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Reactions of nitric oxide and nitrogen dioxide with functionalised alkenes and dienes [†]

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Pure nitric oxide does not add to alkenes containing acceptor or donor substituents, or to conjugated dienes, to afford β-nitrosoalkyl radicals. EPR spectra show that reactions are initiated by NO_2 addition to carbon–carbon double bonds to produce β-nitroalkyl radicals which combine with nitric oxide to yield β-nitro-nitroso-compounds. The latter trap other radicals to afford mixtures of aminoxyl radicals and, where possible, the nitroso-compounds tautomerise to oximes which oxidise to iminoxyl radicals. EPR spectra obtained on reaction of NO–NO_2 mixtures with 2,5-dimethylhexa-2,4-diene have shown the presence of a di-*tert*-alkylaminoxyl plus a *tert*,*sec*-dialkylaminoxyl, providing good support for this mechanism. Product analyses have established that 2-oxo-4-methylpent-3-ene and 1-acetylcyclohexene undergo extensive oxidative degradation. For enol ethers, reaction with NO–NO_2 leads to hydrolysis giving the corresponding carbonyl compound and alcohol, followed by ketal and ester formation.

Introduction

Although NO contains an unpaired electron, on the scale of free radical reactivity it lies at the low rate extremum for most reaction partners.[1] Addition of NO to an alkene, with formation of a β-nitrosoalkyl radical could be envisaged, but previous research showed that pure NO did not react with isobutene or similar alkyl-substituted olefins.[2–5] The main isolated products were found to be nitroalkenes and it was postulated that small amounts of NO_2, formed from the oxidation of NO [reaction (1)], added to the least sterically hindered end of the alkene

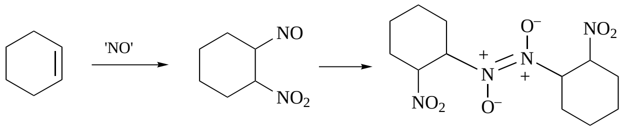
$$2NO + O_2 \longrightarrow 2NO_2 \qquad (1)$$

double bond to produce β-nitroalkyl radicals [equilibrium (2)]

$$NO_2 + CH_2{=}CR_2 \rightleftharpoons O_2NCH_2{-}C^{\bullet}R_2 \qquad (2)$$

which were converted in several steps to nitroalkenes. The NO_2 addition reaction was reversible because (*E*)-alkenes were converted to a mixture of (*E*)- and (*Z*)-isomers.[4]

The product of the reaction of purified NO with cyclohexene, under 7 atm pressure, was shown by X-ray crystallography[6] to be bis(1-nitroso-2-nitrocyclohexane) **1**, *i.e.* the dimer of the



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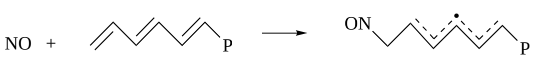
nitroso-compound formed by initial addition of NO_2 to cyclohexene and subsequent coupling of the β-nitrocyclohexyl radical with NO. Similar dimers were isolated from the reaction of NO with other alkenes.[6] The NO used in this study was purified from traces of NO_2 and it was shown, by identification of the by-product (N_2O), that the NO_2 arose from disproportionation of NO [reaction (3)]. Disproportionation was known[6,7] to be important at high pressures and this work showed that it was still significant at 7 atm pressure.

$$3NO \longrightarrow N_2O + NO_2 \qquad (3)$$

It is conceivable that direct addition of NO to an alkene or polyene might be favoured by the presence of a stabilising substituent, or by additional double bonds in the substrate because both of these situations lead to increased resonance stabilisation of the adduct radical by delocalization of the unpaired electron [reaction (4)]. To test this possibility we carried out a



(4)

study, by EPR spectroscopy and product analysis, of the reactions of pure NO and of NO–air mixtures with alkenes containing electron-withdrawing and electron-releasing substituents and with dienes. Recent reports have shown that aminoxyl radicals can be detected by EPR spectroscopy on the reaction of NO with dienes[8] and with β-carotene.[9] Contact between retinyl acetate, another substrate with conjugated double bonds, and NO also led to aminoxyl formation, but initiation by NO_2 in a reaction analogous to equilibrium (2) was postulated to account for the results.[10]

