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Note

Gas chromatographic-mass spectrometric identification of phenylurea herbicides after N-methylation

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Several procedures involving gas chromatography (GC) have been described for the analysis of phenylurea herbicides. Earlier methods were based on the hydrolysis of phenylureas followed by GC of the corresponding anilines, either directly[1,2] or as derivatives[3–5]. The transformation into anilines has the disadvantage that specific determination of such phenylureas as linuron and diuron, which contain the same substituted-phenyl moiety, is not possible without previous and time-consuming separation. In order to overcome this problem, attempts have been made to perform direct GC of phenylureas[6,7]. However, Spengler and Hamroll[8] have pointed out that phenylureas analysed as described by McKone and Hance[6] are pyrolysed and eluted as phenyl isocyanates. According to Katz and Strusz[7], this decomposition was markedly reduced by temperature-programmed GC after aging of the column with a mixture of the compounds under study. However, retention times could not be reproduced, so that the procedure is not applicable for identifying unknown phenylureas.

This paper elucidates the thermal instability of phenylurea compounds and describes the N-methylation of mono-, di- and trisubstituted phenylureas by the use of sodium hydride, dimethyl sulphoxide and iodomethane. Procedures for the GC separation and GC–mass spectrometric (MS) identification of the tetra-substituted derivatives are suggested.

EXPERIMENTAL

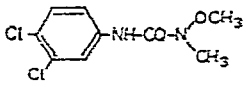
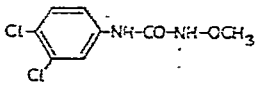
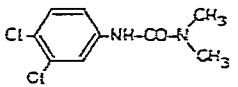
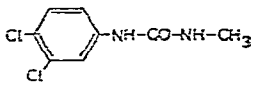
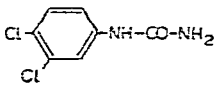
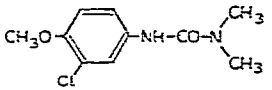
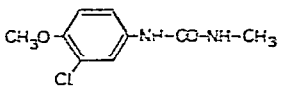
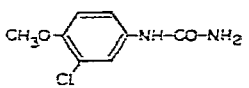
Thermal stability of phenylureas

Initially, the compounds listed in Table I were investigated by GC–MS. This was carried out by using a glass column packed with 5% of OV-101 on Chromosorb W (80–100 mesh); the column temperature was increased from 150° by 4°/min, and the injector temperature was kept at 240°. The column was coupled to a Varian 311 mass spectrometer through a Biemann–Watson separator at 250°. With the ion-source temperature at 200°, mass spectra of the eluted components were recorded at an accelerating voltage of 3 kV and an electron energy of 70 eV.

The analysis demonstrated that linuron (I) and its metabolite (II), each of which has an N-methoxy group, were partly pyrolysed, whereas the remaining compounds (III–VIII) were completely decomposed. Further, an outstanding feature was

TABLE I

PHENYLUREAS STUDIED

Compound No.	*Names*	*Structure*
I	3-(3,4-Dichlorophenyl)-1-methoxy-1-methylurea (linuron)	
II	3-(3,4-Dichlorophenyl)-1-methoxyurea	
III	3-(3,4-Dichlorophenyl)-1,1-dimethylurea (diuron)	
IV	3-(3,4-Dichlorophenyl)-1-methylurea	
V	3-(3,4-Dichlorophenyl)urea	
VI	3-(3-Chloro-4-methoxyphenyl)-1,1-dimethylurea (metoxuron)	
VII	3-(3-Chloro-4-methoxyphenyl)-1-methylurea	
VIII	3-(3-Chloro-4-methoxyphenyl)urea	

that pyrolysis of such trisubstituted phenylureas as linuron (I), diuron (III) and metoxuron (VI) yielded only one aromatic product (identified as the corresponding phenyl isocyanate), while the mono- and di-substituted phenylureas (II, IV, V, VII and VIII) yielded the phenyl isocyanate and the aniline. These results support the observation of Spengler and Hamroll[8] and further demonstrate that the thermal instability of phenylureas is related to the presence of amide-H (see Fig. 1), thus indicating that thermostable compounds can be derived by substitution of this H, as for instance by alkylation to give tetrasubstituted compounds, which can be subjected to GC.

