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Radical-chain Addition of Benzenethiol to Allenic Esters: EPR and Product Studies

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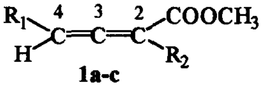
Abstract: The radical-chain addition reaction of benzenethiol to allenic esters has been examined. The reaction products have been separated and identified by means of ^{1}H NMR and mass spectrometry, and the radical intermediates detected by EPR spectroscopy.

In the course of our current studies on the reactivity of allenes,[1] we reported a new method for preparing heterocyclic compounds by reacting a class of allenic esters with disubstituted benzenes under ionic conditions.[2] In order to get a better insight on the behaviour of these compounds we report here an examination of their reactivity towards benzenethiol under free radical conditions.

The addition of PhSH to several substituted allenes has been studied previously by other authors and interpreted as a radical-chain reaction.[3-11] The attack of the PhS• radical to the allenic system was essentially found to take place at the central allenic carbon, thus giving rise to a resonance stabilized allyl radical which, by hydrogen transfer from PhSH, afforded the observed reaction products. The alternative addition to one of the terminal carbon atoms of the allene moiety was found to take place to an almost negligible extent in the majority of the investigated derivatives, this being interpreted in terms of the much lower thermodynamic stability of the resulting vinyl with respect to the allyl radical. In one case, that of tetramethylallene,[8] the intermediate allyl radical, obtained by addition of the methylthiyl radical, MeS•, was detected and identified by EPR spectroscopy.

In the present paper we report the analysis of the products formed when reacting benzenethiol with the allenic esters **1a-c**, their identification using proton magnetic resonance and mass spectrometry, and the EPR detection of the intermediate radical adducts between the examined compounds and the PhS• radical.

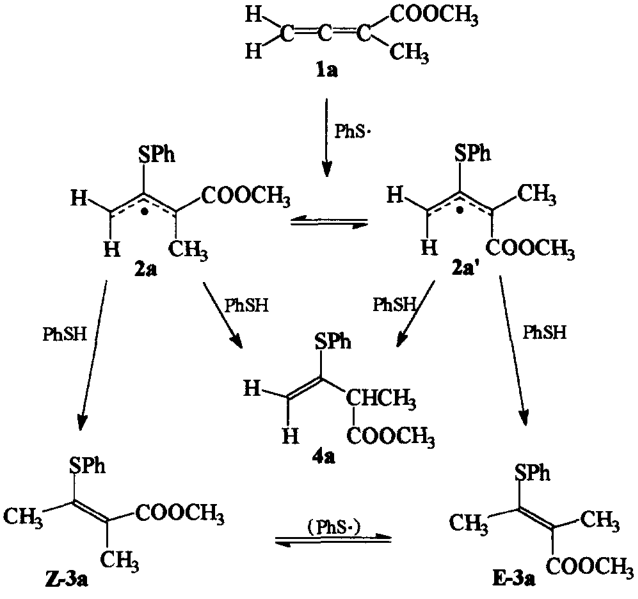


1a-c

1a: $R_1 = H$, $R_2 = CH_3$
1b: $R_1 = CH_3$, $R_2 = H$
1c: $R_1 = CH_3$, $R_2 = CH_3$

RESULTS AND DISCUSSION

All reactions between allenes **1a-c** and PhSH were carried out in refluxing benzene by using α,α'-azo-isobutyronitrile (AIBN) as radical initiator.[3] Compound **1a** afforded the products **E-3a**, **Z-3a** and **4a** in the ratio of 80:18:2 (determined by GC/MS). The products **E-3a** and **Z-3a** were separated by preparative HPLC and identified on the basis of their ^1H NMR spectra as follows: the signals due to the methyl groups linked to the olefinic bond show a splitting caused by the homoallylic coupling of 1.5 Hz in one and of 0.9 Hz in the other isomer. Since such coupling constants are generally larger for groups in the *anti* configuration,[12] we assigned the **E-3a** structure to the former and the **Z-3a** to the latter species.