Results and discussion

The reaction of NO with several alkenes containing electron-withdrawing substituents was examined by bubbling the pure gas into previously degassed solutions of each alkene in benzene, cyclohexane or *tert*-butylbenzene at room temperature. Reaction of 2-oxo-4-methylpent-3-ene (mesityl oxide **2**) (20 cm^3 of 0.25 mol dm^{-3}) with NO was monitored by periodically withdrawing small samples (200 μl) and analysing them by EPR spectroscopy and GC–MS. In the complete absence of air no EPR spectra were obtained. However, when 2 cm^3 of air were introduced into the gas stream with a syringe, spectra due to three radicals appeared after about 0.5 h. The relative intensities of the three radicals depended on the reaction time and on the amount of air introduced. In Fig. 1, which shows the EPR spectrum after 5 h, the radicals are numbered 1–3, starting at low field. The EPR parameters of each species are recorded in Table 1. The spectra were similar to those observed by Fox *et al.*[11] from the reaction of NO_2 with mesityl oxide. The low-field line from radical 1 is shown under high resolution in Fig. 1(*b*) and the best fit hyperfine splittings (hfs) are given in Table 1. We observed the same three radicals when **2** was reacted directly

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Table 1 EPR parameters of radicals generated from the reaction of NO and unsaturated compounds[a]

	Radical					
Substrate	No.	Struct.[b]	Type	*g*-Factor	*a*(N)/G	*a*(other)/G
2	1	**8a**	(*E*)-Iminoxyl	2.0055	30.0	1.75 (3H), 1.22 (3H), 0.49 (3H)
2	2	**8b**	(*Z*)-Iminoxyl	2.0055	27.6	~0.1 (>8 lines)
2	3	**7**	Acylaminoxyl	2.0070	7.1	1.6 (1H)
10	4		Di-*tert*-alkylaminoxyl	2.0060	14.3	
10	5		Acylaminoxyl	2.0055	7.8	0.9 (1H)
12	6		Alkoxyaminoxyl	2.0040	29.5	
12	7		Di-*tert*-alkylaminoxyl	2.0060	13.6	
13	8	**17**	Di-*tert*-alkylaminoxyl	2.0060	15.5	
13	9	**18**	*tert*,*sec*-dialkylaminoxyl	2.0060	14.6	10.8 (1H)

[a] 10 G = 1 mT. [b] Tentative structural assignments; see text.

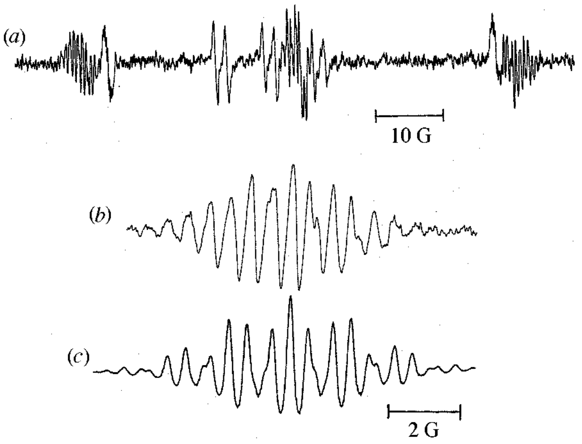
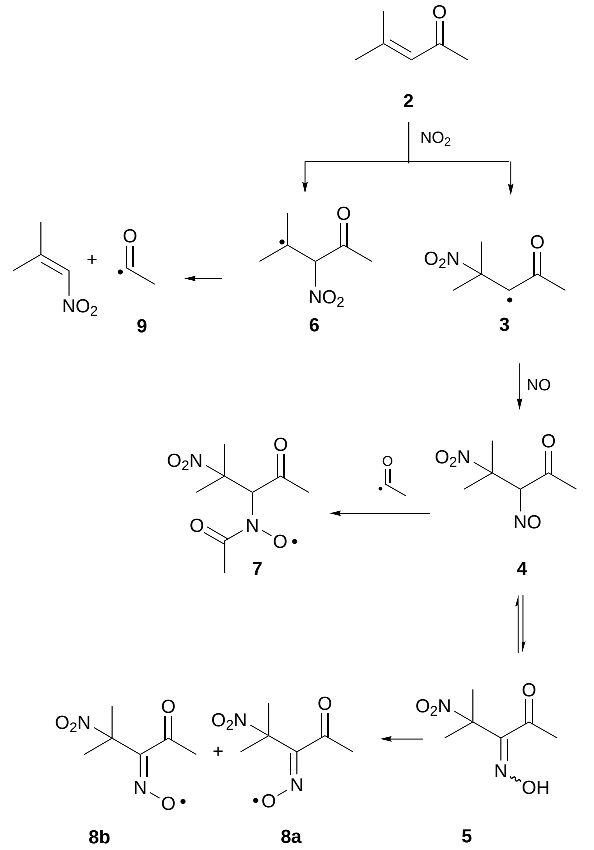


