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Chemical markers from the peracid oxidation of isosafrole

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Abstract

In this work, isomers of 2,4-dimethyl-3,5-bis(3,4-methylenedioxyphenyl)tetrahydrofuran (11) are presented as chemical markers formed during the peracid oxidation of isosafrole. The stereochemical configurations of the major and next most abundant diastereoisomer are presented. Also described is the detection of isomers of (11) in samples from a clandestine laboratory uncovered in South Australia in February 2004.

Keywords: Isosafrole; Peracid oxidation; By-products; MDMA; Profiling; Allylbenzene

1. Introduction

3,4-Methylenedioxymethamphetamine (1) (MDMA, also known as Ecstasy) is produced in clandestine laboratories by a variety of methods. Many parameters can influence the overall organic profile of the ultimate product from such manufacturing sites, including: the skill of the 'cook', the purity of the chemicals used, and the exact reaction technique employed. Consequently, a batch of manufactured drugs might contain a unique chemical profile, which could provide forensic chemists with information relating to the synthetic route and precursor chemicals used. Such knowledge can aid in linking drug seizures and direct government agencies to control particular precursor chemicals. In this regard, route-specific chemical markers produced during the manufacturing process that remain in the finished product are of particular value to 'forensic profiling' [1–4]. Many reports have been devoted to the characterisation of such markers [5–10]. The usual multi-step nature of MDMA synthesis means that by-products and impurities may be carried through the synthetic process and possibly undergo further chemical modification.

One common sequence to MDMA (1) involves the initial isomerisation of safrole (2) to isosafrole (3) followed by peracid oxidation and acidic dehydration to 3,4-methylenedioxyphenyl-2-propanone (MDP2P, also known as PMK) (4) and then reductive amination to (1) (Scheme 1). Noggle et al. reported that performic acid oxidation of isosafrole with acetone produces predominantly the acetonide (5), but when this reaction is performed in tetrahydrofuran a raft of oxygenated compounds is produced that can be subsequently dehydrated to (4) [11]. Acidic hydrolysis of (5) leads to the desired (4) and significant quantities of both diastereomers of methylated isosafrole glycol (6) (Fig. 1). Swist et al. have since reported that some of these oxygenated by-products, among a number of others, may be detected in MDP2P and/or MDMA produced by the chemical sequence illustrated above [12].

Waumans et al. recently reported the detection of isomers of 2,4-dimethyl-3,5-bis(4-methoxyphenyl)tetrahydrofuran in paramethoxyamphetamine (PMA) seizures and confirmed that its presence is a result of peracid oxidation of anethole (7) (Scheme 2) [13]. Ring opening of the epoxide produced by peracid oxidation of anethole is believed to produce a stabilised benzylic carbocation that can be trapped by another molecule of anethole, followed by ring closure to give the furan by-product. This compound had initially been detected as a result of an industrial peracetic acid oxidation of anethole and its stereochemistry was assigned as all *trans* 2,4-dimethyl-3,5-bis(4-methoxyphenyl)tetrahydrofuran (8A) [14]. However, Mori et al. confirmed that the stereochemistry of the product from the peracetic acid oxidation of anethole was 2,3-*cis*, 3,4-*trans*, 4,5-*trans* 2,4-dimethyl-3,5-bis(4-methoxyphenyl)tetrahydrofuran (8B) by single crystal X-ray analysis [15].

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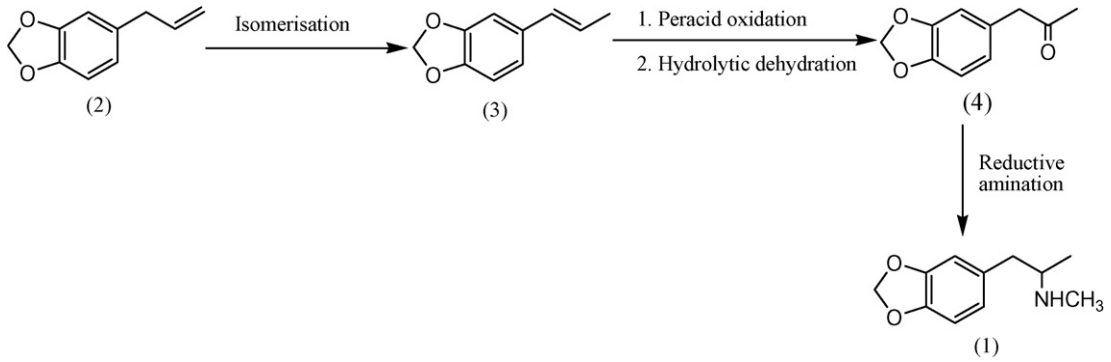


Scheme 1.

