interaction of the hindered C–I bond of **2a**, other than that deriving from the off-line behaviour of 3-iododurene **1a**.<sup>[1]</sup> Ab initio calculations were performed for **2a** at the HF/3–21G(\*) level of theory.<sup>[13]</sup> The result indeed gives the hindered C–I bond of **2a** appreciably longer than the other (2.144 Å vs. 2.132 Å), and the two flanking methyl groups are slightly bent away from the bulky iodine atom (the C<sub>1</sub>–C<sub>2</sub>–CH<sub>3</sub> bond angle is 122.7°, compared with the calculated value of 120.1° for *m*-xylene) (Figure 1).



Figure 1. Bond angle deformation in 2a, from ab initio calculations

At the same level of theory, the  $\Delta E$  values obtained for the two isodesmic reactions of Scheme 11 and 12 (i.e., -0.35 kcal/mol and -1.71 kcal/mol, respectively) once more show that the hindered C-I bond is affected by a steric constraint as high as 1.36 kcal/mol with respect to the other C-I bond, thus giving foundation to the regioselectivity of the tin radical process reported above.









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#### **Experimental Section**

**General Remarks:** Photochemical reactions were conducted in a Rayonet RPR-100 reactor equipped with a set of 16 '350 nm' lamps. Characterisation of the structure of reaction products was by <sup>1</sup>H NMR at 200 MHz in CDCl<sub>3</sub> (vs. TMS) on a Bruker AC 200 instrument, and by GC-MS on an HP 5972 MSD at 70 eV. Calculations were carried out using the Spartan 5.01 package<sup>[14]</sup> on a O2 Silicon Graphics workstation. The synthesis of compounds **3**, **4**, **5** was performed on an analytical scale by means of standard reactions for the exclusive purpose of obtaining a GC and GC-MS characterisation, and no NMR, microanalysis or yield data were determined.

**2,5-Diiodo-1,3-dimethylbenzene (2a):** Commercial 2,6-dimethylaniline (**12**, Aldrich) was iodinated to 4-iodo-2,6-dimethylaniline (**13**) by following *'method a'* (Scheme 13) described in a previous publication (70% yield).<sup>[15]</sup> MS; *m/z*: 247. – <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  = 7.2 (s, 2 H, ArH), 3.5 (bs, 2 H, NH<sub>2</sub>), 2.1 (s, 6 H, CH<sub>3</sub>).





This intermediate was employed without further purification for the preparation of **2a** by means of a standard diazotisation/iododediazotisation procedure. Any residual **13** was then removed by washing the crude reaction product with aqueous acid, and final purification by recrystallisation (EtOH/H<sub>2</sub>O) gave **2a** in 75% yield: m.p. 59–61 °C. MS; *mlz*: 358. – <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  = 7.4 (s, 2 H, ArH), 2.4 (s, 6 H, CH<sub>3</sub>). It was possible to isolate a small sample of iodo-3,5-dimethylbenzene (**3**) from the mother liquor; this was characterised by its MS spectrum (*mlz* 232) and GC retention time. Compound **3**, in this particular case, represents a side-product of hydrodediazotisation in the predominant iododediazotisation route to **2a**.

**2-Iodo-1,3-dimethylbenzene (4):** This was similarly obtained by diazotisation/iododediazotisation of 2,6-dimethylaniline **12**. The crude product was chromatographed on silica gel with petroleum ether (40–70 °C), and obtained as a pure oil. MS; *m/z*: 232. – <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  = 7.1–6.9 (m, 3 H, ArH), 2.5 (s, 6 H, CH<sub>3</sub>). – <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  = 142 ( $C_{\text{ipso}}^{\text{Ph}}$ -Me), 128 ( $C_{\text{para}}^{\text{Ph}}$ ), 127 ( $C_{\text{meta}}^{\text{Ph}}$ ), 108 ( $C_{\text{ipso}}^{\text{Ph}}$ -I), 30 (Me).

**2-Chloro-5-iodo-1,3-dimethylbenzene (2b):** From 4-iodo-2,6-dimethylaniline **13** previously obtained, a standard diazotisation/ chlorodediazotisation gave **2b** (56% yield) as a low-melting solid after column chromatography on silica gel with petroleum ether (40–70 °C). MS; *m/z*: 266 and 268. A small amount of **3** was again obtained as a forerunner.

**2-Chloro-1,3-dimethylbenzene (5):** This was obtained through diazotisation/chlorodediazotisation of **12**, and purified by flash chromatography. MS; *m/z*: 140 and 142.

**Reaction with Tin Radical:** Following the conventional procedure,<sup>[1]</sup> the substrate (either **2a** or **2b**; 1 mmol), AIBN (0.1 mmol), and Bu<sub>3</sub>SnH (0.4 mmol) in dry benzene (3 mL) was irradiated at '350' nm in a Pyrex vessel for 1 h. An aliquot was removed, diluted with diethyl ether and analysed by GC and GC-MS for the determina-

tion of the nature and yield of the hydrodehalogenated product(s). From **2a**, only **3** was obtained; from **2b**, only **5** was obtained. No difference was observed at a shorter or longer sampling time.