N-methylation of phenylureas

The thermal stability of tetrasubstituted phenylureas was demonstrated by

Tanaka and Wien[9], who described an on-column methylation based on the simultaneous injection of phenylurea and trimethylanilinium hydroxide (MethElute; Pierce, Rockford, Ill., U.S.A.). However mono- and di-substituted phenylureas could not be quantitatively converted into tetrasubstituted derivatives by this procedure, which is consequently inadequate for determining metabolites of phenylurea herbicides.

As another approach, N-methylation may be used for substitution of the amide-H; such N-methylation (performed by means of a proton-extracting base and

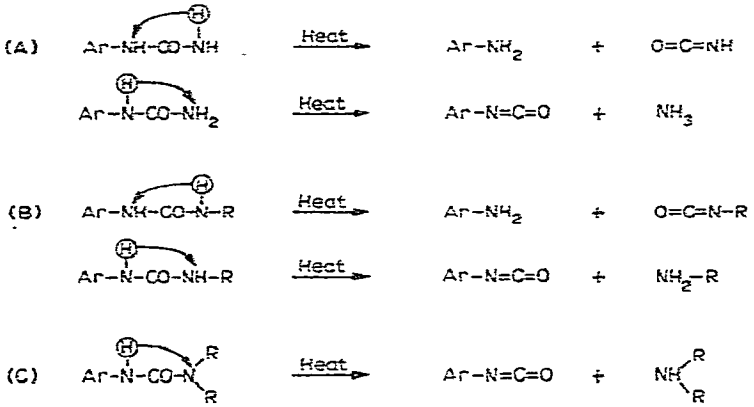


Fig. 1. Suggested pathways for pyrolysis of mono- (A), di- (B) and tri-substituted (C) phenylureas (R = CH_3 or OCH_3). The aromatic fragments were detected by GC–MS, whereas the aliphatic fragments were probably eluted with the solvent.

iodomethane as methyl-group donor) is often used for making derivatives of peptides[10]. Recently, similar methods were described for the N-methylation of phenylurea herbicides by Saunders and Vanatta[11] and by Greenhalgh and Kovacicova[12] using, respectively, potassium *tert.*-butoxide and sodium hydride as base. By heating a mixture of the herbicide, a base and iodomethane, trisubstituted phenylureas were successfully methylated, but no results were reported on the methylation of mono- and di-substituted compounds.

In the present investigation, which parallels that of Greenhalgh and Kovacicova[12], a rapid procedure has been applied for N-methylation of mono-, di- and trisubstituted phenylureas (see Table I). Based on the use of sodium hydride as proton-extracting agent, the N-methylations were performed at room temperature by the following procedure.

About 30 mg of sodium hydride–oil dispersion is washed three times with anhydrous ethyl ether. The sodium hydride is dried in a gentle stream of nitrogen and then suspended in 1 ml of freshly distilled dimethyl sulphoxide (DMSO). A portion (200 μl) of this suspension is added to approx. 1 μmole of the phenylurea dissolved in 100 μl of pure DMSO, and 50 μl of iodomethane are immediately added; the reaction is allowed to proceed, with continuous stirring, for 5 to 10 min. Then 1 ml of water is added, with precautions (sodium hydride is a very corrosive chemical, which is inflammable with water), and the mixture is extracted with three 1-ml portions of ether or light petroleum. The combined organic phases are dried over anhydrous sodium sulphate, filtered and evaporated to dryness in a stream of nitrogen.