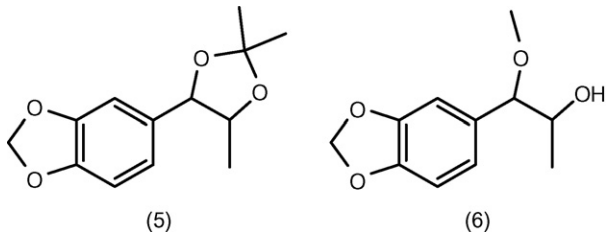
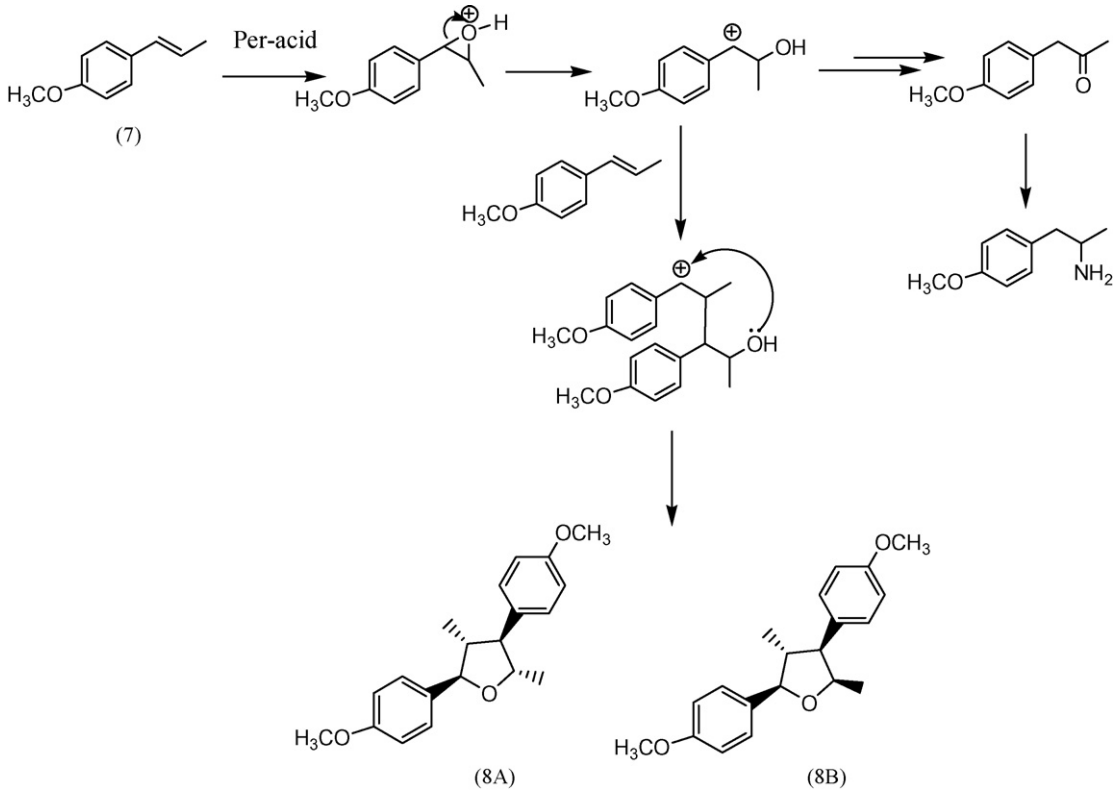


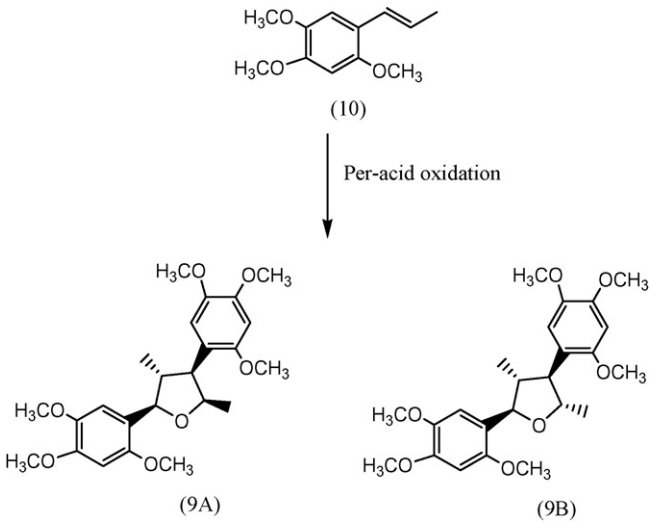
Fig. 1. Products associated with the use of acetone as the solvent for the peracid oxidation of isosafrole.

Furthermore, Mori et al. proved that magnosalicin (9A) (among other isomers) could be synthesised and isolated from the peracid oxidation of α-asarone (10) (Scheme 3).

In February 2004 South Australian Police (SAPOL) uncovered an operating clandestine MDMA laboratory in Findon, Adelaide. The chemicals located at the scene, along with handwritten notes, indicated that MDMA produced by the sequence detailed in Scheme 1 was the target of the laboratory. This was supported by chemical analysis of a number of exhibits, which confirmed that safrole (2) had been isomerised to isosafrole (3) and subsequently oxidised to MDP2P (4) via performic acid oxidation. Some of the compounds mentioned in the above reports were detected in exhibits. Chemical analysis of samples from the 2004 drug laboratory indicated the presence of some unknown impurities with similarities to (8A/8B) and (9A/9B). The mass spectrum of (8A/8B) is shown in Fig. 2. The mass spectrum of (8A/8B) indicates a 44 amu loss, which may correspond to fragmentation of acetaldehyde from the furan ring. This fragmentation produces the base peak ion. The next ion in the mass spectrum is 15 amu less than the base peak and we speculate that this corresponds to the loss of a



Scheme 2.



Scheme 3.

methyl group. The unknown compound shares similar fragmentation with a molecular ion of 340 amu, a base peak of 296 amu and a 281 amu ion (Fig. 3). It was speculated that 2,4-dimethyl-3,5-bis(3,4-methylenedioxyphenyl)tetrahydrofuran (11) was the identity of the unknown chemical from the peracid oxidation of isosafrole (3).

In this report we describe the identification and characterisation of (11) and show examples of the presence of this compound in clandestine laboratory samples (Fig. 4).

2. Experimental procedure

2.1. Chemicals and reagents

All solvents and reagents used in this work were of analytical grade and were purchased from Aldrich Chemical Company. 60 Å 70–230-mesh silica gel with a BET surface area of 500 m^2/g and pore volume of 0.75 cm^3/g was used for column chromatography.

2.2. Instrumentation

Sample analysis was effected with gas chromatography–mass spectrometry (GC/MS), using an Agilent 6890 gas chromatograph equipped with an Agilent 5973 mass selective detector (MSD) and electronic pressure programming. Helium was used as the carrier gas; the column was a 15 m × 0.25 mm × 0.25 μm DB-1 capillary.

The mass spectrometer operated from 30 to 450 amu in electron impact (EI) mode with an ionization energy of 70 eV. A solvent delay of 1.50 min was applied. The injector temperature was 300 °C. The initial column temperature was 90 °C for 2 min and then ramped at 45 °C/min over 4.67 min to 300 °C. The column temperature was then maintained at 300 °C for 4 min.