Fig. 1 9.2 GHz EPR spectrum of radicals formed in the reaction of NO with mesityl oxide (**2**) in cyclohexane at room temperature after introduction of air. (*a*) Complete spectrum (first derivative), (*b*) low field multiplet on an expanded scale with second derivative presentation, (*c*) computer simulation with hfs from Table 1.

with NO_2. The magnitudes of their *g*-factors and nitrogen hfs suggest that radicals 1 and 2 are (*E*)- and (*Z*)-iminoxyls **8a** and **8b** respectively (Scheme 1).

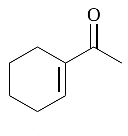
When a solution of mesityl oxide oxime in di-*tert*-butyl peroxide was photolysed in the resonant cavity of the EPR spectrometer, spectra due to an (*E*/*Z*) pair of iminoxyl radicals were obtained. As expected, these were only slightly different from the spectra of radicals 1 and 2, having larger *a*(N) values (that of the major isomer was 33.0 G) and different fine structure (unresolved). This finding supported our assignment of structures **8a**,**b**, to the iminoxyl radicals derived from the NO–**2** reaction. Furthermore, the resolved hfs from **8a** (Table 1) indicated coupling of the unpaired electron with three non-equivalent methyl groups, as required by structure **8**. The NO–**2** reaction was also carried out in CH_3CN solution but no well-defined spectra were obtained.

A mechanism to account for the initial stages of the reaction is shown in Scheme 1. By analogy with previous work[6] initiation occurs by addition of NO_2 to the carbon–carbon double bond, followed by coupling of the β-nitroalkyl radical **3** with NO to afford the nitroso-compound **4**. The latter will exist in tautomeric equilibrium with the pair of oxime conformers **5** which will be easily oxidised (*e.g.* by hydrogen abstraction with NO_2, or any other radical) to produce the pair of long-lived iminoxyl radicals **8a**,**b** which are detected by EPR spectroscopy. In competition with this, nitroso-compound **4** can couple with other radicals to generate persistent aminoxyl radicals. Coupling of **4** with an acetyl radical **9** will produce the acylaminoxyl **7**. This species will have a comparatively small *a*(N) value of *ca.* 7 G and should show coupling to a single β-hydrogen, *i.e.* this corresponds to radical 3 in Table 1. The acetyl radical **9** might be formed by addition of NO_2 to C(3) of mesityl oxide giving adduct radical **6** which could undergo β-scission to afford **9** and a nitroalkene (Scheme 1). Attempts to confirm this mechanism by product analysis were not successful. The GC–MS analyses showed a large number (>25) of volatile, mostly carbonyl-containing products, but none could be identified with certainty. Evidently the radicals and other components shown in Scheme 1 undergo extensive oxidative degradation.



Scheme 1

When similar reactions of NO with 1-acetylcyclohexene **10** (20 cm^3 of 0.20 mol dm^{-3} solution in cyclohexane) were carried out, no EPR spectra were obtained in the absence of air. However, when 2 cm^3 of air was introduced into the NO stream, spectra due to a di-*tert*-alkylaminoxyl (radical 4) and an acylaminoxyl (radical 5) were observed (Table 1). It is probable that the first two steps of the reaction with **10** are analogous to



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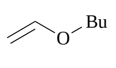

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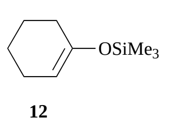

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those with **2**, *i.e.* addition of NO_2 followed by coupling with NO to give a nitroso-compound which, in this instance, will be tertiary so that oxime tautomers are not possible. This explains the absence of iminoxyl signals in the EPR spectra. The nitroso-compound can either pick up another *tert*-radical to give a di-*tert*-alkylaminoxyl (radical 4) or can pick up an acetyl radical, formed by a route analogous to that shown in Scheme 1, to produce acylaminoxyl, radical 5. Analysis of the product mixtures by GC–MS and NMR spectroscopy showed that a large number of carbonyl-containing components were present, but none could be identified with certainty.

