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# Hydrogen–Carbon, Carbon–Carbon Double Rearrangement Induced by Proximity Effects

## 1—Formation of Methoxybenzyl Ions in the Electron Impact Mass Spectra of Substituted 1,1-Bis(dimethoxyphenyl)methanes†

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**The 75 eV electron impact mass spectra of 1,1-bis(dimethoxyphenyl)methanes bearing *o*-methoxy groups are dominated by intense peaks corresponding, at least formally, to benzyl ions $[(CH_3O)_2C_6H_3CH_2]^+$ (*b*). They arise from ions $[((CH_3O)_2C_6H_3)_2CH]^+$ (*a*), which are in turn formed from molecular ions by loss of an alkyl radical through benzylic cleavage. The analysis of compounds labelled with $^2H$ or $^{13}C$ at methoxy groups led to the determination of the mechanism. Hydrogen migration, as hydride, followed by electrophilic substitution by the methylene carbon of the phenyl methylene ether cation through a six-centred transition state is responsible for the formation of benzylic ions *b*.**

## INTRODUCTION

We have previously observed,[2] as the 75 eV electron impact (EI) mass spectrum of 1,1-bis(2,4-dimethoxyphenyl)-2-methylpropane (**1**) (Table 1) shows, in addition to the base peak at *m/z* 287 (ion *a*) formed by loss of an isopropyl radical through benzylic cleavage of the molecular ion, an intense peak at *m/z* 151 corresponding, at least formally, to the dimethoxybenzylic ion *b*. The rearrangement to the corresponding tropylium ion, even if possible,[3] was not investigated in this work and the ion *b* will be indicated as benzylic for simplicity.

Exact mass measurements agree with an elemental composition for ion *b* consistent with $C_9H_{11}O_2$, whereas the presence of the appropriate metastable ion indicates ion *a* as its precursor. A hydride migration (Scheme 1), followed by benzylic cleavage, was suggested.[2] This hypothesis was also in agreement with the commonly encountered *ortho* interaction which involves the transfer of hydrogen atom(s) to the side-chain.[4]

Hence, it seemed of interest to investigate this reaction, in order to confirm the implication of proximity effects and to determine the mechanism responsible for ion *b* formation. We examined several 1,1-bis(dimethoxyphenyl)methanes with different substitution patterns on both the phenyl rings and the aliphatic chain, also with the aid of $^2H$- and $^{13}C$-labelled compounds.

## RESULTS AND DISCUSSION

We examined first the EI mass spectrum of 1,1-bis(3,4-dimethoxyphenyl)-2-methylpropane (**2**), which does not bear any methoxy group at C(2) (Table 1) and, as expected, the ion *b* was not observed.

In contrast, intense peaks at *m/z* 151 are present in the spectra of the 2-methoxy-substituted compounds **3**, **4**, **5** and **6**, and also in those of compounds **7**, **8**, **9** and **10**. Hence the occurrence of this reaction is determined by the presence of the methoxy group at C(2) and neither the different substituents linked to the benzylic carbon nor the different substitution pattern on the aromatic rings impairs the formation of ions *b*.

Further, it seemed useful to investigate compounds bearing deuterium-labelled *o*-methoxy groups. Surprisingly, the mass spectrum of the dodecadeuterio derivative **11** shows a total shift of the ion *b* at *m/z* 159 (Table 1); the occurrence of the previously suggested mechanism should afford, instead, an ion *b* at *m/z* 158 (Scheme 2). It is evident that ion *b* contains two deuterium atoms, which suggests the participation of two deuterium atoms of the *o*-methoxy groups.