Proton spectra were recorded using a Varian 600 MHz NMR spectrometer. Chemical shifts were recorded in parts per million (ppm) and coupling constants in hertz (Hz). The solvent used was deuterochloroform ($CDCl_3$), which contained tetramethylsilane (TMS) as the reference compound.

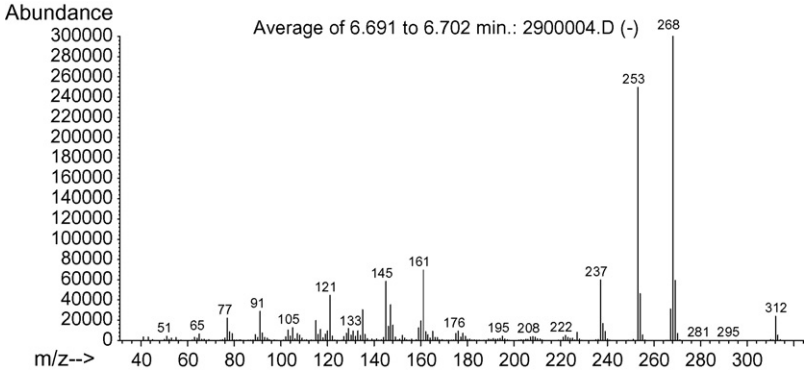


Fig. 2. Mass spectrum of (8A/8B).

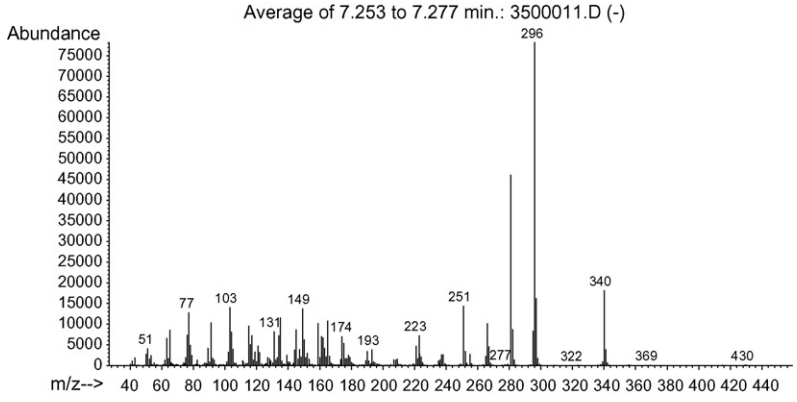


Fig. 3. Mass spectrum of unknown compound detected in exhibits from a MDMA clandestine laboratory.

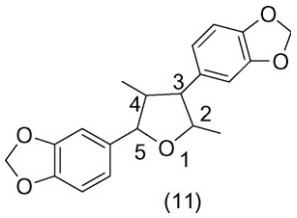


Fig. 4. Proposed structure of an unknown from the peracid oxidation of isosafrole.

2.3. Synthesis procedures

2.3.1. Isomerisation of either safrole (2) or allylbenzene (16)

Potassium hydroxide (10 g) was added to a stirred solution of either safrole (2) or allylbenzene (16) (10 g) dissolved in anhydrous ethanol (10 mL). The reaction mixture was refluxed with vigorous stirring for 24 h, after which distilled water (100 mL) was added. The mixture was extracted with dichloromethane (3× 30 mL) and the combined organic extracts were washed with 5% hydrochloric acid (50 mL), dried (Na_2SO_4), filtered, and evaporated to give either isosafrole (3) or phenylpropene (17), which was used without further purification. Isosafrole (3) was formed as a 10:90 mixture of Z:E isomers. Phenylpropene (17) was formed as a 15:85 mixture of Z:E isomers.

2.3.2. Performic acid oxidation of either isosafrole (3) or phenylpropene (17)

Performic acid was prepared by the addition of 90% formic acid (0.52 mol) to cool 30% hydrogen peroxide (0.20 mol). The reaction mixture was allowed to stir gently at room temperature for 1 h, after which it was ready for use. Performic acid must be prepared before each experiment due to its instability. Performic acid was then added to a stirred solution of either isosafrole (3) or phenylpropene (17) (0.04 mol) dissolved in dichloromethane (5 mL) drop-wise so the reaction mixture did not exceed 30 °C. The mixture was stirred for 16 h, after which distilled water (15 mL) was added and the mixture was extracted with dichloromethane (2× 10 mL). The combined organic extracts were washed with distilled water (15 mL), dried (Na_2SO_4), filtered, and evaporated to give dark orange/red oils. The performic acid oxidation of isosafrole (3) and phenylpropene (17) both resulted in the formation of complex product mixtures. Analysis of the product mixture from performic acid oxidation of isosafrole (3) is represented by the gas chromatogram from Fig. 6. Compounds (11B) and (11A) were isolated as a 3:1 mixture after column chromatography on silica with a 10% ethyl acetate/hexane solvent system. Analysis of the product mixture from performic acid oxidation of phenylpropene (17) is represented by the gas chromatogram from Fig. 11.

2.3.3. Hydrolytic dehydration of the product mixture from the performic acid oxidation of isosafrole (3)

15% sulphuric acid solution (2.2 mL) was added to a stirred solution of the product mixture from the performic acid oxidation of isosafrole (0.51 g, 2.27 mmol) dissolved in methanol (0.63 mL). The mixture was heated at 100 °C for 2 h. After this time the reaction was cooled to room temperature and extracted with dichloromethane (3× 2 mL) and the combined organic extracts were washed with distilled water (3 mL), concentrated potassium hydroxide solution (2 mL) and saturated sodium chloride solution (2 mL). The combined organic extracts were dried (Na_2SO_4), filtered and evaporated to give 0.21 g of a dark orange oil. GC analysis indicated that the major product from this reaction was MDP2P (4). 5-((4-(Benzo[*d*][1,3]dioxol-5-yl)-2,5-dimethyl-1,3-dioxolan-2-yl)methyl)benzo[*d*][1,3]dioxole (12) was detected as a minor product of this reaction.