The effect of four acceptor substituents on the NO addition reaction was examined using tetracyanoethene. No radicals were detected, even after 4 days contact of this substrate with NO in CH_3CN; GC–MS and NMR analysis also showed only unreacted starting materials. When the reaction was carried out in methanol, again no paramagnetic species were detected. After 24 h reaction GC–MS and NMR analysis showed a single product, $(CN)_2C{=}C(CN)OMe$, presumably formed *via* a nucleophilic reaction of the solvent with the substrate.

Two substrates containing donor substituents were next reacted with NO under similar conditions. With butyl vinyl ether (**11**) in cyclohexane no EPR spectra were observed even after 16 h contact with NO. GC–MS analysis showed that the extent of reaction was small but that a complex pattern of products had developed. A matching reaction using NO_2 instead of NO produced a similar pattern of products which suggested that NO_2 was the initiator. The main products were ethanal, butanol, 1,1′-[ethylidenebis(oxy)]bisbutane and an unidentified component together with butyl acetate, 1-nitrobutane and several other minor unidentified components. Clearly the majority of these products were formed by simple hydrolysis of enol ether **11**. The reactants and gas stream had been dried, but hydrogen abstraction by NO_2 from **11** (or a product such as ethanal) would produce nitrous acid which would catalyse the hydrolysis and ketalisation reactions. The nitroso compound, formed by initial addition of NO_2 to **11** in a manner analogous to that shown in Scheme 1, would afford secondary aminoxyl radicals which would be too short-lived for spectroscopic detection, and this explains the absence of EPR signals.

EPR spectra obtained from the reaction of NO with cyclohexen-1-yloxytrimethylsilane (**12**) in cyclohexane showed the rapid development of two main radicals, 6, with $a(N) = 29.5$ G, and 7, a dialkylaminoxyl (Table 1). The large $a(N)$ value of radical 6 would be compatible with an iminoxyl structure, but this is unlikely because the substrate has no appropriate hydrogens at the double bond; furthermore, two conformers would be expected whereas only one species was observed. It is probable therefore that radical 6 is an alkoxyaminoxyl and that radical 7 is a di-*tert*-alkylaminoxyl, both formed from the usual nitroso-intermediate. The main products formed in the early stages of the reaction were found to be: hexamethyldisiloxane, cyclohexyloxytrimethylsilane, cyclohexanone, 1,1-bis(trimethylsiloxy)cyclohexane and 1,1′-bicyclohexyl. The mechanism is therefore probably analogous to that for butyl vinyl ether, *i.e.* hydrolysis and ketalisation. The complementary product, trimethylsilanol, was not identified but it is known to convert readily to hexamethyldisiloxane,[12] plenty of which was produced. Bicyclohexyl and cyclohexyloxytrimethylsilane were presumably formed from solvent-derived radicals.

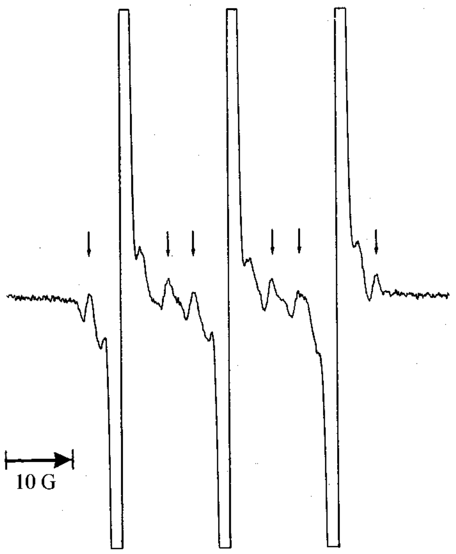
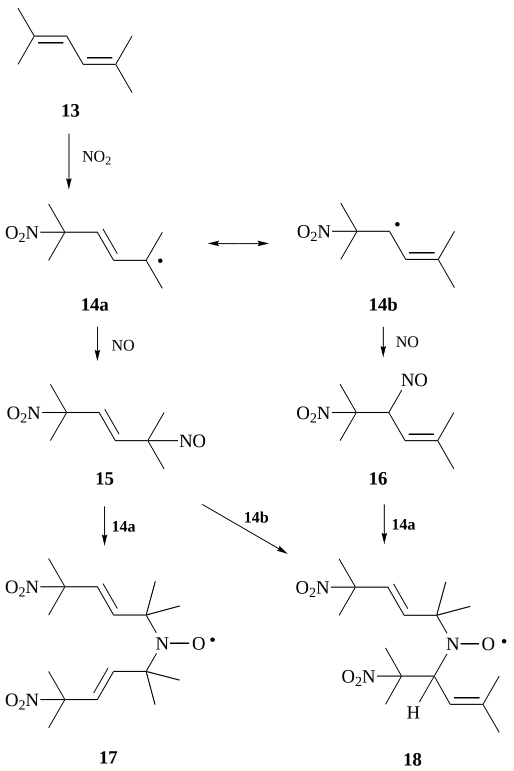