Scheme 1

In addition, the chemical shift values of the same methyl groups are larger in the species we assigned the **E-3a** structure, this being consistent with their proximity to both the deshielding $COOCH_3$ and SPh groups. Compound **4a** was identified by its MS spectrum which showed the M^+ peak at 222 m/e and the major fragment at 135, attributed to the loss of $CH(CH_3)COOCH_3$.

The formation of these products can be explained in terms of the reactions outlined in Scheme 1, implying addition of phenylthiyl radicals to the central carbon of the allenic system to give either of the two isomeric allyl radicals **2a** and **2a'** which undergo hydrogen transfer from PhSH to afford the observed products. The reduced formation of **4a** with respect to **Z-3a** and **E-3a** can be explained in terms of steric hindrance to the hydrogen transfer reaction: in fact the presence of the methyl and carbomethoxy groups on C_2 of the intermediate radical makes the attack to this carbon less favourable than to C_4. We have not found even trace amounts of products resulting from the addition of PhS• to one of the terminal allenic carbons C_2 and C_4, in agreement with previous results.[11]

The final composition of the reaction mixture might give indication on the relative weight of the two intermediate radicals **2a** and **2a'**, and on the ease they undergo hydrogen transfer from PhSH. Since however phenylthiyl radicals were continuously generated in our experimental conditions, the possibility that their reversible addition to the olefins **Z-3a/E-3a** caused isomerization of the latter ones had to be considered.[11] To check if this was the case, pure samples of **Z-3a** and **E-3a** were reacted in refluxing benzene with AIBN and PhSH, *i.e.* under the same conditions used in the synthetic procedure. After four hours, GC analysis of the reaction mixture showed in both cases the presence of the two isomers **Z-3a** and **E-3a** in a ratio of 1:4. This indicates that interconversion of the two geometric isomers takes place under the employed reaction conditions and that the product distribution reflects only the relative thermodynamic stability of compounds **Z-3a** and **E-3a**.

We have also been able to detect by EPR spectroscopy the intermediate allyl radical formed by attack of PhS• to **1a**. The experimental conditions employed to observe the radical adduct were different from those used in the synthetic work. In fact, in the latter case the efficiency of the process, *i.e.* the yield of the reaction, is strictly related to the lenght of the radical chain which in turn depends on the ease by which hydrogen transfer from the thiol to the intermediate allyl radical occurs. On the other hand, in order to obtain a high radical concentration in the EPR experiment, the radical chain reaction should be suppressed; this can be achieved by using diphenyl disulfide as a photolytic source of phenylthiyl radicals.

The hyperfine coupling constants and *g*-factors measured for the PhS• adduct to **1a**, reported in Table 1, are characteristic of the substituted allyl radical shown in Scheme 1.

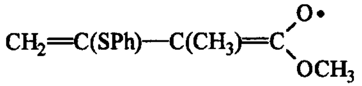
Table 1. EPR Spectral Parameters of the Paramagnetic Adducts Obtained by Reacting PhS• Radical with Allenes **1a-c**.

Radical from	Hyperfine splitting constants (Gauss=10^{-4}T)	*g*-factor
1a	$CH_2 \overset{\cdots}{=} \overset{\bullet}{C}(SPh) \overset{\cdots}{=} C(CH_3)COOCH_3$ 11.58 16.21 0.75 12.60	2.0031
1b	$CH_3CH \overset{\cdots}{=} \overset{\bullet}{C}(SPh) \overset{\cdots}{=} CHCOOCH_3$ 15.24 12.55 13.46 0.93	2.0031
1c	$CH_3CH \overset{\cdots}{=} \overset{\bullet}{C}(SPh) \overset{\cdots}{=} C(CH_3)COOCH_3$ 12.92 10.64 16.36 0.77	2.0030

It should be pointed out that althought this radical might exist in two different conformations, no distinct signals from the two isomers were observed in the EPR spectrum. Several EPR studies[13-19] have shown that the rotational barrier in allyl radicals is large enough (> ca. 15 kcal mol^{-1}) to allow the conformational isomers to be simultaneously observed at or below room temperature. In this case no evidence for the presence of the two possible conformers was found even by lowering the temperature at -50°C.

