Research Article

Reactivity of 2-aryl-1,3-dithiane anions towards neopentyl, neophyl and phenyl iodides. New evidence for an $S_{RN}1$ mechanism

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The reactions of 2-(4-Z-phenyl)-1,3-dithiane anions (Z = H, OMe, Cl, CN) with neopentyl, neophyl and phenyl iodides were studied in DMSO, taking into consideration the effect of the Z substituent on the dithiane anions reactivity as well as on the product distribution. These substitution reactions proceed by an $S_{RN}1$ mechanism with radicals and radical anions as intermediates. Two competitive pathways are possible for the radical anion of the substitution product, namely electron transfer (ET) to the substrate giving the substitution product and C–S bond fragmentation to yield a distonic radical anion. ET is the main pathway for the reactions between dithiane anions bearing electron-donor substituents and neopentyl or its analogue iodides affording the substitution products in moderate yields (41–53%). Copyright © 2011 John Wiley & Sons, Ltd.

Supporting information may be found in the online version of this article.

Keywords: dithiane anion; electron transfer; fragmentation; radical; radical anion

INTRODUCTION

The radical nucleophilic substitution concerning electron transfer (ET) steps or the $S_{RN}1$ mechanism is a chain process involving radicals and radical anions as intermediates. In these reactions, a compound bearing an adequate leaving group is usually substituted by a nucleophile. Over the years, the scope of this process has been considerably extended, and nowadays, it is an important synthetic method to achieve substitution ipso to the leaving group of different substrates.[1–4] Furthermore, non-activated aromatic halides, alkyl halides activated by strong electron withdrawing groups (EWGs; nitroalkyl, nitroallyl, nitro or cyanobenzyl and their heterocyclic analogues) and other simple alkyl halides, can be substituted by nucleophiles through ET mechanisms. These compounds characterised mostly by their low reactivity towards classical polar nucleophilic substitutions, mainly due to steric and strain factors. Examples of this type of compounds include neopentyl halides and derivatives, bridge-head bicyclo- and polycycloalkyl halides. Several nucleophiles are known to react by ET processes to form new C–C or C-heteroatom bonds with good yields, such as carbanions and anions from Sn, Sb, P, As, S, Se and Te.
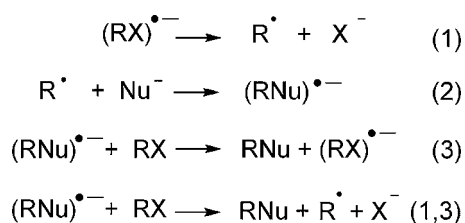
The chain reaction of the $S_{RN}1$ process requires an initiation step, which involves an ET from the nucleophile or from a suitable electron source to the substrate. The most frequently used methods for initiation are chemical initiation by alkali metals in liquid ammonia,[5] electrochemical initiation at a cathode,[4] and photoinitiation,[2,3] with other procedures including the use of Fe^{2+},[6–8] SmI_2,[9] or Na(Hg).[10] In a few systems, a thermal (spontaneous) initiation is observed.[11–14] For example, the $S_{RN}1$ substitution of aliphatic systems with EWGs is in most cases initiated by a thermal ET that can be accelerated by light.[15] Scheme 1 presents the propagation steps of an $S_{RN}1$ mechanism.

In aliphatic systems without a π^* MO to stabilise the radical anion $(RX)^{\cdot-}$, Equations (1) and (3) occur simultaneously (concerted dissociative step),[16] giving the substitution product and the alkyl radical $R^{\cdot}$ (which propagates the chain cycle). Furthermore, since the $S_{RN}1$ is a chain mechanism, the overall reactivity depends on the initiation, propagation, and termination steps. In order for this process to work efficiently, the initiation step may be slow. However, the chain propagation needs to be fast and efficient in order to allow long chains to build up. Finally, the wide variety of nucleophiles that can be used, the great functional group tolerance, and the fact that many C–C and C-heteroatom bonds can be obtained, make the $S_{RN}1$ reaction an effective synthetic tool.[17,18]

The 1,3-dithianes derived from aldehydes and ketones have become highly important in organic synthesis for their role in protecting the carbonyl groups, a strategy commonly used in natural product synthesis.[19,20] Additionally, cyclic thioacetals are versatile synthetic reagents acting as acyl anion equivalents for C–C bond formation by reaction with a wide range of alkyl halides, carbonyl compounds and other electrophilic reagents.[21–24] For example, the reaction between 2-lithio-1,3-dithiane (**1**) and the optically active (R)-2-iodo-octane in THF was found to proceed with complete inversion of configuration.[25] This result implies

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$$(RX)^{\bullet -} \longrightarrow R^{\bullet} + X^{-} \quad (1)$$

$$R^{\bullet} + Nu^{-} \longrightarrow (RNu)^{\bullet -} \quad (2)$$

$$(RNu)^{\bullet -} + RX \longrightarrow RNu + (RX)^{\bullet -} \quad (3)$$

$$(RNu)^{\bullet -} + RX \longrightarrow RNu + R^{\bullet} + X^{-} \quad (1,3)$$

Scheme 1. S$_{RN}$1 mechanism.

Chart 1. Dithiane anions and iodides studied.

	Z
3a	H
3b	OMe
3c	Cl
3d	CN

that the S$_N$2 mechanism is the preferred pathway between **1** and unhindered alkyl halides. However, when the neopentyl type probe (**2**) was used, both uncyclised and cyclised substitution products were found at low yields, suggesting that this occurred, at least in part, by an ET reaction (Scheme 2).[25] For these reactions a chain mechanism with radical and radical anions as intermediates, such as the S$_{RN}$1 mechanism, was discarded by the authors; they proposed instead the occurrence of an ET process with cage collapse of the radical pair.

