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Identification of the isomers from mono- and dinitration of α -hydroxydiphenylacetic acid by capillary gas chromatography with Fourier transform infrared and mass spectrometric detection

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Abstract

All three mononitro and all six heteronuclear dinitro isomers from nitration of α -hydroxydiphenylacetic (benzilig) acid were separated as methyl esters by capillary gas chromatography and their retention indices were measured. Heteronuclear dinitro substitution of α -hydroxydiphenylacetic acid was confirmed by inspection of the MS fragmentation patterns of the eluted compounds. The mononitro and dinitro derivatives were identified on the basis of their Fourier transform IR spectra and, in part, of the MS spectra recorded in the positive-ion mode.

1. Introduction

In previous work [1] we solved the problem of the separation and identification of all the isomers from the mono- and dinitration of phenyl- and diphenylacetic acids, as their corresponding methyl esters, by capillary gas chromatography (GC) with Fourier transform infrared (FT-IR) and mass spectrometric (MS) detection.

The use of an OV-1 coated capillary column working between 150 and 300°C with a gradient 10°C min⁻¹ allowed the separation of all the isomers actually present in the available mixtures. GC-MS established that all the dinitro derivatives had both rings bearing a nitro group.

The positional assignments were essentially established by extrapolation of the observations of the IR stretching vibrations of both the nitro group and the benzene ring in the methyl esters of mononitrophenylacetic acid isomers.

In continuation of synthetic work on the mono- and dinitration of α - and α,α -substituted toluenes and diphenylmethanes, we encountered the problem of the prompt identification of the isomers produced in the nitration of α -hydroxydiphenylacetic (benzilig) acid and its methyl ester under a variety of experimental conditions.

This paper describes the investigation of this problem by the procedure successfully used previously [1], i.e., the separation of the nitration products of α -hydroxydiphenylacetic acid (after methylation with diazomethane) by capil-

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lary GC and identification of the separated peaks by FT-IR spectrometry, in part supported by MS. However, the introduction of the hydroxyl group into the structure of phenylacetic acid derivatives causes a significant change in both the symmetry and polarity of the molecule, creating a new identification problem in respect of the nitro derivatives of diphenylacetic acid. This problem has not been reported previously; moreover, all these nitro derivatives are unknown or poorly characterized compounds.

2. Experimental

2.1. Materials

α -Hydroxydiphenylacetic acid (benzilic acid) was provided by Chimica del Friuli (Torviscosa, Udine, Italy). Nitration experiments on α -hydroxydiphenylacetic acid and its methyl ester, obtained by Fisher methylation [2], yielding the corresponding mono and dinitro derivatives, were carried out in a standard fashion. Mixtures of nitrated acids were methylated by the action of diazomethane in diethyl ether. Pure *o*-nitrobenzilic acid was obtained by crystallization from a mononitration reaction mixture; *p,p'*-dinitrobenzilic acid was analogously obtained from a dinitration mixture.

2.2. GC-FT-IR and GC-MS measurements

GC separations were carried out on a capillary column (8 m \times 320 μ m I.D.) coated with HP-5 as the stationary phase with a 0.17- μ m film thickness (Hewlett-Packard, Avondale, PA, USA). The carrier gas was helium at an inlet pressure of 50 kPa and a linear velocity of 44 cm s⁻¹. Samples were injected on to the column with a 1- μ l syringe with the aid of a splitter operating at a splitting ratio of 1:50. The column efficiency was 20 000 effective plates for *m,m'*-dinitrobenzilic acid methyl ester with $k' = 30$ at 200°C. *n*-Alkanes were added to the mixtures of nitration products in order to evaluate retention indices in isothermal and temperature-programmed experiments. Retention indices were

measured with an average repeatability of ± 1 index unit (i.u.). The column temperature was programmed from 110 to 300°C at 10°C min⁻¹.

A Hewlett-Packard (Palo Alto, CA, USA) Model 5890 Series II gas chromatograph equipped with an HP Model 5965 A IR detector was used to record FT-IR spectra.

Mass spectra were recorded using a Fisons VG TRIO 2000 gas chromatograph-mass spectrometer (VG Biotech, Cheshire, UK), equipped with automated data retrieval, under electron impact (EI) (70 eV) conditions working in the positive-ion mode. Each individual GC peak was carefully inspected for constancy of the MS pattern in order to detect possibly overlapping components and to ensure homogeneity of the eluates.