MS data for (12) *m/z*: 356 (1%, M^+), 221 (70), 203 (2), 179 (100), 161 (25), 149 (7), 135 (35), 121, 107, 91, 77, 65, 53, 43 (40).

2.3.4. Synthesis of 1-(3,4-methylenedioxyphenyl)-1,2-propandiol (13)

Potassium permanganate (0.16 g, 1.03 mmol) dissolved in distilled water (10 mL) was added drop-wise to an ice-cold (0 °C) stirred solution of isosafrole (3) (0.21g, 1.31 mmol) dissolved in methanol (5 mL). The reaction was stirred at 0 °C for 1 h after which, the reaction mixture was poured onto distilled water (50 mL). The reaction mixture was extracted with dichloromethane (3× 20 mL) and the combined organic extracts were washed with distilled water (40 mL), dried (Na_2SO_4) and filtered. Evaporation of the solvent gave 0.04 g (25%) of 1-(3,4-methylenedioxyphenyl)-1,2-propandiol (13) as a white solid.

MS data for 1-(3,4-methylenedioxyphenyl)-1,2-propandiol (13) *m/z*: 196 (23%, M^+), 178 (2), 162 (1), 151 (100), 135 (4), 123 (18), 93 (95), 77, 65 (56).

2.3.5. Synthesis of 5-((4-(benzo[d][1,3]dioxol-5-yl)-2,5-dimethyl-1,3-dioxolan-2-yl)methyl)benzo[d][1,3]dioxole (12)

1-(3,4-Methylenedioxyphenyl)-1,2-propandiol (13) (0.04 g) was heated with a drop of 10% hydrochloric acid solution for 10 min. The reaction mixture was basified with potassium hydroxide (2 mL) and extracted with dichloromethane (2× 2 mL). The combined organic phase was dried (Na_2SO_4), filtered and evaporated to give a yellow oil which contained (4) and isomers of (12). A single isomer of (12) was isolated by silica gel chromatography (10% ethyl acetate/hexane).

MS data for (12) *m/z*: 356 (1%, M^+), 221 (70), 203 (2), 179 (100), 161 (25), 149 (7), 135 (35), 121, 107, 91, 77, 65, 53, 43 (40).

^{1}H NMR data for (12): δ 1.15 (d, 3H, 6 Hz), 1.49 (s, 3H), 2.95 (d, 1H, 13.8), 3.03 (d, 1H, 13.8), 3.77 (dq, 1H, 8.6, 6), 3.90 (d, 1H, 8.6), 5.94 (s, 4H), 6.71–6.84 (m, 6H).

3. Results and discussion

In this study commercial safrole (2) was dissolved in ethanol and heated with potassium hydroxide for a period of 24 h. This resulted in the formation of isosafrole (3) as a 10:90 mixture of Z:E isomers.

A variety of reaction conditions were trialled for the peracid oxidation of isosafrole (3) and the unknown from Fig. 3 was detected in every case. The proposed furan was detected from both the peracetic acid and performic acid oxidation of isosafrole. Performic acid was used in the majority of experiments conducted. The unknown was also detected when acetone, dichloromethane or tetrahydrofuran was used as the reaction solvent with performic acid. Although the unknown was detected in the acetone mediated oxidation of isosafrole, the acetonide (5) interfered with the isolation of the unknown and consequently dichloromethane was the reaction solvent of choice. The optimal molar ratio of isosafrole (3) to hydrogen peroxide to formic acid was determined to be 1:5:13 which was identical to that used by Waumans et al. for the performic acid oxidation of anethole (7) [13] and similar to several illicit recipes. In most cases the yield of the suspected furan (11) was approximately 5–10% from isosafrole (3).

The suspected furans were found to survive the subsequent hydrolytic dehydration used to produce MDP2P (4). This process introduced two new unknown components, which eluted in the same region as the suspected furans. The similarity of the mass spectra of these two new unknown compounds suggested that they were likely to be isomers (Fig. 5).

The presence of these possible isomers complicated the attempted isolation of the suspected furans as they were found to co-elute when isolation was attempted by column chromatography on silica. It was speculated that the two peaks might represent two of four possible diastereomers of the condensation product (12) derived from MDP2P (4) (the major product of hydrolytic dehydration) and isosafrole glycol (13) (an oxygenated product reported in the peracid oxidation of isosafrole (3) [11]) (Scheme 4).

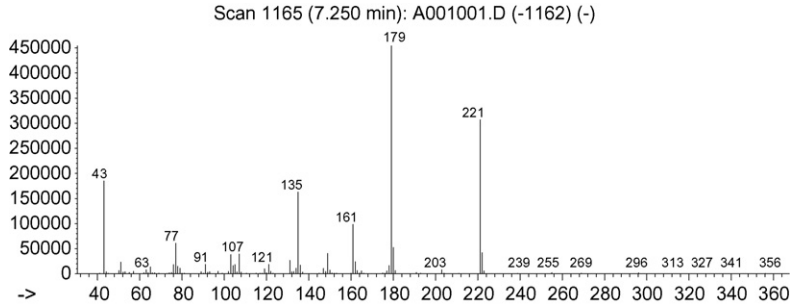
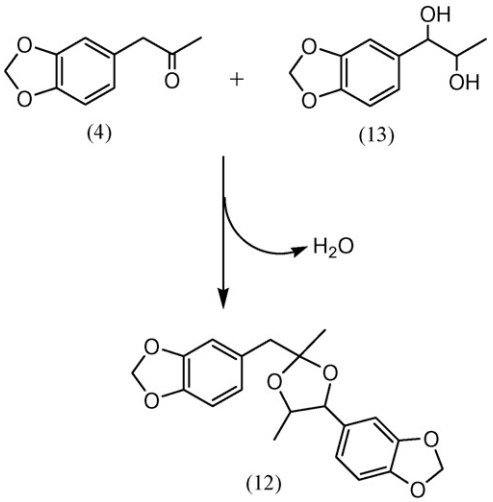


Fig. 5. Mass spectrum representing two possible isomeric compounds produced during hydrolytic dehydration to (4).



Scheme 4.