The reactivity of neopentyl and neophyl iodides by the S$_{RN}$1 process has been well established, for carbanions as well as for sulphur, phosphorous, selenide and telluride anions.[26–28] A kinetic study of the reaction of neopentyl bromide with PhS$^-$ and Ph$_2$P$^-$ ions was performed in liquid ammonia and MeCN, with the rate constants for the coupling of neopentyl radicals with PhS$^-$ ions determined to be about 1.2×10^8 M^{-1} s^{-1}.[29] More recently, detailed photochemical studies were conducted to investigate the reactions of neophyl iodide with carbanions such as the enolate anion of acetophenone ($^-$CH$_2$COPh) and the nitromethane anion ($^-$CH$_2$NO$_2$) in DMSO, with the rate constant for the coupling of $^-$CH$_2$COPh anion with the neophyl radical found to be 1.2×10^5 M^{-1} s^{-1}. In relation to this, on the basis of determinations of quantum yields for the initiation step, these reactions were proposed to occur by the S$_{RN}$1 mechanism, with chain lengths of 127 ($^-$CH$_2$COPh) and 2 ($^-$CH$_2$NO$_2$), although the overall quantum yields were below 1.[30] Conversely, in the reaction of iodide **2** with lithium propiophenone in HMPA (lab. light), *O*-alkylation was the principal reaction (66%), accompanied by a small yield of *C*-alkylation (11%) and a small amount of the cyclic hydrocarbon. It was suggested that this reaction takes place, at least partly, with radicals as intermediates.[31] The effects of leaving groups, solvents, and hydrogen atom donors have been investigated in the reaction of probe **2** with *i*-PrSLi, with quantitative straightforward substitution being obtained in THF. However, the same reaction, in the presence of the radical trap dicyclohexylphosphine (DCPH), yielded up to 19% of the cyclic and 3% of the straightforward hydrocarbon products, respectively. These results were also attributed to an ET pathway with geminate radical coupling within the solvent cage, to some extent, for the reaction of probe **2** with *i*-PrSLi in THF.[32]

The aim of this study is to explore further the reactivity of dithiane anions as electron donors in radical nucleophilic substitution by the S$_{RN}$1 mechanism. Thus, we herein report a comprehensive study of the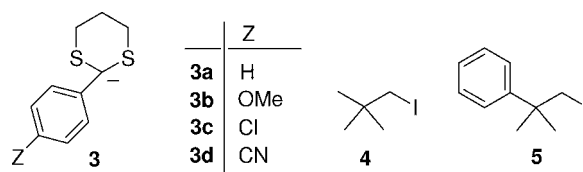 reactions of 2-aryl-1,3-dithiane anion (**3**) with neopentyl (**4**) and neophyl (**5**) iodides, under a variety of conditions in DMSO at 20 °C (Chart 1). For comparison purposes, the reactivity towards phenyl iodide has also been investigated. New evidence for the operating mechanism is presented and discussed.

EXPERIMENTAL

Chemicals

tert-BuOK, neopentyl iodide (**4**), neophyl iodide (**5**), MeI, DTBN, thiophenol, iodobenzene, *p*-dinitrobenzene, benzaldehyde, 4-methoxybenzaldehyde, 4-chlorobenzaldehyde, 4-formylbenzo-nitrile and 1,3-propanedithiol were all high-purity commercial samples, used without further purification. DMSO was distilled under vacuum and stored over molecular sieves (4 Å). Anions **3a–d** were generated *in situ* by acid–base deprotonation using *tert*-BuOK. Dithiane precursors of anions **3a–d** were synthesised by standard procedures from the reaction between commercial benzaldehydes and 1,3-propanedithiol in CH$_3$Cl, in the presence of a catalytic amount of iodine.[33] 5-(Iodomethyl)-5-methyl-1-hexene **2** was synthesised as previously reported.[25,32]

General methods

Irradiation was conducted with two 400 W medium pressure Hg lamps emitting maximally at 365 nm. All the reaction products were isolated by radial chromatography from the reaction mixture, and characterised by ^{1}H and ^{13}C NMR and mass spectrometry. All the dithiane[34] precursors of anions **3a–d** and 4-benzylbenzonitrile (**24**)[35] are well known and exhibited physical properties identical to those reported in the literature. ^{1}H and ^{13}C NMR spectra were recorded at 400.16 and 100.62 MHz respectively on a 400 spectrometer, and all spectra were reported in δ (ppm) relative to Me$_4$Si, with CDCl$_3$ as solvent at 30 °C. Gas chromatographic analyses were performed with a flame-ionisation detector, on 30 m capillary column of a 0.32 mm × 0.25 μm film thickness, with a 5% phenylpolysiloxane phase. GS-MS analyses were performed employing a 25 m × 0.2 mm × 0.33 μm with a 5% phenylpolysiloxane phase column.

Representative experimental procedure

These reactions were carried out in a 10 mL three-necked Schlenk tube, equipped with a nitrogen gas inlet and a magnetic stirrer.

1	**2**	N$_2$ -20 to 25 ºC THF THF/TMEDA	1.7% 2.5%	6% 11%
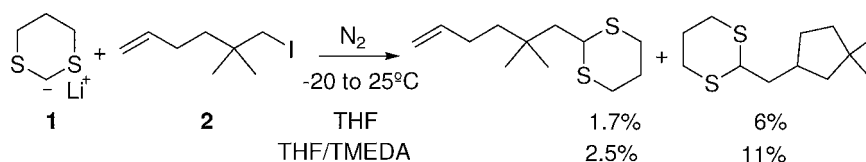
Scheme 2. ET reaction between 2-lithio-1,3-dithiane (**1**) and 5-(iodomethyl)-5-methyl-1-hexene (**2**).