Fig. 2 9.2 GHz EPR spectrum obtained from reaction of NO–air with 2,5-dimethylhexa-2,4-diene (**13**) in *tert*-butylbenzene at room temperature. The main triplet, plus ^{13}C satellites, corresponds to aminoxyl **17**; the resonance lines of the *tert*,*sec*-dialkylaminoxyl **18** are indicated with arrows.

To test if increased π-conjugation in the substrate would favour direct NO addition, as implied in reaction (4), the reactions of NO with several conjugated dienes were examined. EPR spectra were not observed with *trans*,*trans*-1,4-diphenylbuta-1,3-diene, however, when 2,5-dimethylhexa-2,4-diene (**13**) in *tert*-butylbenzene was treated with NO an intense three-line spectrum, similar to that reported previously,[7] was obtained (Fig. 2). Initial NO_2 addition to **13** will produce adduct radical **14**, as suggested by Rockenbauer and Korecz[13] and also by Korth and Sustmann.[14] However, an important feature of radical **14** is that it contains a delocalised allyl unit (**14a** and **14b**, Scheme 2). It follows that NO can couple at each end of the allyl system to give two different nitroso-compounds, **15** and **16**, both of which may couple with another allyl radical (**14**) at either end to give a mixture of the dialkylaminoxyl radicals **17** and **18**. The di-*tert*-alkylaminoxyl **17** will be the most stable and longest lived and hence dominates the EPR spectrum. The one β-hydrogen of the *tert*,*sec*-dialkylaminoxyl **18** enables disproportionation to occur and hence its lifetime will be much shorter and its stationary-state concentration much lower. A third, di-*sec*-alkylaminoxyl could be formed by coupling of **16** and **14b** (not shown in Scheme 2)



Scheme 2

but its lifetime, and hence concentration, will be even lower. The main three-line spectrum in Fig. 2 (radical 8 in Table 1) corresponds to the di-*tert*-alkylaminoxyl **17** and satellites due to hfs from ^{13}C can be observed adjacent to each component. Close inspection shows a much weaker triplet of doublets (radical 9 in Table 1) which we attribute to the *tert*,*sec*-dialkylaminoxyl **18**. The ratio [**18**]/[**17**] was initially *ca.* 0.02 but decreased as contact time increased. As expected, no trace of the *sec*,*sec*-dialkylaminoxyl was found. The observation of **18** provides strong support for the mechanism outlined in Scheme 2.

Conclusions

Pure NO did not add directly to alkenes containing acceptor or donor substituents or to dienes and hence thermodynamic stabilisation due to electron delocalisation [eqn. (4)] was not sufficient to tip the balance in favour of formation of β-nitrosoalkyl radicals. Reaction could be initiated by addition of NO_2 to the double bond of each unsaturated molecule, but whether the NO–O_2 reaction [reaction (1)] or the disproportionation reaction [reaction (3)] is the main source of NO_2 was not established. The β-nitro-nitroso-compounds trap other radicals to give various aminoxyl radicals and, when tautomerism to oximes is possible, are oxidised to iminoxyl radicals. For alkenes containing conjugated carbonyl groups subsequent reactions lead to many oxidation products. For enol ethers, these reactions were accompanied by hydrolysis and ketalisation.