Support for this theory was gained when pure isosafrole glycol (13) (synthesised by permanganate oxidation of isosafrole (3)) was heated in dilute hydrochloric acid. Analysis of this mixture by gas chromatography–mass spectrometry (GC/MS) indicated the presence of (4) as well as two peaks with identical mass spectral fragmentation and retention time as those observed in the hydrolytic dehydration. Confirmation of the ketal structure (12) was obtained following proton nuclear magnetic resonance (NMR) analysis. Subsequently the isolation and characterisation of the suspected furans was attempted post peracid oxidation and prior to hydrolytic dehydration.

In all cases of peracid oxidation of isosafrole (3), the suspected furans were detected as a cluster of three apparent diastereomeric isomers (11A), (11B) and (11C) with identical mass spectra (Fig. 6). In every case (11B) was the major isomer, followed by the earlier eluting (11A) and then the later eluting (11C); this pattern closely follows the formation of anethole-derived furans [13].

Partial isolation of these suspected furan diastereomers was achieved using silica column chromatography with a 10% ethyl acetate/hexane solvent system. Isomers (11A) and (11B) were obtained as a 1:3 mixture from combined fractions after chromatography. ^{1}H NMR spectroscopy confirmed that (11A) and (11B) were indeed diastereomeric isomers of 2,4-dimethyl-3,5-bis(3,4-methylenedioxyphenyl)tetrahydrofuran. The furan ring protons, which provide critical stereochemical data for both (11A) and (11B), resonated as various multiplets between 2 and 4.6 ppm as shown in Fig. 7.

Our stereochemical argument is based on the unambiguously established 2,3-*cis*, 3,4-*trans*, 4,5-*trans* configuration of

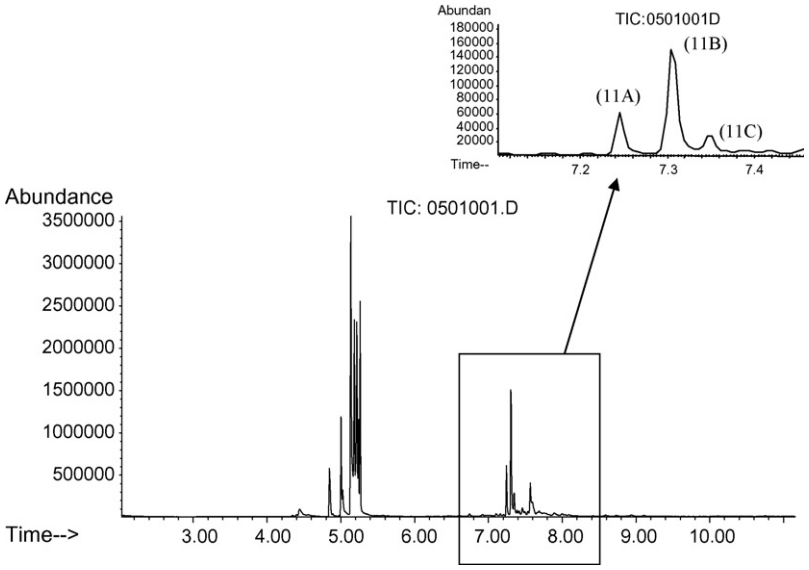


Fig. 6. Gas chromatogram of the peracid oxidation of isosafrole (3).

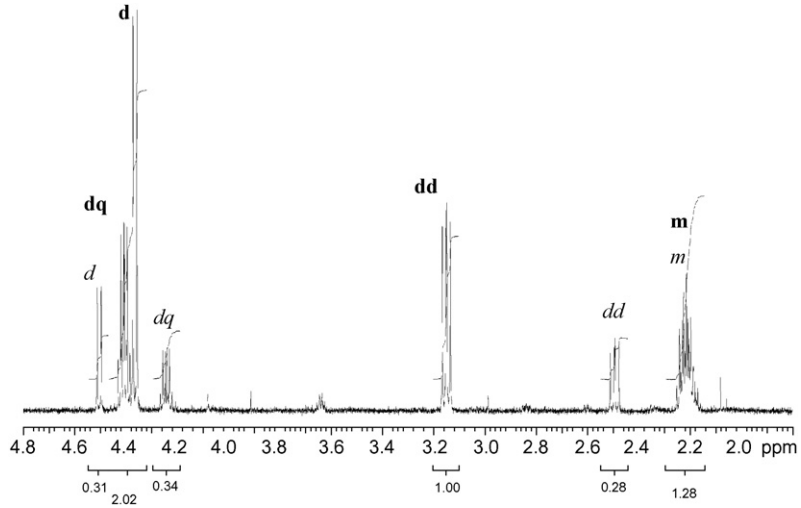


Fig. 7. ^{1}H NMR spectrum of a 1:3 mixture of (11A) and (11B). *Note*: Signals corresponding to the major isomer (11B) are denoted with bold font while signals corresponding to (11A) are denoted by italics.

both magnosalicin (9A) and the isolated and fully characterised anethole-derived isomer (8B). The splitting pattern of the protons attached to the tetrahydrofuran ring of the major isomer (11B) exhibit remarkable similarity to those reported for magnosalicin (9A) and particularly the anethole-derived isomer (8B) [15] (Table 1).