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The tube was dried under vacuum, filled with nitrogen and then with dried DMSO (5 mL). *tert*-BuOK (336.7 mg, 3.0 mmol), dithiane precursor of **3a–d** (294.0 mg, 1.5 mmol), and neopentyl iodide (99.0 mg, 0.5 mmol), were added to the degassed solvent under nitrogen. After 1 h of irradiation with a medium pressure Hg lamp emitting maximally at 365 nm, the reaction was quenched by the addition of ammonium nitrate in excess and 10 mL of water, and the mixture was extracted with methylene chloride (3 mL × 20 mL). The organic extract was washed twice with water and dried over anhydrous MgSO$_4$, and the products were quantified by GC using the internal standard method, or isolated by radial chromatography from the crude product reaction mixture.

2-Neopentyl-2-phenyl-1,3-dithiane (6a)

White solid, m.p.: 147.8–148.1 °C. ^{1}H NMR: $\delta = 0.722$ (s, 9 H), 1.90–1.93 (m, 2 H), 2.16 (s, 2 H), 2.58–2.73 (m, 4 H), 7.24–7.37 (m, 3 H) ppm, 7.96–7.98 (m, 2 H). ^{13}C NMR: $\delta = 25.05$, 27.86, 31.29, 33.44, 58.11, 58.95, 126.80, 128.24, 129.89, 141.35 ppm. MS (EI$^+$), m/z (relative intensity), 266 (26, M$^+$); 209 (6); 195 (48); 136 (68); 121 (37); 103 (100); 91 (11); 77 (37); 57 (74). HRMS, calcd for C$_{15}$H$_{22}$S$_2$ 266.1163, found 266.1164.

2-(4-Methoxyphenyl)-2-neopentyl-1,3-dithiane (6b)

Solid, m.p. 69.5–69.8 °C. ^{1}H NMR: $\delta = 0.75$ (s, 9 H), 1.88–1.95 (m, 2 H), 2.15 (s, 2 H), 2.57–2.63 (m, 2 H), 2.72–2.79 (m, 2 H), 3.85 (s, 3 H), 6.89–6.91 (d, 2 H, J = 8.8), 7.86–7.88 (d, 2 H, J = 8.8) ppm. ^{13}C NMR: $\delta = 25.1$, 27.8, 31.3, 33.4, 55.3, 58.2, 58.7, 113.4, 131.1, 133.2, 158.4 ppm. HRMS (MH+), calcd for C$_{16}$H$_{25}$OS$_2$ 297.1347, found 297.1344.

2-(4-Clorophenyl)-2-neopentyl-1,3-dithiane (6c)

Solid, m.p. 83.9–84.2 °C. ^{1}H NMR: $\delta = 0.75$ (s, 9 H), 1.92–1.95 (m, 2 H), 2.15 (s, 2 H), 2.59–2.71 (m, 4 H), 7.33–7.35 (d, 2 H, J = 8.8), 7.92–7.94 (d, 2 H, J = 8.8) ppm. ^{13}C NMR: $\delta = 24.9$, 27.8, 31.4, 33.5, 58.2, 58.3, 128.3, 131.5, 132.8, 140.3 ppm. MS (EI$^+$), m/z (relative intensity), 302 (16, M^{+2}); 300 (39 M$^+$); 243 (51); 229 (67); 191 (40); 170 (94); 155 (41); 139 (41); 137 (100); 107 (34); 57 (86). HRMS (MH+), calcd for C$_{15}$H$_{22}$ClS$_2$ 301.0851, found 301.0846.

4-(2-Neopentyl-1,3-dithian-2-yl)benzonitrile (6d)

Solid, m.p. 98.8–99.2 °C. ^{1}H NMR: $\delta = 0.73$ (s, 9 H), 1.96–1.99 (m, 2 H), 2.18 (s, 2 H), 2.63–2.665 (m, 4 H), 7.67–7.70 (d, 2 H, J = 8.8), 8.13–8.16 (d, 2 H, J = 8.8) ppm. ^{13}C NMR: $\delta = 24.6$, 27.8, 31.4, 33.6, 58.1, 130.8, 132.0 ppm. MS (EI$^+$), m/z (relative intensity), 293 (4, M^{+2}); 291 (38 M$^+$); 234 (100); 220 (91); 161 (83); 146 (51); 128 (55); 107 (98); 57 (96); 41 (72). HRMS, calcd for C$_{16}$H$_{21}$NS$_2$ 291.1115, found 291.1105.

1,3-bis(Neopentylthio)propane (7)

Liquid, ^{1}H NMR: $\delta = 1.00$ (s, 18 H), 1.83–1.90 (q, 2 H, J = 7.2), 2.46 (s, 4 H), 2.61–2.64 (t, 4 H J = 7.2) ppm. ^{13}C NMR: $\delta = 28.94$, 29.92, 32.32, 33.11, 47.60 ppm. MS (EI$^+$), m/z (relative intensity), 248 (24, M$^+$); 177 (79); 121 (20); 107 (100); 57 (25); 43 (71). HRMS, calcd for C$_{13}$H$_{28}$S$_2$ 248.1632, found 248.1633.