Useful information was also obtained from the EI mass spectrum of the hexadeuterio derivative **12**, which

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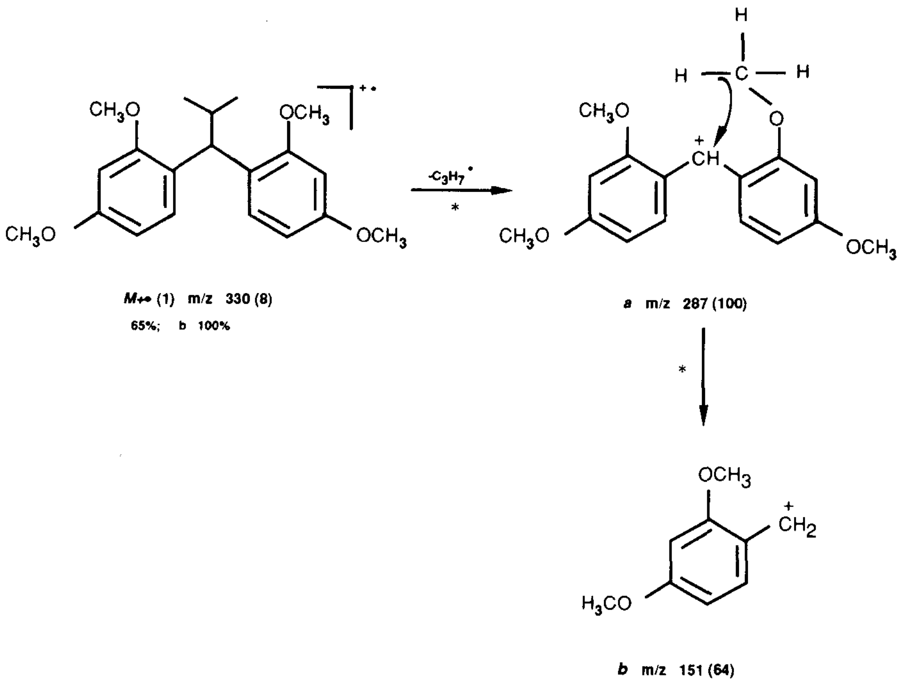


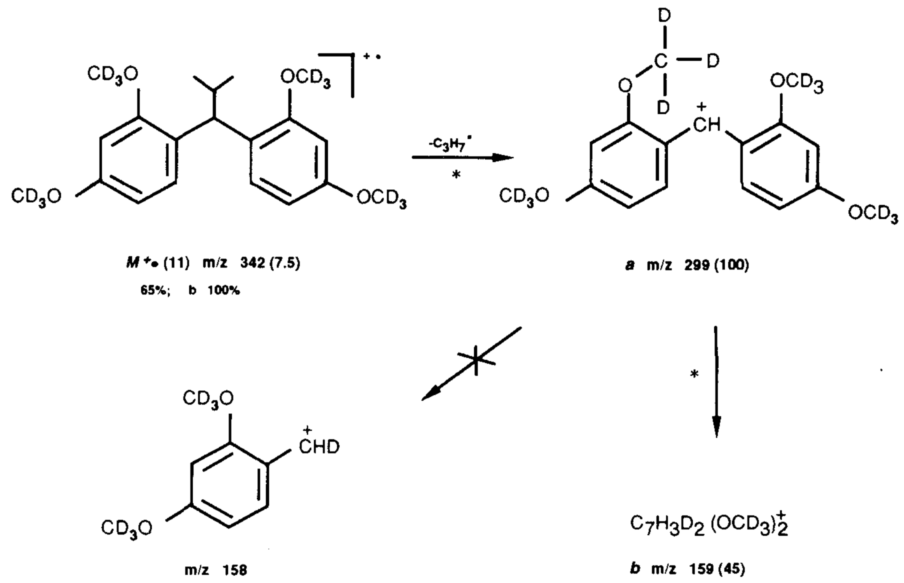
**Scheme 1**. Electron impact-induced fragmentation of **1**.

shows two ions *b*, at *m/z* 153 and 157 (Table 1), respectively. The *m/z* 153 ion contains two deuterium atoms arising from the *ortho*-labelled methoxy group, whereas that at *m/z* 157 bears two hydrogen atoms arising from the *ortho*-unlabelled methoxy group (Scheme 3)