However, given the poor signal to noise ratio, the second isomer might be present at concentrations lower than 15-20% without being detected. Moreover, it is also possible that the small differences expected in the spectra of the two species are hidden by the unusually large EPR line width (ca. 0.5 G), presumably due to unresolved coupling with the protons of the phenylthio group. In any case, the spectral parameters did not allow us to identify which of the two isomeric radicals **2a** and **2a'** is that one detected. On the basis of the greater stability of olefin **E-3a** with respect to **Z-3a**, we may only tentatively infer that radical **2a'**, having the PhS and $COOCH_3$ groups *anti*, is more stable than **2a**.

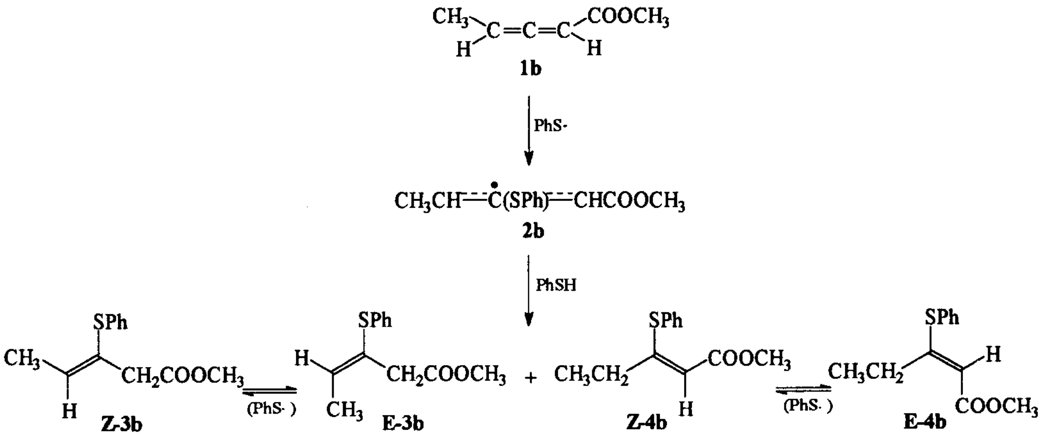
When comparing the spectral parameters measured in the radical from **1a** with those reported for allyl,[19] it appears that the hyperfine coupling constants at the two protons linked to C_4 are reduced from 14.84 and 13.92 G to 12.60 and 11.58 G upon substitution. This indicates that in the radical from **1a** the spin density is slightly more delocalized on C_2 than on C_4 and/or that a mesomeric structure such **A** bearing the unpaired electron on the carbonyl oxygen is of some importance.



$$CH_2{=}C(SPh){-}C(CH_3){=}C\begin{matrix}O\bullet\\ OCH_3\end{matrix}$$

A

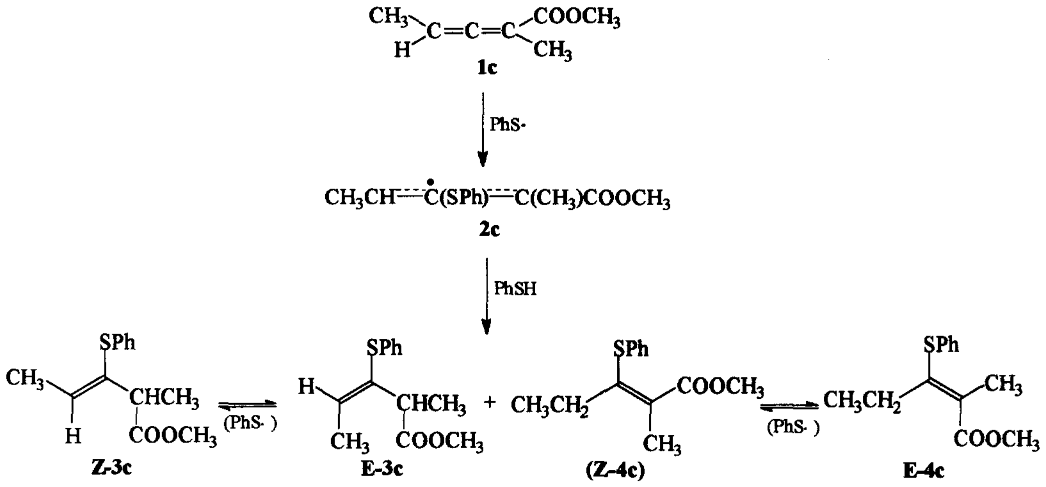
Compound **1b** afforded all the four possible isomeric products in the ratio of 38:23:34:5 (GC/MS). We assigned to these species structures **Z-3b**, **E-3b**, **E-4b** and **Z-4b**, respectively (Scheme 2), by analyzing the ^1H NMR spectrum of the mixture of the four products.