The vicinal coupling constant between the proton attached to C-3 and the proton attached to C-4 was 10.3 Hz and the vicinal relationship between the proton of C-4 and the proton of C-5 had a coupling constant of 9.4 Hz. These coupling constants indicate dihedral angles of approximately 180° and are symptomatic of an anti peri-planar arrangement existing between the protons attached to C-3, C-4 and C-5. Thus, an assignment of 3,4-*trans* and 4,5-*trans* is proposed for the major isomer (11B). Since the vicinal relationship between the protons attached to C-2 and C-3 of (11B) is characterised by a coupling constant of 8.4 Hz the stereochemical assignment is ambiguous. Such coupling indicates the possibility of either *cis* or *trans*. We propose that this coupling represents a *cis* arrangement, which is consistent with the characterised isomers (8B) and (9A). This proposition is supported by the assignment of (11A) as the all *trans* isomer, which would otherwise be the alternative assignment for (11B). Mori et al. assigned the all *trans* isomer of 2,4-dimethyl-3,5-bis(2,4,5-trimethoxyphenyl)-

Table 1
^{1}H NMR spectral data for (11B) and reported data for (8B) and (9A)

Chemical shifts δ (ppm) and coupling constants J (Hz)			
Protons	(11B)	(8B)	(9A)
C-2 CH_3	0.95 or 0.98 (d, 3H, 6.5)	0.94 (d, 3H, 6.5)	0.90 (d, 3H, 6.5)
C-4 CH_3	0.95 or 0.98 (d, 3H, 6.5)	0.98 (d, 3H, 6.5)	1.04 (d, 3H, 6.5)
C-2 H	4.40 (dq, 1H, 8.4, 6.5)	4.43 (dq, 1H, 8.5, 6.5)	4.60 (dq, 1H, 8.5, 6.5)
C-3 H	3.14 (dd, 1H, 8.4, 10.3)	3.19 (dd, 1H, 8.5, 10.5)	3.60 (dd, 1H, 8.5, 10.5)
C-4 H	2.20 (m, 1H)	2.30 (ddq, 1H, 10.5, 9.5, 6.5)	2.31 (ddq, 1H, 10.5, 9.0, 6.5)
C-5 H	4.36 (d, 1H, 9.4)	4.42 (d, 1H, 9.5)	4.97 (d, 1H, 9.0)
Ar–O–CH_3	N/A	3.80 (3H) 3.82 (3H)	3.79 (3H) 3.81 (3H) 3.82 (3H) 3.87 (3H) 3.90 (3H) 3.91 (3H)
–O–CH_2–O–	5.84 (m, 4H)	N/A	N/A
Ar–H	6.61–6.95 (6H)	6.87 (d, 2H, 7) 6.91 (d, 2H, 7) 7.10 (d, 2H, 7) 7.36 (d, 2H, 7)	6.545 (1H) 6.540 (1H) 6.69 (1H) 7.14 (1H)

Table 2
^{1}H NMR spectral data for (11A) and reported data for (9B)

Chemical shifts δ (ppm) and coupling constants J (Hz)		
Protons	(11A)	(9B)
C-2 CH_3	0.98 (d, 3H, 6.1)	1.27 (d, 3H, 6.0)
C-4 CH_3	0.95 (d, 3H, 6.5)	0.90 (d, 3H, 6.5)
C-2 H	4.2 (dq, 1H, 6.1, 9.5)	4.35 (dq, 1H, 6.0, 9.5)
C-3 H	2.49 (dd, 1H, 9.5, 11.2)	3.13 (dd, 1H, 9.5, 10.5)
C-4 H	2.20 (m, 1H)	2.45 (ddq, 1H, 6.5, 9.5, 10.5)
C-5 H	4.50 (d, 1H, 9.4)	5.02 (d, 1H, 9.5)
Ar–O–CH_3	N/A	3.82 (s, 3H) 3.84 (s, 3H) 3.86 (s, 3H) 3.91 (s, 9H)
–O–CH_2–O–	5.84 (m, 4H)	N/A
Ar–H	6.61–6.95 (m, 6H)	6.53 (s, 1H) 6.56 (s, 1H) 6.76 (s, 1H) 7.08 (s, 1H)

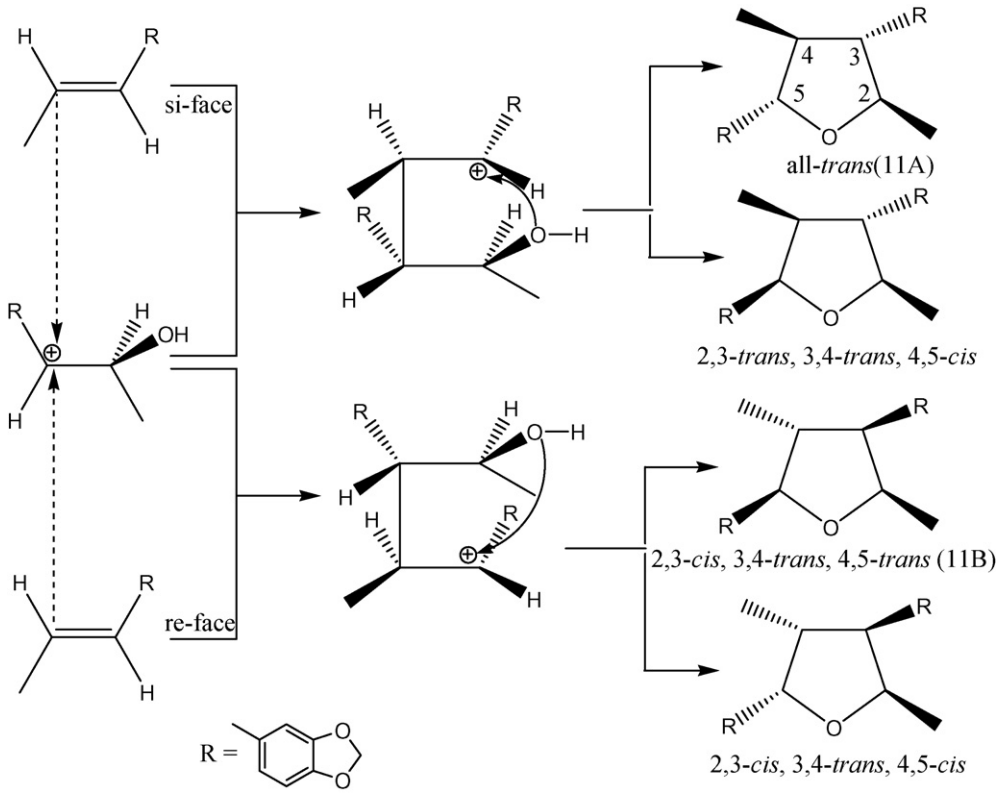
tetrahydrofuran (9B) on the basis of an up-field shift of the C-3 proton signal [15] (Table 2).