2-(2-Methyl-2-phenylpropyl)-2-phenyl-1,3-dithiane (15)

Solid, m.p. 57.3–57.8 °C. ^{1}H NMR: $\delta = 1.15$ (s, 6 H), 1.80–1.83 (m, 2 H)ppm. 2.45–2.63 (m, 6 H), 7.15–7.25 (m, 8 H), 7.77–7.78 (m, 2 H). ^{13}C NMR: $\delta = 24.9$, 27.9, 28.1, 30.5, 39.19, 58.7, 58.99, 125.5, 125.86, 126.05, 126.18, 126.64, 127.67, 128.11, 129.81, 141.12, 148.7 ppm. MS (EI$^+$), m/z (relative intensity), 328 (5, M$^+$); 209 (8); 121 (20); 119 (64); 103 (70); 91 (100); 77 (41); 51 (27). HRMS, calcd for C$_{20}$H$_{24}$S$_2$ 328.1319, found 328.1319.

2-(2,2-Dimethylhex-5-enyl)-2-phenyl-1,3-dithiane (16)

Solid, ^{1}H NMR: $\delta = 0.70$ (s, 6 H), 1.08–1.12 (m, 2 H), 1.86–1.93 (m, 4 H), 2.15 (s, 2 H), 2.56–2.76 (m, 4 H), 4.83–4.90 (m, 2 H), 5.60–5.69 (m, 1 H), 7.26–7.38 (m, 3 H), 7.97–7.99 (m, 2 H) ppm. ^{13}C NMR: $\delta = 25.0$, 27.9, 28.5, 28.6, 35.9, 42.9, 55.9, 58.96, 113.7, 126.8, 128.3, 129.9, 139.5, 141.4 ppm. MS (EI$^+$), m/z (relative intensity), 306 (4, M$^+$); 231 (14); 209 (24); 195 (25); 121 (42); 106 (100); 103 (68); 91 (24); 77 (27); 55 (70). HRMS (MH+), calcd for C$_{18}$H$_{27}$S$_2$ 307.1554, found 307.1553.

2-((3,3-Dimethylcyclopentyl)methyl)-2-phenyl-1,3-dithiane (17)

Solid, ^{1}H NMR: $\delta = 0.85$ (s, 3 H), 0.92 (s, 3 H), 1.03–1.43 (m, 6 H), 1.94–2.12 (m, 5 H), 2.61–2.76 (m, 4 H), 7.25–7.29 (m, 1 H), 7.37–7.41 (m, 2 H), 7.94–7.96 (m, 2 H) ppm. ^{13}C NMR: $\delta = 25.2$, 27.67, 27.69, 29.5, 30.3, 30.7, 35.2, 38.5, 40.5, 49.7, 52.7, 59.4, 126.8, 128.4, 129.1, 141.9 ppm. MS (EI$^+$), m/z (relative intensity), 306 (19, M$^+$); 231 (16); 217 (18); 195 (100); 136 (73); 121 (38); 103 (18); 91 (15); 69 (26); 55 (32). HRMS (MH+), calcd for C$_{18}$H$_{27}$S$_2$ 307.1554, found 307.1553.

1,3-bis(2,2-dimethylhex-5-enylthio)propane (18)

Liquid, ^{1}H NMR: $\delta = 0.98$ (s, 12 H), 1.38–1.42 (m, 4 H), 1.85–1.89 (q, 2 H, J = 7.2), 2.00–2.06 (m, 4 H), 2.48 (s, 4 H), 2.60–2.64 (t, 4 H, J = 7.2), 4.94–5.06 (dd, 4 H), 5.79–5.87 (m, 2 H) ppm. ^{13}C NMR: $\delta = 26.7$, 28.6, 29.9, 32.97, 34.6, 40.4, 45.8, 114.0, 139.3 ppm. MS (EI$^+$), m/z (relative intensity), 328 (5, M$^+$); 217 (65); 121 (18); 107 (26); 95 (27); 69 (100); 55 (76). HRMS (MH+), calcd for C$_{19}$H$_{37}$S$_2$ 329.2337, found 329.2341.

4-(2-Phenyl-1,3-dithian-2-yl)benzonitrile (23)

Solid, ^{1}H NMR: $\delta = 2.03$–2.06 (m, 2 H), 2.72–2.81 (m, 4 H), 7.30–7.38 (m, 3 H), 7.63–7.65 (d, 4 H, J = 8.4), 7.84–7.86 (d, 2 H, J = 8.4) ppm. ^{13}C NMR: $\delta = 24.1$, 29.3, 111.4, 118.6, 128.1, 128.7, 129.1, 130.25, 132.2 ppm. MS (EI$^+$), m/z (relative intensity), 297 (28, M$^+$); 223 (100); 190 (95); 146 (18); 121 (24); 105 (5). HRMS (MH+), calcd for C$_{17}$H$_{16}$NS$_2$ 298.0724, found 298.0725.

### 4-((3-Mercaptopropylthio)(phenyl)methyl)benzonitrile (25)

Solid, m.p: 139.5–140.0 °C. ^{1}H NMR: $\delta = 1.88$–1.92 (m, 1 H), 2.08–2.16 (m, 1 H), 2.80–2.90 (m, 4 H), 5.12 (s, 1 H), 7.47–7.48 (m, 5 H), 7.53–7.54 (m, 1 H), 7.62–7.65 (m, 2 H), 7.67–7.89 (m, 1 H) ppm. ^{13}C NMR: $\delta = 24.8$, 32.0, 48.0, 112.0, 118.4, 128.4, 128.7, 128,8, 129.9, 131.4, 133.8, 138.1, 141.7, 141.9 ppm. MS (EI$^+$), m/z (relative intensity), 299 (3, M$^+$); 297 (27); 223 (24); 222 (83); 191 (100); 106 (38). HRMS (MH+), calcd for C$_{17}$H$_{18}$NS$_2$ 300.0875, found 300.0856.