Scheme 2

The structural assignment of the two geometric isomers **Z-3b** and **E-3b** was made by comparing the relative magnitudes of the allylic (^4J) and homoallylic (^5J) coupling constants. The quartet due to the vinylic hydrogen was further split into a triplet of 0.9 Hz in one isomer and of 0.5 Hz in the other one, attributable to the allylic coupling with the CH_2 group. Since the values of the allylic coupling constants (^4J) between groups in the *syn* conformation are larger than in the *anti*[12] we assigned the geometry **Z-3b** to the species showing the 0.9 Hz splitting and the geometry **E-3b** to the other one. Consistent with this assignment was also the magnitude of the homoallylic coupling with the CH_2 groups observed in the signals due to the CH_3 group directly linked to the double bond, which is larger in **Z-3b** (1.2 Hz) than in **E-3b** (0.9 Hz). The couple of isomers **Z-4b** and **E-4b** were identified on similar bases; here the signal due to the vinylic hydrogen was split into a triplet, J 0.9, by an allylic coupling with the CH_2 group in **Z-4b** while in **E-4b** no splitting was measurable.

Compound **1c** afforded three products, in the ratio of 40:3:57 (GC/MS), which were assigned structures **Z-3c**, **E-3c** and **E** (or **Z**)**-4c**, respectively (Scheme 3).



Scheme 3

The two isomers **Z-3c** and **E-3c**, separated by flash-chromatography and obtained as a mixture, were identified on the basis of their ^1H NMR spectra. The signal due to the vinylic hydrogen in the major component of the mixture showed a splitting of 0.9 Hz attributable to an allylic coupling with the CH group directly linked to the olefinic bond, while the corresponding signal in the other isomer showed no splitting. Since allylic coupling constants are generally larger in the *syn* geometry,[12] we assigned the structure **Z-3c** to the more abundant isomer. This assignment was further supported by the fact that, in the latter compound, the signal due to the CH_3 group directly linked to the olefinic bond showed a splitting of 0.6 Hz attributable to an homoallylic coupling with the *anti* CH group;[12] such a coupling is not detectable in the other isomer.

The other isolated compound showed a ^1H NMR spectrum consistent with either of the two geometries **Z-4c** and **E-4c**. On the basis of the larger stability of the homologous isomeric olefins formed from **1a** and **1b** where the PhS and $COOCH_3$ are *anti* (**E-3a** and **E-4b**), we tentatively assign structure **E-4c** to this species.

Also with allenes **1b** and **1c** photolytic reaction with PhSSPh in degassed benzene solution within the EPR cavity, afforded the EPR spectra of the corresponding allyl adducts (**2b** and **2c**) with PhS• radicals. As an example, Figure 1 shows the spectrum of radical **2c**. As previously stated for the radical from **1a**, also in these two cases no signals due to different conformational isomers could be detected, although we can not discarde the possibility that a 15-20% of a second isomer is present. The measured coupling constants are reported in Table 1 together with the assignment to the various protons. It should be mentioned that in radical **1b** the assignment of the 12.55 and 13.46 G splittings may be interchanged. Also in these two cases the spin density distribution is similar to that one reported for the unsubstituted allyl radical,[19] apart from a slight increase on C_2, i.e. the carbon atom directly linked to the estereal group.