The proton attached to C-3 from (11A) exhibits a similar up-field shift of $\Delta\delta$ 0.63 ppm (when compared to the C-3 proton signal from (11B)). The all *trans* stereochemical assignment of (11A) is further supported by consideration of the coupling constants between the protons attached to C-2, C-3, C-4 and C-5. The vicinal protons are characterised by coupling constants of 9.5 Hz (C-2 H and C-3 H), 11.2 Hz (C-3 H and C-4 H) and 9.4 Hz (C-4 H and C-5 H). These large coupling constants are consistent with *trans* arrangements and are very close to the reported values for the all *trans* isomer (9B). Thus (11A) is assigned as the all *trans* isomer, which supports the assignment of the major isomer (11B) as the 2,3-*cis*, 3,4-*trans*, 4,5-*trans* configuration. Unfortunately we have been unable to isolate isomer (11C) in sufficient quantity and purity for stereochemical determination.

The oxidative coupling of *trans* isosafrole (3) may yield four diastereomers (each as a racemate) as shown in Scheme 5. This scheme has been adapted from Mori et al. [15].

Further mass spectral analysis of both crude (Fig. 8) and pure (Fig. 9) MDP2P from the 2004 MDMA laboratory by way of ion extraction indicates the presence of three furan diastereomers in a similar ratio to those seen in our laboratory experiments. Co-injection of a mixture of the furan isomers from the performic acid oxidation of isosafrole prepared in the laboratory with samples from the clandestine laboratory, confirmed that (11A), (11B) and (11C) were formed in a similar ratio by the laboratory operators.

In the case of both the crude and purified MDP2P (4) from the scene we believe that the molecular ion of the furan is contaminated with co-eluting compound(s) and the relative amount of the furan isomers is more accurately represented by the 296 and 281 ions. Extraction of 221 and 179 ions from the crude MDP2P (4) from the laboratory indicates the presence of two isomers of the condensation product (12) (Fig. 10).



Scheme 5.

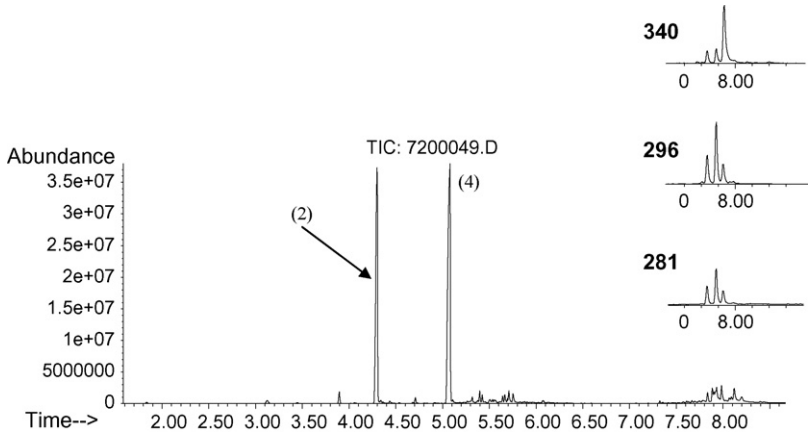


Fig. 8. Gas chromatogram of crude MDP2P (4) from the 2004 clandestine laboratory. (Retention times are different to those from Fig. 6 owing to a change in chromatography conditions.) Inset: 340, 296 and 281 reconstructed ion chromatograms.

Symmetrical enhancement of these peaks was observed when independently synthesised and purified (12) was co-injected with the crude MDP2P from the drug laboratory. The condensation product (12) was not observed in the apparently purified MDP2P from the clandestine laboratory.

All of the chemicals and equipment for the final conversion of (4) to (1) (by way of the nitromethane mercury/aluminium amalgam method) were located at the scene of the clandestine laboratory, but there was no evidence that this conversion had taken place. Consequently we have not attempted to detect the

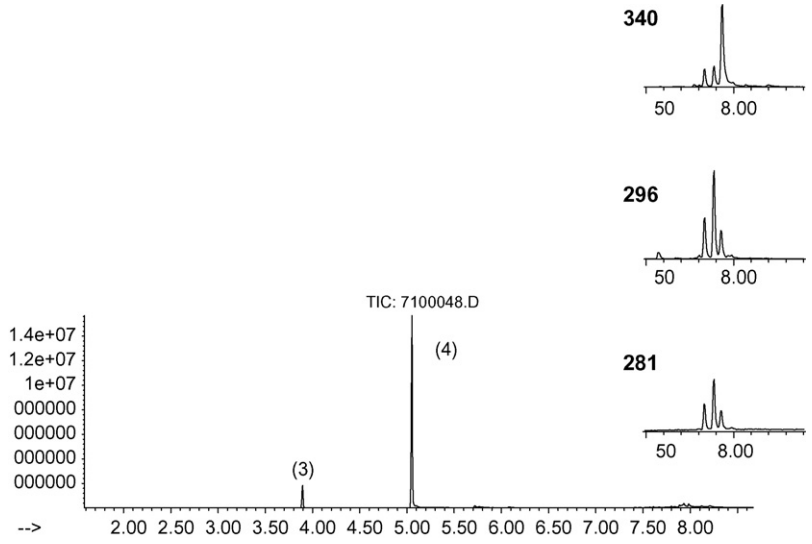


Fig. 9. Gas chromatogram of purified MDP2P (4) from the 2004 clandestine laboratory. (Retention times are different to those from Fig. 6 owing to a change in chromatography conditions.) Inset: 340, 296 and 281 reconstructed ion chromatograms.