3. Results and discussion

3.1. Gas chromatography

The chromatogram of the methyl esters of the nitration products of α -hydroxydiphenylacetic acid obtained with temperature programming on a capillary column with HP-5 as the stationary phase is shown in Fig. 1. In a short capillary column with an efficiency of 20 000 plates, complete separation of the isomeric mononitro and dinitro derivatives was obtained. The measured values of their retention indices with temperature programming [3] and isothermally at 200°C, and their temperature coefficients, are given in Table 1.

The retention orders of the isomeric mononitro (*ortho* < *meta* < *para*) and dinitro (*ortho*, *ortho'* < *ortho,meta'* < *ortho,para'* < *meta*, *meta'* < *meta,para'* < *para,para'*) methyl esters of α -hydroxydiphenylacetic acid were identical with those of the mono- and dinitromethyl esters of diphenylacetic acid [1], and also with those of methyl- and dimethylbiphenyls [4]. When a second methyl group is introduced in the second ring of a methylbiphenyl, additivity of the retention index contribution acts in a range of a few units. Similarly, with a change in substitution from mono- to dinitromethyl esters of α -hydroxydiphenylacetic acid the measured values

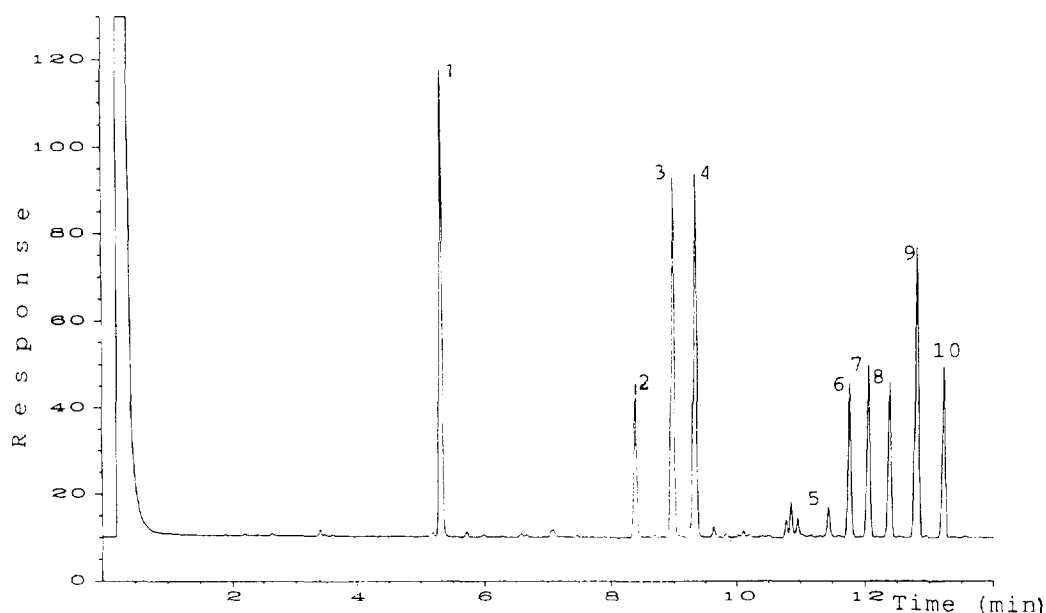


Fig. 1. Chromatogram of the methyl esters of the products from the nitration of α -hydroxydiphenylacetic acid. Peak identification as in Table 1.

are on average only 11 i.u. higher than those calculated from the retention index contribution of mononitro derivatives. This value is about five times smaller than the value of the retention

index difference of neighbouring eluted isomers, which for mononitro isomers is 41–68 i.u. and for dinitro isomers 38–57 i.u. It follows from the retention index data in Table 1 that substitution

Table 1

Temperature-programmed retention indices (TP- I), isothermal (200°C) retention indices (I) and temperature coefficients (dI/dT) of methyl esters of products from the nitration of α -hydroxydiphenylacetic acid on HP-5