RESULTS AND DISCUSSION

Reaction of 2-phenyl-1,3-dithiane anion (3a) with neopentyl iodide (4) in DMSO

2-Phenyl-1,3-dithiane anion (**3a**) can be generated in DMSO under nitrogen atmosphere by deprotonation of the dithiane precursor (p$Ka = 30.5$)[36] with *tert*-BuOK (p$Ka = 32.2$).[33] Accordingly, the addition of an excess of MeI to a solution of anion **3a** (produced with 3 equiv of base) afforded 2-methyl-2-phenyl-1,3-dithiane in a 71% yield (determined by GC quantification). In the presence of only 1.5 equiv of *tert*-BuOK, a 60% yield of the methylated derivative was obtained.

When a solution[37] of 2-phenyl-1,3-dithiane anion (**3a**) and **4** was stirred for 1 h under irradiation at $\lambda_{max} > 350$ nm, the substitution product 2-neopentyl-2-phenyl-1,3-dithiane (**6a**) was obtained in 42% yield, together with small amounts of the neopentyl substituted product **7** (7% yield) and traces of the hydrocarbons **8a** and **9a** (Eqn 4, Table 1, entry 1). This reaction proceeded to a similar conversion in the dark to afford **6a** as the major product, with a minor amount of product **7** (Table 1, entry 2). Both experiments were performed using a **3a:4** ratio of 3:1 and 1 equiv of *tert*-BuOK.
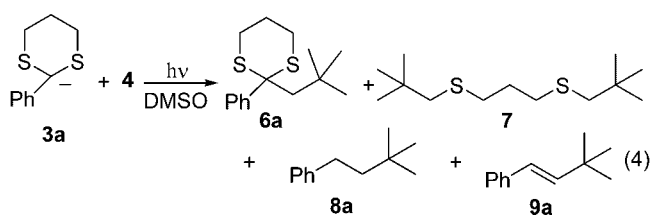
When equimolar amounts of dithiane and *tert*-BuOK were employed, a slight improvement in the yields of the substitution products **6a** and **7** was observed after 60 min (51% and 10% yields, respectively; Table 1, entry 3). A comparable performance of this reaction was achieved by using a ratio dithiane:*tert*-BuOK:**4** of 1:1:1, giving a 50% yield of **6a** after 60 min. In order to assess the participation of radicals and radical anions in these dark reactions, the following experiments were conducted under different conditions. The addition of 10 mol.% of *p*-dinitrobenzene (*p*-DNB), a well-known electron acceptor, caused a small inhibition of the reaction. However, in the presence of 1 equiv of *p*-DNB, the reaction was completely inhibited (Table 1, entries 5 and 6). Finally, when the reaction was performed to a minor conversion after only 5 min of stirring, the yield of **6a** was reduced from 30% to 9% by adding 10 mol.% of *p*-DNB, and was slightly catalysed by light (Table 1, entries 7–9). The effect of light and the inhibition results clearly indicate the participation of ET process in these reactions. On the other hand, in the presence of a very efficient radical trap such as di-*tert*-butylnitroxide (DTBN), there was no inhibition in these reactions (Table 1, entries 10 and 11). A possible oxidation of the dithiane anion **3** by DTBN may have taken place, thus avoiding inhibition.[38,39]

In view of the absence of the corresponding aldehyde, the possible formation of 1,3-propane dithiolate anion (**10**) by deprotection of the dithiane precursor of anion **3a** can be disregarded, during photochemically and thermally induced reactions. Furthermore, for the control experiment, the substitution product **6a** was added to a solution of anion **3a** in DMSO. Then, after stirring for 1 h the mixture was quenched with MeI.

Table 1. Dark reactions of anion 3a with neopentyl iodide (4) in DMSO[a]

| Entry | Conditions | | Product yield (%)[b] | | |
	3a:4:*t*-BuOK (eq)	Time (min)	I$^-$	6a	7[c]
1[d]	3:1:6	60	82	42	7
2	3:1:6	60	81	42	4
3	3:1:3	60	76	51	10
4	1:1:1	60	60	50	3
5[e]	3:1:6	60	84	32	14
6[f]	3:1:6	60	9	0	0
7	1:1:1	5	62	30	8
8[e]	1:1:1	5	20	9	3
9[d]	1:1:1	5	49	43	7
10[g]	3:1:6	60	79	43	9
11[h]	3:1:6	60	81	32	7
12[i]	1:—:1	60	—	92	—
13[d,i]	—:—:1	180	—	90	—
14[i,j]	—:—:3	180	—	24	[k]
15[l]	3:1:6	180	35	10	—
16[l]	3:1:6	180	—	—	—

[a] Under nitrogen atmosphere, at room temperature; [**3a**] $= 0.3$ M (ratio **3a:4** $= 3:1$ or 1:1 as indicated). This reaction was quenched with NH$_4$NO$_3$.
[b] Product yield determined by CG using the internal method, error $<5\%$, and iodide ions potentiometrically.
[c] Together with **8a** and **9a**, detected by GC-MS but not quantified ($<5\%$).
[d] Under irradiation, $\lambda_{max} > 350$ nm.
[e] In the presence of 10 mol.% of *p*-DNB.
[f] In the presence of 1 equiv of *p*-DNB.
[g] In the presence of 14 mol.% of DTBN.
[h] In the presence of 1 equiv of DTBN.
[i] Control experiment of **6a**, quenched by addition of MeI after irradiation.
[j] Under irradiation, $\lambda_{max} = 300$ nm using a quartz tube.
[k] Hydrocarbons **8** and **9** were quantified by GC, showing yields of 38% and 26%, respectively.
[l] Performed in NH$_3$ (liq) at $-33\,°$C with [**3a**] $= 0.012$ M, and quenched by the addition of MeI after the indicated time.