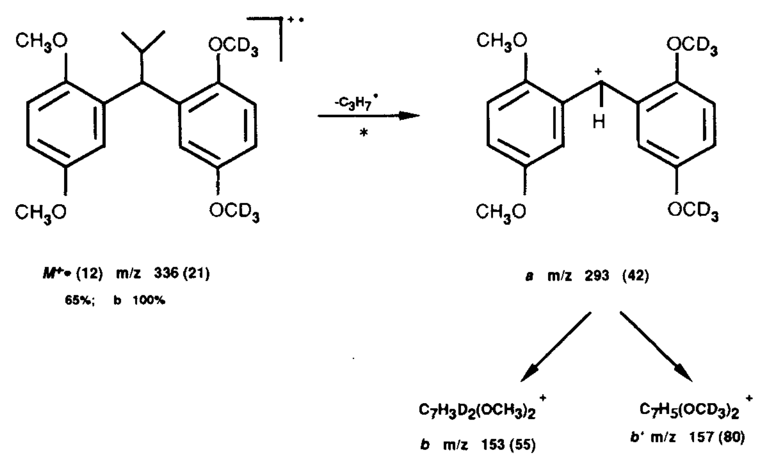
In addition, the presence of identical labelled and unlabelled moieties allows the accurate determination of the isotopic effect, which is $K_H/K_D = [m/z\ 157]/[m/z\ 153] = 1.45$. This value is that expected on the basis of the quasi-equilibrium theory ($\nu_H/\nu_D = \sqrt{2}$) for highly energetic decomposing ions[5] as those generated in the 75 eV EI mass spectrum. Hence in this reaction the migration of a hydrogen (or deuterium) atom from the methoxy group constitutes the rate-determining process.

However, the shift of two mass units in the labelled compounds does not agree with the proposed mechanism[2] and cannot be explained by consecutive scrambling between the methoxy hydrogens and benzylic or aromatic hydrogens. In fact, in both cases mixtures of ions *b* shifted 1–2 u in comparable amounts should be obtained.

All these findings can be rationalized by assuming that the methylene of the *o*-methoxy group becomes part of the benzyl ion *b*. Hence it was necessary to synthesize compounds with $^{13}$C-labelled *o*-methoxy groups. Thus the EI mass spectrum of the **13** unequivocally demonstrates that the labelled carbon atom is part of the ion *b* as it is shifted at *m/z* 152 (Table 1).