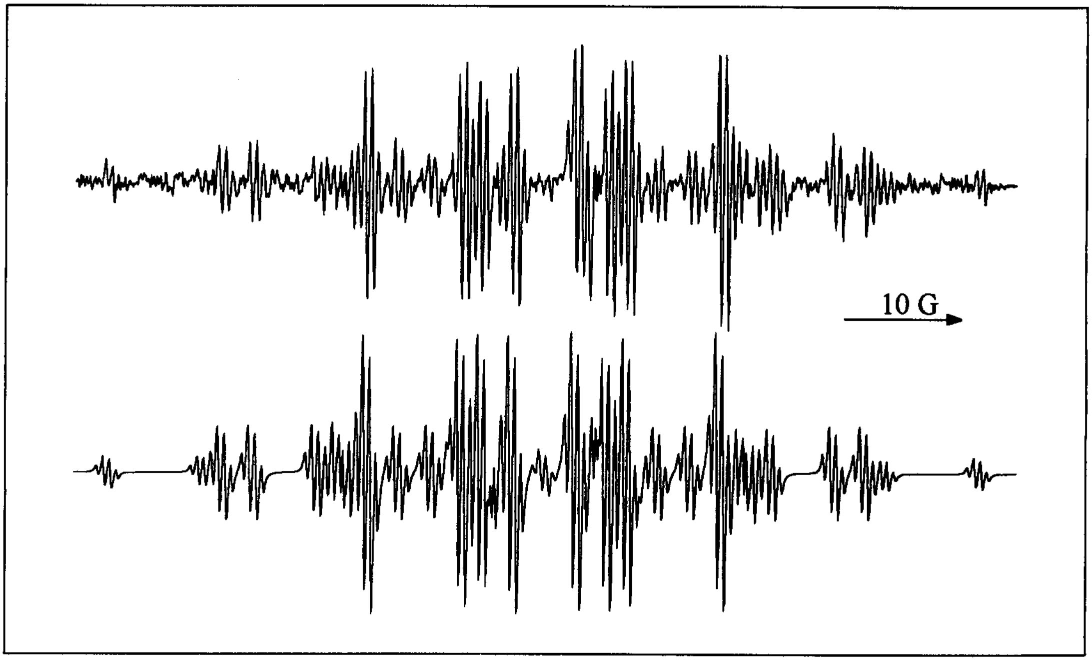


Figure 1. Experimental (top) and computer simulated (bottom) EPR spectrum of radical **2c** obtained by photolysing a deoxygenated benzene solution of **1c** in the presence of PhSSPh at room temperature.

EXPERIMENTAL

Compounds **1a-c** were prepared by literature methods.[20] Benzenethiol and AIBN were purchased from Aldrich. ^1H NMR spectra were recorded on a Varian VXR-300 spectrometer using $CDCl_3$ as solvent and TMS as internal standard. GC/MS analyses were performed at 70 eV with a Hewlett Packard 5989A GC/MS system with HP 5890 GC fitted with a capillary column (50 m x 0.2 mm) packed with DH 50.2 Petrocol (0.50 μm film thickness). The preparative HPLC was performed by using a Waters 600 apparatus with an ODS column (10 x

250 mm) and UV detector, using methanol-water (4:1) as eluent. Flash-chromatographies were performed on silica G60 (Merck) columns.

The EPR spectra were recorded by means of a Bruker ESP 300 spectrometer equipped with an NMR gaussmeter and a frequency counter. The measured *g* factors were corrected with respect to that of the radical cation of perylene in concentrated sulfuric acid (2.00258).

The radicals were generated by UV photolysis of diphenyl disulfide in deoxygenated benzene or toluene (for low temperature experiments) within the cavity of the spectrometer, in the presence of the allenic compound. The UV light source was a 500 W high pressure mercury lamp.

*General procedure for the addition of benzenethiol to the compounds **1a-c***[3]

To a solution of the allenic compound (0.03 mol) and AIBN (3-5% molar) in benzene (30 ml) was added 1 mol equiv of benzenethiol (0.03 mol, 3.3 g) and the mixture was stirred under reflux for 4 hours. After cooling at room temperature, the mixture was poured into water, extracted with diethyl ether, the organic layer was washed with 10% NaOH to remove the unreacted thiol and then dried (Na_2SO_4). The solvent was evaporated and the crude product was analyzed by GC/MS. Then the mixture was flash-chromatographed (hexane) or separated by HPLC.