GC peak No. ^a (Fig. 1)	Identification	TP- I	I	dI/dT
1		1825	1868	0.8
2	<i>ortho</i>	2152	2183	1.0
3	<i>meta</i>	2220	2245	1.0
4	<i>para</i>	2261	2285	1.0
5	<i>ortho.ortho'</i>	2516	2519	1.1
6	<i>ortho.meta'</i>	2557	2558	1.2
7	<i>ortho.para'</i>	2595	2592	1.2
8	<i>meta.meta'</i>	2638	2632	1.1
9	<i>meta.para'</i>	2693	2677	1.4
10	<i>para.para'</i>	2750	2732	1.3

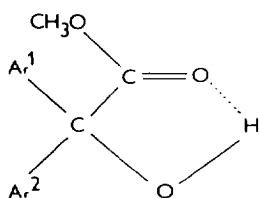
^a 1 = Methyl ester of α -hydroxydiphenylacetic acid; 2–4 = methyl esters of α -hydroxymononitrodiphenylacetic acid; 5–10 = methyl esters of α -hydroxydinitrodiphenylacetic acid with one nitro group in each phenyl ring.

of one NO₂ group in the parent compound increased the retention index of the *ortho* isomer by 315 i.u., of the *meta* isomer by 377 i.u. and of the *para* isomer by 417 i.u. Heteronuclear substitution of two NO₂ groups in the parent compound increased the retention indices by 651–864 i.u. and substitution of NO₂ in mononitro derivatives by 336–447 i.u.

None of the products is commercially available for comparison purposes and they do not appear to be easily produced by any reported method. Positive identification of isomeric nitration products was achieved with the highly informative detection of capillary column eluates both by FT-IR spectrometry and EI-MS.

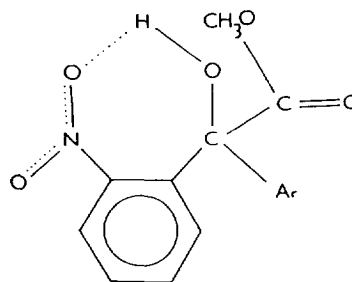
3.2. GC-FT-IR

The GC peak identification and the FT-IR data for the methyl esters of α -hydroxydiphenylacetic acid and the products of its mononitration are given in Table 2. The carbonyl stretching frequencies of *m*- and *p*-nitro derivatives of the methyl esters of α -hydroxydiphenylacetic acid are observed in a region close to the $\nu(\text{C}=\text{O})$ value of the parent methyl ester and can be assigned to the molecules stabilized by an intramolecular hydrogen bond between the C=O and OH groups [5], as illustrated.



The structure shown is also reflected by absorption in the O–H stretching frequency region, the $\Delta\nu(\text{OH})$ value being 75–80 cm⁻¹, which corresponds to a hydrogen bond energy of 7.6–8.0 kJ mol⁻¹. On the other hand, the carbonyl stretching frequency of the *o*-nitro derivative of the methyl ester of α -hydroxydiphenylacetic acid is 11–14 cm⁻¹ higher than those of α -hydroxydiphenylacetic methyl ester derivatives lacking any NO₂ group in the *ortho* position of the

benzene ring. It follows from the above data that with an *o*-nitro derivative of the methyl ester of α -hydroxydiphenylacetic acid the C=O group becomes free of intramolecular hydrogen bonding as the equilibrium is shifted towards the formation of a new hydrogen bond between the OH and the NO₂ groups [6], as shown.



The above results show that the IR frequency of the carbonyl stretching vibration in α -hydroxydiphenylacetic acid esters can be advantageously used as a reliable criterion for identification and distinction of the *o*-nitro derivatives. The second characteristic feature of an *o*-nitro derivative in comparison with *para*- and *meta*-substituted nitro compounds is the increase in $\nu_s(\text{NO}_2)$ frequency by 7 cm⁻¹, as a consequence of a decrease in coplanarity, i.e., deconjugation between the NO₂ and OH groups. It must be pointed out that the FT-IR spectrum of the *o*-nitro derivative of the methyl ester of α -hydroxydiphenylacetic acid obtained from the mixture by GC separation was identical with that measured for the isolated pure compound. Analogously to the nitration products of phenyl- and diphenylacetic acids [1], the *p*- and *m*-nitro derivatives of the methyl ester of α -hydroxydiphenylacetic acid can be clearly distinguished comparing the values of $\nu_{as}(\text{NO}_2)$ frequencies, and in the case of *para* substitution, by the occurrence of the characteristic aromatic absorption $\nu(\text{arom.})$ at ca. 1600 cm⁻¹. Finally, the *para* position of the nitro group on the benzene ring of the methyl ester of α -hydroxydiphenylacetic acid was also assigned using the characteristic position of the absorption band belonging to the out-of-plane wagging deformation of the benzene ring $\omega(\text{CH})$.