**Scheme 2**. Electron impact-induced fragmentation of **11**.

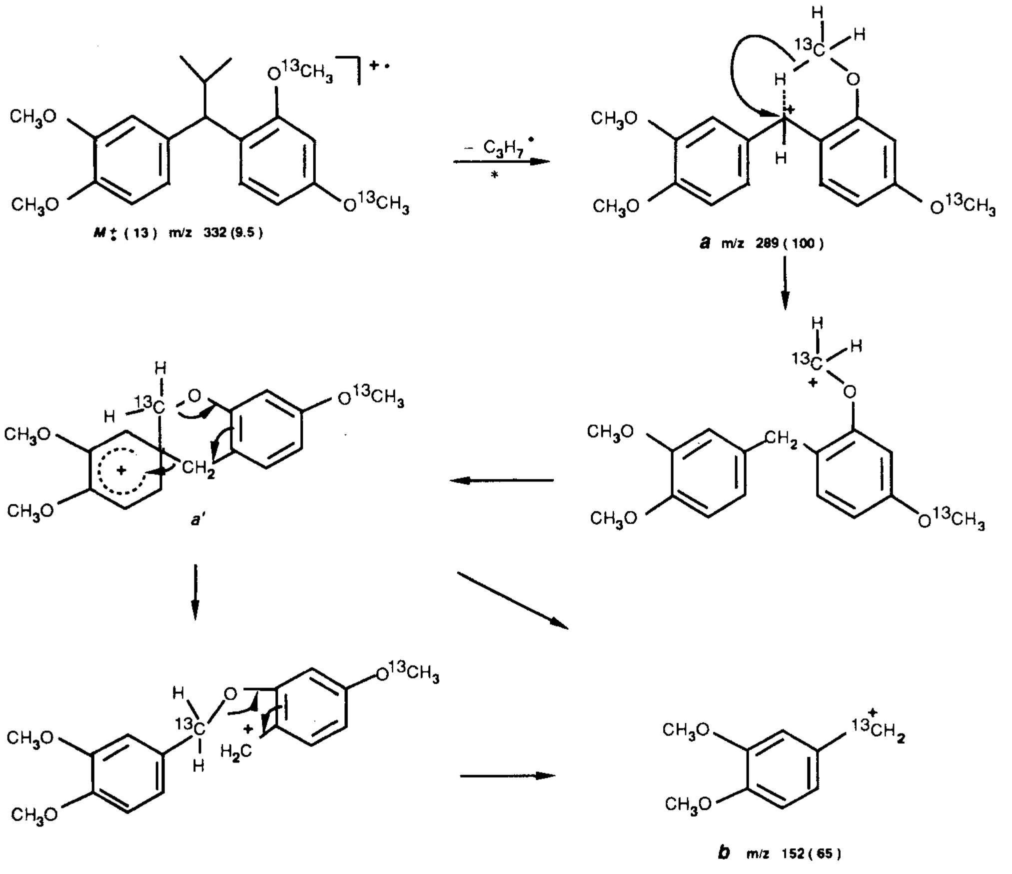


Scheme 3. Electron impact-induced fragmentation of **12**.

The formation of the benzylic ion *b* in the EI mass spectra of these compounds can be rationalized, as shown in the Scheme 4 for **13**, with a double H—C and C—C rearrangement. The first step involves the migration of hydrogen (as hydride) of the *o*-methoxy group, through a six-centred transition state, to the benzylic carbon (ion *a*); this hydrogen migration is responsible for the rate-determining process. The second step involves the electrophilic attack of the charged carbon atom of the methylene phenyl ether cation *a*, again through a six-centred transition state. Hence, the resulting ion *a*′ gives, by a concerted or stepwise process, either charged (benzyl or tropylium ion) or neutral (5-methylenecyclohexa-2,4-dienone) thermodynamically stable products.

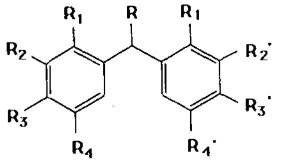
## CONCLUSION

By use of $^2$H- and especially $^{13}$C-labelled compounds the occurrence of a new double rearrangement in mass spectrometry involving hydrogen—carbon followed by carbon—carbon transposition due to proximity effects of the methoxy group in a series of diphenylmethane derivatives was demonstrated. As this reaction has not



Scheme 4. Electron impact-induced fragmentation of **13**.