Synthesis of the Products of the  $S_{RN}1$  Reaction: *meta*-Xylene 11 is commercially available. An apparently sound synthetic strategy to obtain reaction products 7 and 9 was through the  $S_{RN}1$  reaction of 13 with the enolate ion of pinacolone, to give the pinacolyl-substituted aniline 14. Diazotisation of this, followed by iododediazotisation, would give 7 (Scheme 14), while hydrodediazotisation would give 9.



Unfortunately, the photostimulated  $S_{RN}$  reaction<sup>[10d]</sup> of 13 with  $Me_3CCOCH_2^-$  gave only a trace amount of 14, thus supporting a previous report on adverse effects of an NH<sub>2</sub> substituent on the viability of an aryl halide S<sub>RN</sub>1 process.<sup>[9]</sup> In order to circumvent this problem, we carried out an  $S_{RN}1$  reaction of 2a (0.041 M) with Me<sub>3</sub>CCOCH<sub>2</sub><sup>-</sup> (0.062 M) in DMSO (55 mL, distilled from CaH<sub>2</sub>) under photostimulation with 16 '350' nm lamps for 20 min.[10d] Conventional workup with brine and diethyl ether, followed by removal of the organic solvent, gave a crude mixture of products, which was chromatographed on silica gel with petroleum ether (40-70 °C) to separate a mixture of 3 + 4, followed by a small amount of unchanged 2a, along with a small amount of 9; the latter was characterized by its GC and GC-MS retention times and MS spectrum (m/z 204). The residue of this chromatography was chromatographed once more on silica gel with a toluene/hexane 1:3 eluent and, as a first pure fraction, afforded 15 mg of 7 as an oil.  $- {}^{1}$ H NMR (CDCl<sub>3</sub>):  $\delta = 6.8$  (bt, 2 H, ArH), 3.7 (s, 2 H, ArCH<sub>2</sub>CO), 2.4 (s, 6 H, ArCH<sub>3</sub>), 1.2 (s, 9 H, CMe<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>) 213 (C=O), 147 (C<sup>Ar</sup><sub>ipso</sub>-Me), 130 (C<sup>Ar</sup><sub>ipso</sub>-pinac.), 128, 98 (C Ar <sub>ipso</sub>-I), 45 (CMe<sub>3</sub>), 43 (ArCH<sub>2</sub>CO), 30 (ArCH<sub>3</sub>), 27.5 (Me<sub>3</sub>). -MS; m/z: 330 (M<sup>+</sup>), 273 (M<sup>+</sup> - CMe<sub>3</sub>), 245 (M<sup>+</sup> - COCMe<sub>3</sub>), 203 (M<sup>+</sup> - I), 127 (I<sup>+</sup>), 85 (COCMe<sub>3</sub><sup>+</sup>), 57 (CMe<sub>3</sub><sup>+</sup>).

A sample of **6** (25 mg), slightly contaminated with **7**, was eluted from the column next: <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  = 7.4 (s, 2 H, ArH), 3.8 (s, 2 H, ArCH<sub>2</sub>CO), 2.1 (s, 6 H, ArCH<sub>3</sub>), 1.27 (s, 9 H, CMe<sub>3</sub>). – <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  = 212 (*C*=O), 140 (*C*<sup>Ar</sup><sub>1pso</sub>-Me), 136, 131 (*C* <sup>Aro</sup><sub>1pso</sub>-pinac.), 96 (*C*<sup>Ar</sup><sub>1pso</sub>-I), 45.5 (*C*Me<sub>3</sub>), 38 (ArCH<sub>2</sub>CO), 27 (Me<sub>3</sub>), 20 (ArCH<sub>3</sub>). – MS; *m/z*: 330 (M<sup>+</sup>), 273 (M<sup>+</sup> – CMe<sub>3</sub>), 245 (M<sup>+</sup> – COCMe<sub>3</sub>), 203 (M<sup>+</sup> – I), 127 (I<sup>+</sup>), 85 (COCMe<sub>3</sub><sup>+</sup>), 57 (CMe<sub>3</sub><sup>+</sup>).

Finally, 10 mg of **10** was separated: MS; m/z: 302 (M<sup>+</sup>), 245 (M<sup>+</sup> – CMe<sub>3</sub>), 217 (M<sup>+</sup> – COCMe<sub>3</sub>), 132 (M<sup>+</sup> – 2 × COCMe<sub>3</sub>), 85 (COCMe<sub>3</sub><sup>+</sup>), 57 (CMe<sub>3</sub><sup>+</sup>). Its <sup>1</sup>H NMR spectrum compared very well to the one reported in the literature.<sup>[16]</sup>

Another  $S_{RN}$  reaction was carried out as above with 4 (see Scheme 10), and gave 8 as an oil (45% yield) after column chromatography.

- <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ = 7.1–6.9 (bs, 3 H, ArH), 3.9 (s, 2 H, ArCH<sub>2</sub>CO), 2.2 (s, 6 H, ArCH<sub>3</sub>), 1.18 (s, 9 H, CMe<sub>3</sub>). – MS; *m/z*: 204 (M<sup>+</sup>), 147 (M<sup>+</sup> – CMe<sub>3</sub>), 119 (M<sup>+</sup> – COCMe<sub>3</sub>), 85 (COCMe<sub>3</sub><sup>+</sup>), 57 (CMe<sub>3</sub><sup>+</sup>). Preliminary GC-MS and GC analyses of the crude mixture of this reaction had revealed the formation of a sizeable quantity (13%) of *m*-xylene **11**.

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