Table 2
FT-IR data for the methyl esters of α -hydroxydiphenylacetic acid and its products of mononitration

GC peak No. (Fig. 1)	Position of NO ₂ group on benzene ring	ν (cm ⁻¹)		$\Delta\nu(\text{OH})^a$	$\nu(\text{C}=\text{O})$	$\nu_{\text{as}}(\text{NO}_2)$	$\nu_{\text{s}}(\text{NO}_2)$	$\nu(\text{C}-\text{O})$	$\omega(\text{CH})$
		$\nu(\text{OH})_{\text{free}}$	$\nu(\text{OH})_{\text{bond}}$						
1	- ^b	3623	3548	75	1744	-	-	1243	- ^c
2	<i>ortho</i>	3622	3536	86	1758	1547	1359	1241	763
3	<i>meta</i>	3622	3543	79	1747	1546	1352	1245	- ^c
4	<i>para</i> ^d	3622	3542	80	1746	1538	1352	1245	851, 754

^a $\Delta\nu(\text{OH}) = \nu(\text{OH})_{\text{free}} - \nu(\text{OH})_{\text{bond}}$.

^b Methyl ester of α -hydroxydiphenylacetic acid.

^c Unresolved.

^d Additional absorption band of $\nu(\text{arom.}) = 1599 \text{ cm}^{-1}$.

The identification rules discussed above for simple mononitration products of α -hydroxydiphenylacetic acid enabled a strategy for the identification of structurally more complex dinitro derivatives to be elaborated. The GC peak assignments and the FT-IR features of the dinitration products of methyl esters of α -hydroxydiphenylacetic acid are listed in Table 3. The knowledge of the position of the stretching vibration of free and hydrogen-bonded C=O groups was implemental for identification and distinction of the *ortho* substitution. Further, the $\nu_{as}(\text{NO}_2)$, $\nu(\text{arom.})$ and, in some instances, also the $\omega(\text{CH})$ bands were successfully employed to identify *meta* and *para* substitution.

In addition, it has been observed that for all the dinitro derivatives the intensity ratio $\nu_{as}(\text{NO}_2):\nu(\text{C=O})$ is always >1 , whereas the same ratio for mononitro compounds is ≤ 1 . This general rule allows one to distinguish reliably all the products of dinitration from those of mononitration. Finally the identity of the *p,p'*-dinitro derivative was confirmed by recording the FT-IR spectrum of the isolated substance. It must also be mentioned that these results are in good agreement with those obtained previously [1] for the corresponding nitration products of phenyl- and diphenylacetic acids.

3.3. GC-MS

The mass spectral patterns of the three methyl mononitrobenzylates **1**, **2** and **3** (Fig. 2) showed essentially the same main features, i.e., a base

peak for the loss of the methyl carboxylate function from the parent ion [m/z 228 (**4**)] and an intense ion (**5**) at m/z 150, corresponding to the composition $\text{O}_2\text{NC}_6\text{H}_4\text{CO}$, believed to originate from the former by elimination of a benzene molecule. This could be formed by the acidic proton on the oxygen in **4** being transferred to the more electron-rich phenyl group rather than to the less electron-rich nitrophenyl group; eventually, both **5** and **6** should lose carbon monoxide, but only the latter did. This was completely unexpected behaviour, and we therefore have to assume that the true nature of the fragment had by this time changed to that of a mesomerically favourable nitrite derivative **7** from that of a nitro derivative **5**. We also noticed the presence of an ion at m/z 104 (**8**) for the *meta* and *para* isomers (**2** and **3**); the ion at m/z 77 is always present and larger than any at m/z 76. In the spectrum of the *para* isomer **3**, the ion at m/z 150 (**7**) underwent loss of a nitrogen monoxide molecule (m/z 120, **9**) to some extent, which eventually collapsed to **10** (m/z 92). The direct inlet mass spectrum of the isolated *ortho* isomer **1** was identical with that obtained for the first GC peak of the mononitro isomers.