**Table 1. Structures and EI mass spectra (75 eV) of compounds 1–13**[a]



| | | | | | | | | | | m/z (relative abundance, %) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Compound | R | $R_1$ | $R_2$ | $R_3$ | $R_4$ | $R_1'$ | $R_2'$ | $R_3'$ | $R_4'$ | $M^{+\cdot}$ | *a* | *b* |
| **1** | $(CH_3)_2CH$ | $OCH_3$ | H | $OCH_3$ | H | $OCH_3$ | H | $OCH_3$ | H | 330 (8) | 287 (100) | 151 (64) |
| **2** | $(CH_3)_2CH$ | H | $OCH_3$ | $OCH_3$ | H | H | $OCH_3$ | $OCH_3$ | H | 330 (15) | 287 (100) | — |
| **3** | H | $OCH_3$ | H | $OCH_3$ | H | $OCH_3$ | H | $OCH_3$ | H | 288 (100) | 287 (10) | 151 (39) |
| **4** | $CH_3$ | $OCH_3$ | H | $OCH_3$ | H | $OCH_3$ | H | $OCH_3$ | H | 302 (47) | 287 (81) | 151 (100) |
| **5** | $CHCl_2$ | $OCH_3$ | H | $OCH_3$ | H | $OCH_3$ | H | $OCH_3$ | H | 370 (65) | 287 (100) | 151 (45) |
| **6** | $CCl_3$ | $OCH_3$ | H | $OCH_3$ | H | $OCH_3$ | H | $OCH_3$ | H | 404 (5) | 287 (65) | 151 (100) |
| **7** | $(CH_3)_2CH$ | H | $OCH_3$ | $OCH_3$ | H | $OCH_3$ | H | $OCH_3$ | H | 330 (17) | 287 (100) | 151 (55) |
| **8** | $(CH_3)_2CH$ | $OCH_3$ | H | H | $OCH_3$ | $OCH_3$ | H | H | $OCH_3$ | 330 (34) | 287 (60) | 151 (100) |
| **9** | $(CH_3)_2CH$ | $OCH_3$ | $OCH_3$ | H | H | H | $OCH_3$ | $OCH_3$ | H | 330 (20) | 287 (100) | 151 (55) |
| **10** | $(CH_3)_2CH$ | $OCH_3$ | H | $OCH_3$ | $OCH_3$ | H | $OCH_3$ | $OCH_3$ | H | 360 (14) | 317 (92) | 151 (100) |
| **11** | $(CH_3)_2CH$ | $OCD_3$ | H | $OCD_3$ | H | $OCD_3$ | H | $OCD_3$ | H | 342 (7.5) | 299 (100) | 159 (45) |
| **12**[b] | $(CH_3)_2CH$ | $OCD_3$ | H | $OCD_3$ | H | $OCH_3$ | H | $OCH_3$ | H | 336 (21) | 293 (42) | 157 (80)<br>153 (55) |
| **13** | $(CH_3)_2CH$ | $O^{13}CH_3$ | H | $O^{13}CH_3$ | H | H | $OCH_3$ | $OCH_3$ | H | 332 (10) | 289 (100) | 152 (65) |

[a] For labelled compounds the degree of complete $^2H$ and $^{13}C$ incorporation is 96–98%. The contribution of the partially labelled compounds was not taken into account.

[b] The base peak is at *m/z* 43.

hitherto been reported, studies are in progress to determine the essential structural requirements, the effects of substituents on both aromatic rings and that of a second radical on the benzylic group in addition to the possibility of such a reaction by modifications of the *ortho* substituent.

## EXPERIMENTAL

Low-resolution mass spectra were measured on a Jeol JMS-01-SG-2 mass spectrometer with an electron beam energy of 75 eV, an accelerating voltage of 10 kV and a total emission current of 100 μA. Exact mass measurements were performed at 15000 resolving power, using a photoplate detection technique and perfluorokerosene as standard, and to an accuracy of ±10 ppm of the theoretical value. First field-free metastable ions were detected by the accelerating voltage scan technique. The samples were introduced into the ionization chamber with a glass probe.

$^1H$ NMR spectra were measured with a Varian EM-360A instrument, using tetramethylsilane as internal standard.

Compounds **1**,[2] **2**,[6] **3**,[7] **4**,[8] **7**[8] and **8**[8] were obtained by literature methods. Compounds **5** and **6** were synthesized as **1** using 1,3-dimethoxybenzene and dichloroacetaldehyde and chloralium hydrate, respectively, instead of isobutyraldehyde.

### 1,1-Bis(2,4-dimethoxyphenyl)-2,2-dichloroethane (5)

This was obtained as white crystals from ethanol, m.p. 103–104 °C (yield 74%). $^1H$ NMR ($CDCl_3$), $\delta$: 3.74 (6H, s, 2 $OCH_3$), 3.78 (6H, s, 2 $OCH_3$), 5.20 (1H, d, $J = 9.0$ Hz, $CHCHCl_2$), 6.30–6.50 (4H, m, 2 3-H and 2 5-H), 6.70 (1H, d, $J = 9.0$ Hz, $CHCHCl_2$), 7.30 (2H, d, $J_o = 8.5$ Hz, 2 6-H).