*Reaction of **1a***

GC/MS analysis of the reaction mixture showed the presence of three compounds, **Z-3a** (18%), **E-3a** (80%) and **4a** (2%), m/e 222 (M^+). **Z-3a**: ^{1}H NMR δ 1.80 (3H, q, J 0.9 Hz, CH_3), 1.95 (3H, q, J 0.9 Hz, CH_3), 3.76 (3H, s, OCH_3), 7.35 (5H, m, Ar-H). **E-3a**: ^{1}H NMR δ 2.06 (3H, q, J 1.5 Hz, CH_3), 2.10 (3H, q, J 1.5 Hz, CH_3), 3.71 (3H, s, OCH_3), 7.20 (5H, m, Ar-H). **4a**: MS, m/e 222 (M^+, 18), 163 (M^+-$COOCH_3$, 10), 135 (M^+-$C_4H_7O_2$, 73), 110 ($PhSH^+$, 19), 88 ($C_4H_8O_2^+$, 100).

*Reaction of **1b***

GC/MS analysis of the reaction mixture showed the presence of four compounds: **Z-3b** (38%), **E-3b** (23%), **E-4b** (34%), **Z-4b** (5%), m/e 222 (M^+). **Z-3b**: ^{1}H NMR δ 1.89 (3H, double triplet, J 6.9, 1.2, CH_3-CH), 3.17 (2H, m, CH_2), 3.57 (3H, s, OCH_3), 6.10 (1H, triple quartet, J 6.9, 0.9, CH_3-*CH*), 7.25 (5H, m, Ar-H). **E-3b**: ^{1}H NMR δ 1.76 (3H, double triplet, J 7.2, 0.9, CH_3-CH), 3.22 (2H, m, CH_2), 3.60 (3H, s, OCH_3), 6.17 (1H, triple quartet, J 7.2, 0.5, CH_3-*CH*), 7.30 (5H, m, Ar-H). **E-4b**: ^{1}H NMR δ 1.23 (3H, t, J 7.3, CH_3), 2.82 (2H, q, J 7.3, CH_2), 3.55 (3H, s, OCH_3), 5.10 (1H, s, CH), 7.40 (5H, m, Ar-H). **Z-4b**: ^{1}H NMR δ 1.04 (3H, t, J 7.3, CH_3), 2.52 (2H, double quartet, J 7.3, 0.9, CH_2), 3.42 (3H, s, OCH_3), 5.82 (1H, t, J 0.9, CH), 7.35 (5H, m, Ar-H).

*Reaction of **1c***

GC/MS analysis of the reaction mixture showed the presence of three compounds: **Z-3c** (40%), **E-3c** (3%) and **E-4c** (57%), m/e 236 (M^+). **Z-3c**: ^{1}H NMR δ 1.33 (3H, d, J 7.3, CH_3-CH), 1.89 (3H, dd, J 6.6, 0.6, CH_3-CH=C), 3.34 (1H, m, CH_3-*CH*), 3.58 (3H, s, OCH_3), 6.22 (1H, double quartet, J 6.6, 0.9, CH_3-*CH*=C), 7.20 (5H, m, Ar-H). **E-3c**: ^{1}H NMR δ 0.98 (3H, d, J 6.6, CH_3-CH), 1.80 (3H, d, J 7.2, CH_3-CH=C), 3.51 (3H, s, OCH_3), 3.72 (1H, q, J 6.6, CH_3-*CH*), 6.04 (1H, q, J 7.2, CH_3-*CH*=C), 7.20 (5H, m, Ar-H). **E-4c**: ^{1}H NMR δ 1.01 (3H, t, J 7.2, CH_3-CH_2), 2.12 (3H, t, J 0.6, CH_3), 2.45 (2H, m, CH_3-CH_2), 3.75 (3H, s, OCH_3), 7.30 (5H, m, Ar-H).

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