Experimental

^{1}H and ^{13}C NMR spectra were obtained at 300 and 75 MHz, respectively, on a Bruker AM 300 spectrometer for $CDCl_3$ solutions containing $SiMe_4$ as internal standard. GC–MS analyses were carried out with a Finnigan Incos 50 quadrupole mass spectrometer coupled to a Hewlett Packard HP5890 capillary gas chromatograph fitted with a 25 m HP 17 column (50% phenyl methyl silicone). EPR spectra were obtained with a Bruker ER 200D spectrometer operating at 9.4 GHz with 100 kHz modulation. Samples were prepared in 4 mm od quartz tubes or, for solutions in H_2O or CH_3CN, in capillary tubes (1 mm id) and degassed by bubbling nitrogen for 15 min. Photolyses were carried out in the EPR resonant cavity with unfiltered light from a 500 W super pressure Hg lamp focused onto the sample tubes by a series of quartz lenses. Spectra were simulated with a program created originally by Heinzer.[15]

Nitric oxide

Pure nitric oxide[16] was made by dropwise addition of a solution of sodium nitrite (3.45 g, 0.05 mol in 25 cm^3 H_2O) to an L-ascorbic acid solution (3.52 g, 0.02 mol in 20 cm^3 H_2O) with stirring. Both solutions, together with that containing the substrates, were degassed by bubbling nitrogen for *ca.* 40 min prior to the start of NO generation. The NO gas was passed through a bubbler of conc. H_2SO_4 and the outlets from the apparatus were protected from air seepage with bubblers containing paraffin oil.

Mesityl oxide oxime

Mesityl oxide (5 g, 0.051 mol), hydroxylamine hydrochloride (5 g, 0.07 mol), ethanol (5 cm^3) and pyridine (5 cm^3) were refluxed on a water bath for 1 h. The ethanol was removed on a rotary evaporator and the oxime separated on cooling as a red oil; ν/cm^{-1} 3250 (OH), 1680 (C=N); δ_H 1.7 (3H, m), 1.9 (6H, m), 5.6 (1H, d).

General method for reaction of NO with substrates

The substrate (*ca.* 0.5 g) was dissolved in cyclohexane (sometimes *tert*-butylbenzene or CH_3CN), degassed by bubbling nitrogen for *ca.* 40 min, and then pure NO was bubbled through the stirred mixture for up to 4 h at room temperature in the dark. Samples were withdrawn for analysis from time to time by means of a syringe. Measured amounts of air were introduced into the NO stream by means of a syringe and reaction was allowed to proceed sometimes for up to 4 days. Details of the EPR spectra are given in Table 1.

Reaction of NO with mesityl oxide 2. The initial reaction was carried out with a 5 mmol solution in cyclohexane (20 cm^3). GC–MS analyses at various reaction times showed many product peaks most of which were carbonyl compounds; only 1,1′-bicyclohexyl was identified with certainty. An attempt was made to isolate major products by column chromatography on silica gel, using diethyl ether, ethyl acetate and finally methanol as eluents. Many of the products were too volatile for this technique and no individual component was obtained in sufficient quantity for identification. Experiments in *tert*-butylbenzene showed similar results.

Reaction of NO with 1-acetylcyclohexene 10. GC–MS of the products of the reaction of NO with 1-acetylcyclohexene (0.2 mol dm^{-3}) again showed many peaks none of which were identified with certainty.

Reaction of NO with tetracyanoethene. The reaction of tetracyanoethene (20 cm^3 of 0.2 mol dm^{-3}) in CH_3OH with NO showed no EPR spectra but after 20 h contact with NO–NO_2 GC–MS analysis indicated that $(NC)_2C{=}C(CN)OCH_3$ was the sole significant product.

Reaction of NO with butyl vinyl ether 11. After 16 h contact of butyl vinyl ether (0.25 mol dm^{-3}) with NO–NO_2 GC–MS analysis showed the major products to be ethanal, butanol, 1,1′-ethylidenebis(oxy)butane, butyl acetate, butyl formate, 1-nitrobutane plus one major (probably $C_9H_{20}O_2$) and several minor unidentified components.

Reaction of NO with cyclohexen-1-yloxytrimethylsilane 12. GC–MS analysis of the products of the reaction of NO with cyclohexen-1-yloxytrimethylsilane (20 cm^3 of 0.15 mol dm^{-3}) in cyclohexane established that the main products of the reaction were hexamethyldisiloxane, cyclohexyloxytrimethylsilane, cyclohexanone, 1,1-bis(trimethylsiloxy)cyclohexane and 1,1′-bicyclohexyl, accompanied by several minor unidentified components.

Reaction of NO with 2,5-dimethylhexa-2,4-diene 13. The diene (0.4 g, 3.6 mmol) in *tert*-butylbenzene (20 cm^3) showed no EPR spectra until air was introduced. The spectra persisted overnight; the initial ratio [**18**]/[**17**] after 2 h was estimated from the average of the peak heights and found to be 0.019 ± 0.002. GC–MS analysis showed only unreacted **13**.

Acknowledgements

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