The six dinitro derivatives of the methyl ester of α -hydroxydiphenylacetic acid (**12–17**) present in the nitration mixture also exhibited mass spectral patterns (Fig. 3) that were so similar that they could not be used even as fingerprints to distinguish them one from another. Their parent ions were absent or barely observable from a regular spectrum recorded at 70 eV; the

Table 3
FT-IR data for the methyl esters of the products of the heteronuclear dinitration of α -hydroxydiphenylacetic acid

GC peak No. (Fig. 1)	Position of NO_2 group on the benzene rings	ν (cm^{-1})					$\omega(\text{CH})$
		$\nu(\text{C=O})$	$\nu(\text{arom.})$	$\nu_{as}(\text{NO}_2)$	$\nu_s(\text{NO}_2)$	$\nu(\text{C-O})$	
5	<i>ortho.ortho'</i>	1760	1603 ^a	1548	1359	1243	– ^b
6	<i>ortho.meta'</i>	1760	–	1547	1353	1244	– ^b
7	<i>ortho.para'</i>	1759	1602	1546	1352	1248	851
8	<i>meta.meta'</i>	1749	–	1547	1351	1247	– ^b
9	<i>meta.para'</i>	1749	1600	1546	1351	1248	851
10	<i>para.para'</i>	1749	1600	1543	1351	1250	848

^a Exception: see also the methyl ester of 2-nitrobenzeneacetic acid [1].

^b Unresolved.

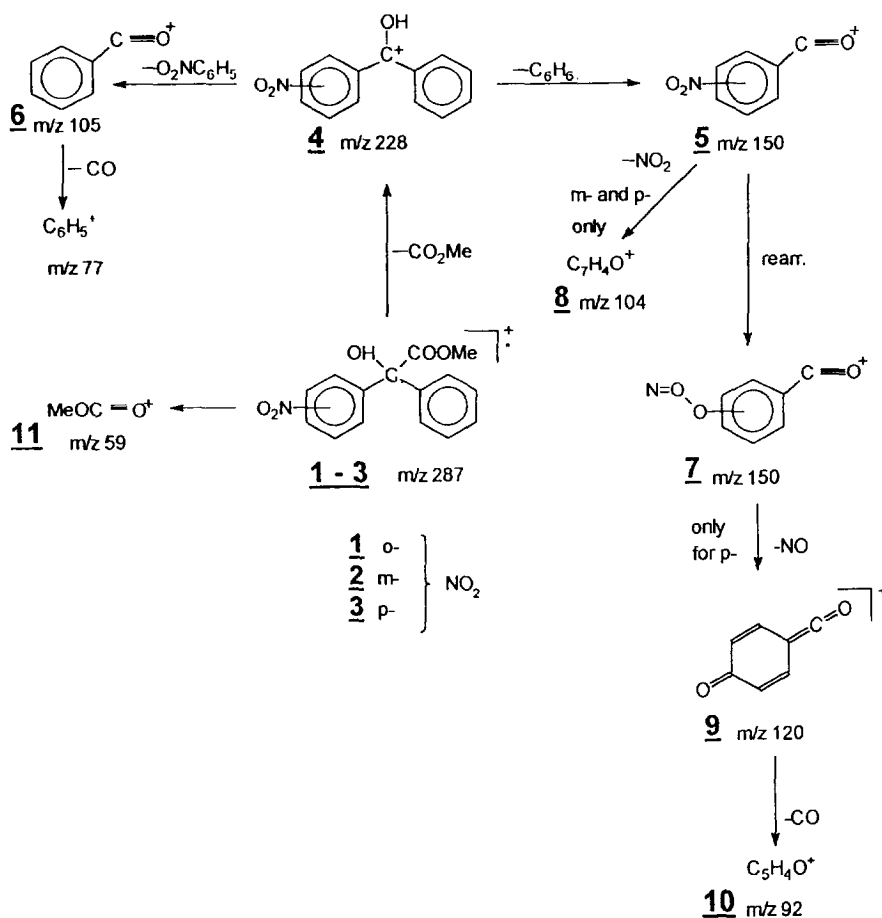


Fig. 2. Mass spectral patterns of the mononitro derivatives of the methyl ester of α -hydroxydiphenylacetic acid.