From this mixture, **6a** was recovered at a 92% yield, showing no evidence of 1,3-bis(methylthio)propane being detected. Finally, when product **6a** was irradiated at $\lambda_{max} > 350$ nm for 3 h in the presence of 1 equiv of *tert*-BuOK and then quenched with MeI, **6a** was recovered at a 90% yield revealing no trace of other products being detected by GC-MS (Table 1, entries 12 and 13). These control experiments clearly point out the stability of **6a** in the presence of an excess of anion **3a**, even after irradiation with *tert*-BuOK under the photoinduced reaction conditions used in the present study. In order to force the reduction of **6a**, a solution of this dithiane in the presence of 3 equiv of *tert*-BuOK was irradiated at $\lambda = 300$ nm, using a quartz tube. After 3 h, hydrocarbons **8a** and **9a** were obtained at 38% and 26% yields, respectively; dithiane **6a** recovered at a 24% yield (Table 1, entry

14). Finally, liquid ammonia ($-33\,^{\circ}$C) was tested as a solvent. After 3 h of irradiation, a mixture of anion **3a** with iodide **4** was quenched with MeI, resulting in only the substitution product **6a** being obtained (10% yield), where derivative **7** was not observed. This reaction was completely inhibited in the dark (Table 1, entries 15 and 16).

The formation of the secondary substitution product **7** by the reaction of iodide **4** with the 1,3-propane dithiolate anion (**10**), generated in the reaction medium (see results above) was unequivocally confirmed by a series of independent experiments (Eqn 5, supplementary material, Table S1). The reaction between **4** and **10** was thermally induced, occurred very fast (within <5 min) and was slightly catalysed by light. The ET ability of lithium thiolate ions towards alkyl iodide has been previously established; from the above results and the low reactivity of neopentyl halides in the polar process, the participation of an ET reaction is the main plausible mechanism to account for the formation of the derivative **7**.[32]

(5)
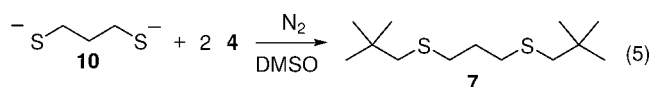
Reaction of 2-phenyl-1,3-dithiane anion (3a) with radical probe iodides 2 and 5 in DMSO

The rearrangement of the neophyl radical (**11**) to a tertiary radical **12** ($k_r = 4.02 \times 10^2\,s^{-1}$)[40] and also the cyclisation of the 2,2-dimethyl-5-hexenyl radical (**13**) to the cyclopentylmethyl radical **14** ($k_c = 3.6 \times 10^6\,s^{-1}$)[41] are well-known processes, with the Arrhenius functions for both reactions determined previously,[42,43] In order to investigate the presence of free radicals, the photoinduced reactions between anion **3a** and neophyl iodide (**5**) and the neopentyl-type probe **2** were carried out in a nitrogen atmosphere. The reactions of iodide **5** with anion **3a** were performed under different concentrations and nucleophile:substrate ratios, but afforded only the unrearranged product **15** (Eqn 6, Table 2, entries 1 and 2). The fact that no rearranged product was observed could arise from a nucleophilic addition rate to radical **11** occurring faster than that of radical rearrangement.[30]

(6)
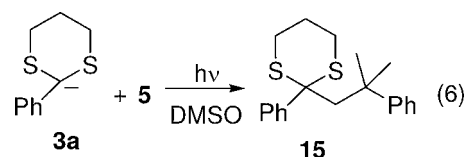
On the other hand, the reaction between **3a** and iodide **2** gave a 53% yield of the un-cyclised substitution product **16**, while the cyclised derivative **17** was not detected. The secondary product **18**, produced from substitution of iodide **2** with the 1,3-propane dithiolate anion (**10**) that was generated in the reaction medium, was obtained at a 10% yield (Eqn 7, Table 2, entry 3).[44] However, when the reaction was performed with a ratio substrate:nucleophile of 2:1 in a 10-fold more diluted solution, it was possible to observe, both the un-cyclised and cyclised substitution products **16** and **17**, respectively, together with **18** (Table 2, entry 4). Similar cyclised and un-cyclised derivatives were previously observed in the dark reaction of dithiane anion **1** with iodide **2**, (Scheme 2).[25]

(7)
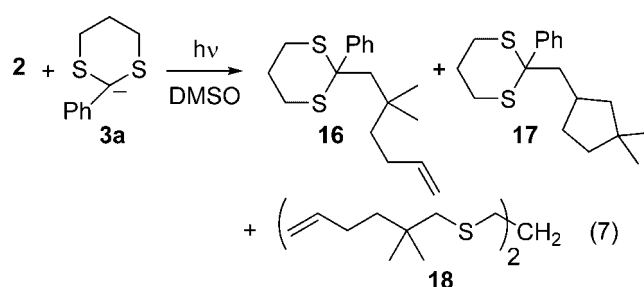
Reaction with other 2-aryl-1,3-dithiane anions (3b–d) in DMSO