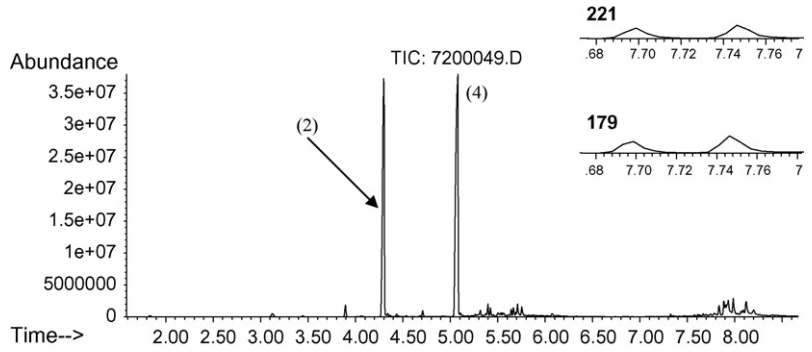
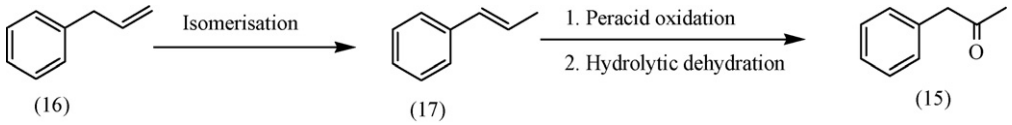


Fig. 10. Gas chromatogram of crude MDP2P (4) from the 2004 clandestine laboratory. (Retention times are different to those from Fig. 6 owing to a change in chromatography conditions.) Inset: 221 and 179 reconstructed ion chromatograms.



Scheme 6.

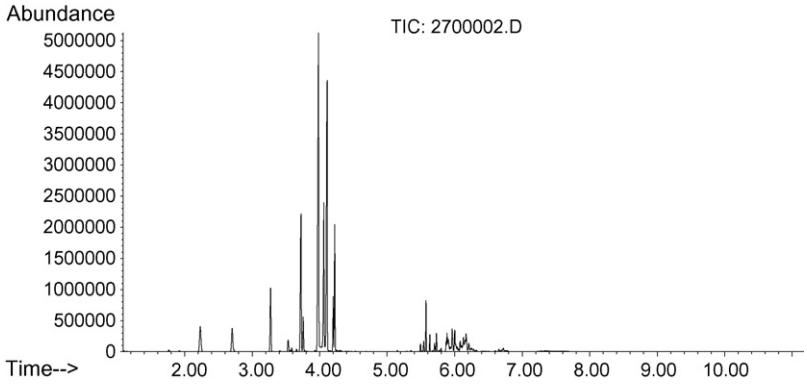


Fig. 11. Gas chromatogram of the product from peracid oxidation of (17).

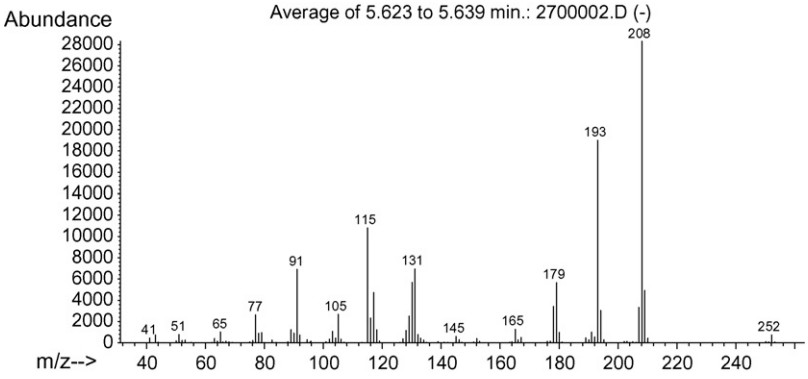


Fig. 12. Mass spectrum of suspected 2,4-dimethyl-3,5-diphenyltetrahydrofuran (18).

furan isomers in seized samples but we have detected these products in MDMA produced by this method in the laboratory.

It was considered likely that analogous furans would be produced by the peracid oxidation of other types of phenylpropenes. Phenyl-2-propanone (P2P) (15) is a key precursor chemical in the synthesis of both amphetamine and methylamphetamine. One method to prepare P2P involves the isomerisation of allylbenzene (16) to phenylpropene (17) followed by peracid oxidation and hydrolytic dehydration to produce (15) (Scheme 6).

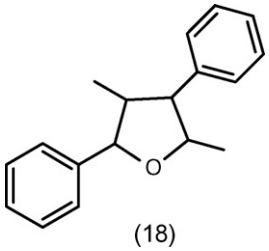


Fig. 13. Structure of 2,4-dimethyl-3,5-diphenyltetrahydrofuran (18).

When this was attempted in the laboratory, GC/MS analysis indicated that a number of analogous oxygenated products were produced from the performic acid oxidation of (17) (Fig. 11).

Also produced were a number of products, which appeared to have identical mass spectra and, by analogy, a great deal of similarity with previously detected furans (Fig. 12).

All peaks at 5.63, 5.70 and 5.73 min from Fig. 11 contain the 252 amu molecular ion, the 208 amu base peak and the 193 amu fragment, indicating the possible initial loss of acetaldehyde followed by the fragmentation of a methyl group. We propose that the identity of the compounds eluting at 5.63, 5.70 and 5.73 min are diastereomers of 2,4-dimethyl-3,5-diphenyltetrahydrofuran (18) (Fig. 13).

No attempt has been made in the present study to unambiguously characterise (18) from the peracid oxidation of (17) and therefore the identification of (18) remains tentative.

4. Conclusion

It has been found that 2,4-dimethyl-3,5-bis(3,4-methylenedioxyphenyl)tetrahydrofuran (11) is produced as a mixture of

three diastereomeric isomers during the peracid oxidation of isosafrole. The most abundant stereoisomer formed contains a 2,3-*cis*, 3,4-*trans*, 4,5-*trans* configuration, while the next most abundant diastereoisomer contains the all *trans* configuration. We have demonstrated the detection of these isomers in clandestinely produced MDP2P. Laboratory experiments indicate that isomers of (11) may be detected in samples of MDMA but the presence of this impurity may depend upon the exact technique of purification. The presence of other high boiling co-eluting compounds in forensic samples may complicate the detection of these isomers. The detection of (11) in forensic samples may also be accompanied by the detection of the ketal (12). We have tentatively identified 2,4-dimethyl-3,5-diphenyltetrahydrofuran (18) as a product of the peracid oxidation of allylbenzene.

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