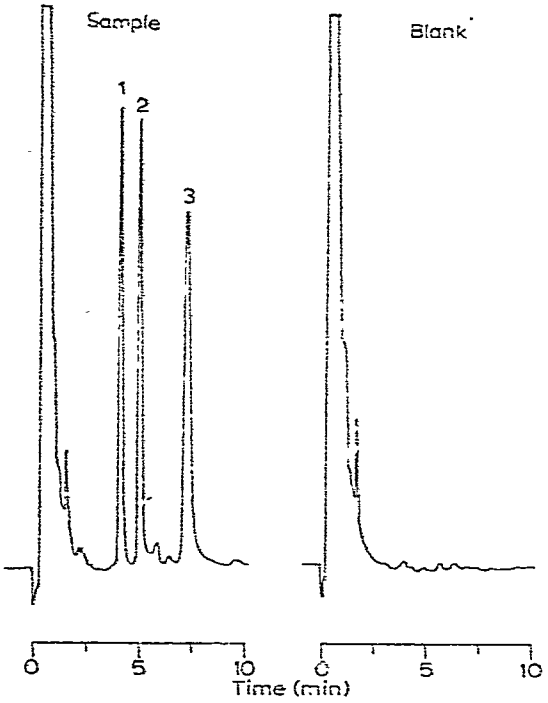


Fig. 2. Chromatogram of methylated phenylurea herbicides obtained by GC with electron-capture detection. 1, linuron (1 ng); 2, diuron (1 ng); and 3, metoxuron (10 ng). Column temperature, 180°; stationary phase, OV-225.

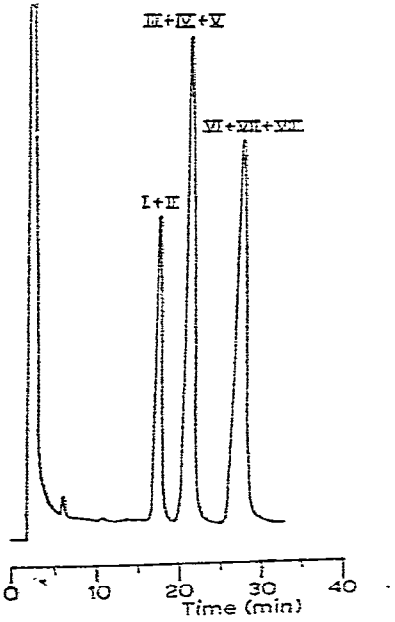


Fig. 3. Total-ion-monitor chromatogram at the 1-μg level of a methylated mixture of compounds I–VIII. Column temperature, 170°; stationary phase, DC 200 and QF-1 (1:3).

RESULTS AND DISCUSSION

The methylated products of the phenylurea compounds listed in Table I were analysed by GC–MS. For each compound, only one GC peak was detected and the corresponding component was identified from the mass spectrum as the expected N-methylated derivative. This indicates that the procedure is generally applicable for the N-methylation of mono-, di- and tri-substituted phenylureas, yielding tetra-substituted thermostable derivatives.

As part of this investigation, the method was applied at the ng level, for the simultaneous determination of closely related chlorophenylurea herbicides by GC with electron-capture detection; the resulting chromatogram is shown in Fig. 2.

N-methylation of metabolites (*e.g.*, IV and V) and the parent phenylurea herbicide (*e.g.*, III) results in the same compound (see Fig. 3). Consequently, distinction between the herbicides and their individual metabolites is not possible by the method in its present form. However, preliminary experiments have shown that specific analysis for metabolites and herbicides can be performed using trideuteromethylated derivatives and GC–MS. Trideuteromethylation is accomplished by the described methylation procedure, but with trideuteroiodomethane in place of iodomethane. In a trideuteromethylated derivative, the methyl groups originally bonded in the phenylurea molecule differ in weight from those introduced by methylation; this difference can be detected by MS, either by recording the total mass spectrum or by mass fragmentography.

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