The reactivity of iodide **4** towards the anions from 2-(4-*Z*-phenyl)-1,3-dithiane (**3b–d**, *Z* = OMe, Cl, CN) was also studied. In the reaction between iodide **4** and the *para*-OMe substituted anion **3b**, the major product found was the substitution one (**6b**) in the dark and under irradiation (Table 3, entries 1 and 2). The behaviour of anion **3b** was comparable to that of anion **3a**. However, the photoinduced reaction of **4** with anion **3d** (*Z* = CN) after 3 h afforded a 19% yield of the substitution product (**6d**) and a 20% yield of **7**, together with 4-(3,3-dimethylbutyl)benzonitrile

Table 2. Reactions of anion 3a with neophyl iodide (5) and 5-(iodomethyl)-5-methyl-1-hexene (2) in DMSO[a]

			Product yield (%)[b]			
Entry	Substrate	3a/substrate (M)	**15**	**16**	**17**	**18**[c]
1	**5**	0.3/0.1	10			
2	**5**	0.1/0.1	26			
3	**2**	0.15/0.1		53	[d]	10
4	**2**	0.021/0.012		19	5	15

[a] Irradiation for 3 h under nitrogen atmosphere. This reaction was quenched with NH$_4$NO$_3$.
[b] Determined by CG using the internal method, error <5%.
[c] Together with the reduced product analogous to **8** and **9**, which were detected by GC-MS but not quantified.
[d] Not detected.

Table 3. Reactions with other derivatives 2-aryl-1,3-dithiane anions with substrate 4 in DMSO[a]

Entry	Anion	Product yield (%)[b]		
		6	7	6/7
1	**3b** (OMe)	42 (**6b**)	4	10
2[c]	**3b**	41 (**6b**)	<5	—
3	**3c** (Cl)	22 (**6c**)	10[d]	2
4[c]	**3c**	13 (**6c**)	—	—
5	**3d** (CN)	19 (**6d**)	20[e]	1
6[c]	**3d**	9 (**6d**)	—	—

[a] Irradiation for 3 h under nitrogen atmosphere, at room temperature; [**3**] = 0.3 M (ratio **3:4** = 3:1). This reaction was quenched with NH$_4$NO$_3$.
[b] Determined by CG using the internal method, error <5%.
[c] Dark reaction.
[d] Together with **8c**, detected by GC-MS but not quantified.
[e] Together with **8d**, detected by GC-MS but not quantified.

(**8d**), which was detected by GC-MS but not quantified. This reaction was strongly inhibited in the dark, with only 9% yield of **6d** being quantified after 3 h. For the *para*-Cl substituted anion **3c**, the substitution **6c** and the fragmentation product **7** were obtained under irradiation, while this reaction was partially inhibited in the dark (Table 3, entries 3–6).

Mechanistic Consideration

The occurrence of the reaction between anions **3** and **4** in the dark, and the inhibition by *p*-DNB strongly suggest the participation of a spontaneous or thermal ET as a possible initiation for a chain reaction, which is light catalysed, and imply the involvement of radical anions as intermediates. The latter is undoubtedly supported by the presence of the desulphurised hydrocarbons **8a,b** and **9a** and the disubstitution product **7** from reaction between iodide **4** and 1,3-propanedithiolate dianion (**10**), as minor products. These secondary products (**8–10**) arose from fragmentation of the radical anion intermediate of the primary substitution product (**6a**$^{\bullet-}$). The stability of the primary product **6a** under the reaction conditions has been shown by different control experiments. Finally, C–S bond fragmentation was avoided when the reaction was performed in liquid ammonia (−33 °C) under photostimulation, attributed to stabilisation of the radical anion intermediate by lowering 60° the reaction temperature. Although the radical trap DTBN showed no inhibition of these reactions,[35] the participation of free radicals as intermediates was established by the observation of the cyclised substitution product (**17**) in the reaction of the radical-type probe **2** and anion **3a**. Thus, a radical substitution S$_{RN}$1 mechanism is proposed to account for all the results described above and is presented in Scheme 3. After initial interaction between anion **3a–d** and iodide **4**, an ET occurs as the initial step A of the process, with formation of the alkyl radical **19**. These free alkyl radicals (**19**) add to the anion to afford the radical anion of the primary substitution product (**6a–d**$^{\bullet-}$), this following two competitive reaction channels: pathway B, ET to the substrate affords the substitution product (**6a–d**) and the alkyl radical **19**, the latter being able to continue with the chain

propagation of the reaction; and pathway C, the radical anion (**6a–d**$^{\bullet-}$) intermediate can cleave by fragmentation of the C–S bond to provide a distonic radical anion **20**. By subsequent hydrogen abstraction, reduction and fragmentation, **20** gives the dianion **10** and the alkyl radical **21**. Disproportionation of **21** affords hydrocarbons **8** and **9**, while the secondary substitution reaction between anion **10** and iodide **4** yields the disubstitution product **7** (Scheme 3).