ion at m/z 59 for the MeCO_2 ion (**11**) was constantly present, but of definitively small intensity. The common feature was a fragment ion at m/z 273 (loss of MeCO_2 from the parent ion, **18**), which corresponded in all instances to the base peak. A peak at m/z 150 (**5** and/or **7**) was the second highest (65–80%), accompanied by weaker ions at m/z 151 and 152 (**19** and **20**). The weaker peak at m/z 105 could be ascribed to a different route, namely loss of NO_2 from **19**. A weak ion at m/z 180 (**21**) was equally ubiquitous and is believed to yield the ion at m/z 152 (**20**) by loss of carbon monoxide. Loss of nitrogen dioxide from the ion at m/z 150 (**5** and/or **7**) yielded the ubiquitous ion of medium intensity at m/z 104 (**8**), as we saw before. The *para* deriva-

tives **14**, **16** and **17** all showed a small but distinct ion at m/z 120 (**9**), a feature observed in the *p*-mononitro isomer **3**.

The above observations, coupled with the peak homogeneity for all the dinitro isomers **12–17**, allowed us to discard the possibility of the presence of any significant concentrations of isomers with both the nitro groups in a single phenyl ring in the analysed mixture. The direct inlet mass spectrum obtained for isolated pure methyl *p,p'*-dinitrobenzilate (**17**), independently identified by ^1H NMR and IR spectrometry, was identical in all details with the mass spectrum of the sixth GC peak of the dinitro isomers GC sequence.

Nitration of methyl *o*-nitrobenzilate (**1**) with

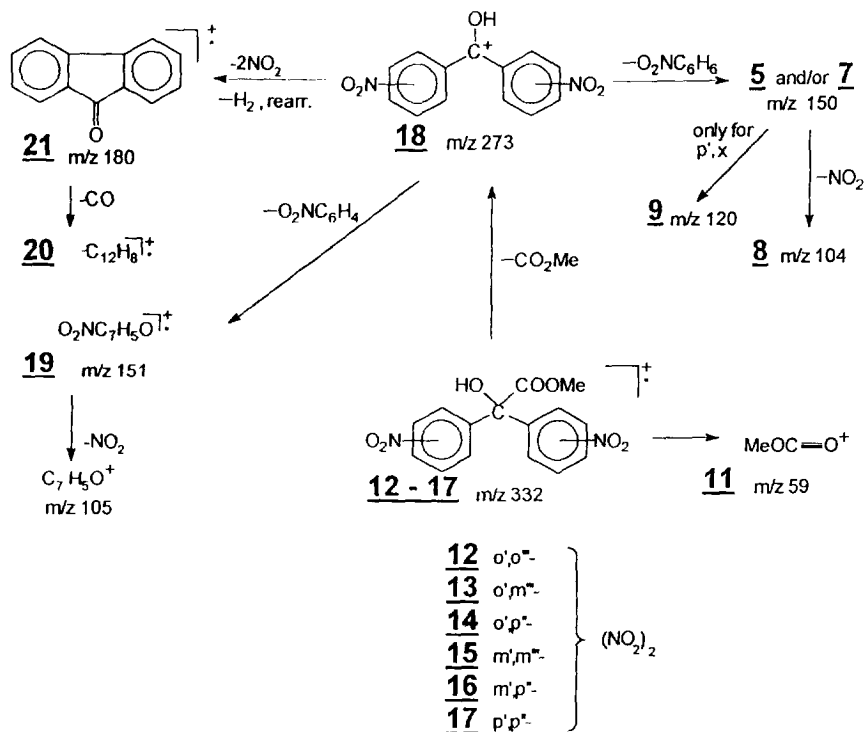


Fig. 3. Mass spectral patterns of the dinitro derivatives of the methyl ester of α -hydroxydiphenylacetic acid.

100% nitric acid yielded three *ortho,x*-isomers, which overlapped the first three GC peaks of the whole nitration mixture and exhibited identical mass spectra.

The minor peaks detected in the chromatogram (Fig. 1) were found to be side-products of a different nature.

4. Conclusions

The coupling of capillary GC with FT-IR spectrometry and EI-MS allowed the identification of all the isomers arising from the mononitration and dinitration of α -hydroxydiphenylacetic acid.

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