The different reactivity observed in the reactions of iodide **4** with anions **3a–d** gives further support to the mechanism proposed. The ET from anions **3a–d** to **4** depends mainly on the oxidation potential of the anion, which determines its ability as an electron donor. Bordwell *et al.* developed a linear correlation of E_{ox} (A$^-$) versus pK_{HA}, with slopes near unity, which established the presence of an intrinsic relationship between the oxidation potential of carbanions and their equilibrium acidities in DMSO. These authors showed that for an increase in the ion basicity, there was an E_{ox} (A$^-$) shift to a more negative potential. In general, it has been observed that the higher the pK_{HA}, the higher the electron donor capability of its conjugate base, and consequently the higher the probability of a spontaneous ET reaction.[45–47] Our experimental data reveal that the electron donor ability of anions **3** followed the order: **3a** = **3b** > **3c** > **3d**. Unfortunately, there have been no pKa values reported for dithiane **3b–d**, the electron donor ability order observed was in good agreement with the Hammett σ substituent constant: OMe: −0.28; Cl: 0.24 and CN: 0.65, as expected.[48]

The competition between ET and the C–S bond fragmentation pathways (B and C, respectively), could be measured by the **6:7** ratio, and followed the order: CN: 1; Cl: 2; OMe: 10. This trend agrees with the stability order of the distonic radical anions **20a–d**, the Cl and CN derivatives being further stabilised by a captodative effect.[49,50]

The results obtained for the photostimulated reaction of anion **3d** with the aryl substrates are mechanistically interesting.[51] In these reactions, the fragmentation step was the most favoured pathway. For example, when the anion **3d** (3 equiv) reacted with IPh (**22**) under irradiation, the substitution product 4-(2-phenyl-1,3-dithian-2-yl) benzonitrile (**23**) was found at a 7% yield with the fragmentation products 4-benzylbenzonitrile (**24**) (17%), thiophenol[52] (4%), and 3-mercaptopropylthio derivative **25** (4%), and also with other minor products that could not be separated or identified satisfactorily (Eqn 8). This result can be explained by considering the stability of the distonic radical anion arising from the fragmentation step of **23**$^{\bullet-}$ (analogous to **20**, pathway C, Scheme 3, and confirmed by isolation of product **25**). There was no reaction in the dark, but the photoinduced reaction in the presence of substrate **22** in excess (5 equiv) afforded the substitution product **23** and the fragmentation product **24** with yields of 14% and 4%, respectively. As expected, under the latter conditions, a rise in the concentration of the electron acceptor (PhI) increased the rate of the intermolecular ET and competed efficiently with the fragmentation step.
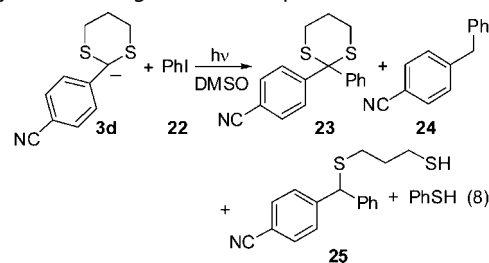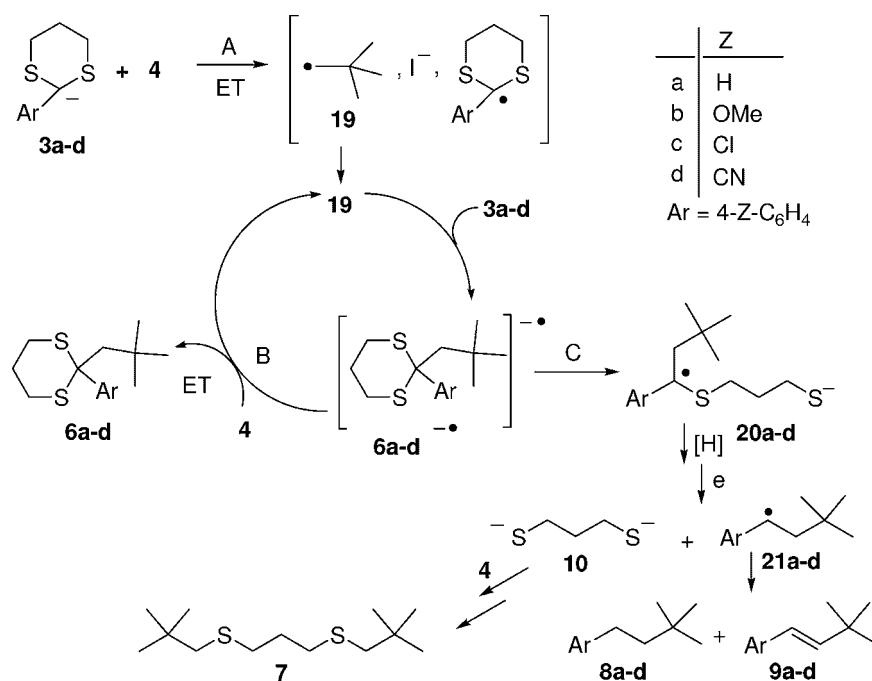
Scheme 3. $S_{RN}1$ reaction between 2-aryl-1,3-dithiane anions (**3a–d**) and neopentyl iodide (**4**).

CONCLUSIONS

Neopentyl iodide (**4**) reacted with dithiane anions **3a–d** by a $S_{RN}1$ mechanism with radicals and radical anions as intermediates. The occurrence of this mechanism was suggested mainly from observation of the products from the C–S bond fragmentation of the radical anion of the substitution product. Due to the fact that the fragmentation process of the intermediate radical anion was a competitive reaction, the chain may have been short or even non-existent. As a consequence, the yields of the substitution product for the reactions between dithianes anions substituted with electron-donor substituents **3a,b** with neopentyl and their analogue iodides were moderate (41–53%) in DMSO. On the other hand, in liquid ammonia the fragmentation was avoided, but as the initiation of the reaction was not effective enough, the performance of the reaction was poor.

On the basis of our findings, further studies are currently in progress in order to develop this photoinduced reductive process of dithiane derivatives as an environmentally friendly alternative to the current reduction methodologies for the de-oxygenation of carbonyl groups.

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