### 1,1-Bis(2,4-dimethoxyphenyl)-2,2,2-trichloroethane (6)

White crystals were obtained from ethanol, m.p. 105 °C (yield 95%). $^1H$ NMR ($CDCl_3$), $\delta$: 3.73 (6H, s, 2 $OCH_3$), 3.76 (6H, s, 2 $OCH_3$), 6.30 (1H, s, $CHCCl_3$), 6.43 (2H, d, $J_m = 2.5$ Hz, 2 3-H), 6.50 (2H, dd, $J_o = 8.5$ Hz, $J_m = 2.5$ Hz, 2 5-H), 7.76 (2H, d, $J_o = 8.5$ Hz, 2 6-H).

### 1-(2,3-Dimethoxyphenyl)-1-(3,4-dimethoxyphenyl)-2-methylpropane (9)

By a Grignard reaction, 2,3-dimethoxybenzaldehyde (10 g) and isopropylmagnesium bromide (obtained from magnesium (10 g) and isopropylbromide (42 g)) in anhydrous diethyl ether afforded 1-(2,3-dimethoxyphenyl)-2-methylpropan-1-ol (12 g) as an oil (yield 95%). IR (Nujol), $\nu_{max}$: 3450 cm$^{-1}$ (OH). $^1H$ NMR ($CDCl_3$), $\delta$: 0.80 (3H, d, $J = 6.8$ Hz, $CHCH_3$), 1.02 (3H, d, $J = 6.8$ Hz, $CHCH_3$), 2.00 (1H, m, $CH(CH_3)_2$), 2.85 (1H, s broad, exchangeable with $D_2O$, $OH$), 3.85 (6H, s, 2 $OCH_3$), 4.63 (1H, d, $J = 7.2$ Hz, $CHOH$), 6.85–7.15 (3H, m, aromatic-H). Compound **9** was synthesized as **8** using the 1-(2,3-dimethoxyphenyl)-2-methylpropan-1- ol obtained as described above and 1,2-dimethoxybenzene as a yellow oil (yield 90%). $^1H$ NMR ($CDCl_3$), $\delta$: 0.87 (3H, d, $J = 6.5$ Hz, $CHCH_3$), 0.90 (3H, d, $J = 6.5$ Hz, $CHCH_3$), 2.40 (1H, m, $CH(CH_3)_2$), 3.67 (3H, s, $OCH_3$), 3.70 (6H, s, 2 $OCH_3$), 3.75 (3H, s, $OCH_3$), 3.90 (1H, d, $J = 11.0$ Hz, $CHCH(CH_3)_2$), 6.70–7.00 (6H, m, aromatic-H).

### 1-(2,4,5-Trimethoxyphenyl)-1-(3,4-dimethoxyphenyl)-2-methylpropane (10)

This was synthesized as **7** using 1,2,4-trimethoxybenzene instead of 1,3-dimethoxybenzene as a yellow oil (yield 83%). $^1$H NMR [$(CD_3)_2CO$)], $\delta$: 0.85 (6H, d, $J = 6.5$ Hz, $CH(CH_3)_2$), 2.50 (1H, m, $CH(CH_3)_2$), 3.63 (3H, s, $OCH_3$), 3.70 (3H, s, $OCH_3$), 3.72 (9H, s, 3 $OCH_3$), 3.88 (1H, d, $J = 11.0$ Hz, $CHCH(CH_3)_2$), 6.58 (1H, s, 3-H), 6.75–7.00 (3H, m, 2′-, 5′- and 6′-H), 7.00 (1H, s, 6-H).

### 1,1-Bis(2,4-[dimethoxy-$^2H_{12}$]phenyl)-2-methylpropane (11)

This was synthesized as **1** using 1,3-hexadeuteriodimethoxybenzene[9] instead of 1,3-dimethoxybenzene as white crystals from ethanol, m.p. 112 °C (yield 60%) (degree of complete D incorporation, 96%). $^1$H NMR ($CDCl_3$), $\delta$: 0.88 (6H, d, $J = 6.8$ Hz, $CH(CH_3)_2$), 2.50 (1H, m, $CH(CH_3)_2$), 4.30 (1H, d, $J = 11.0$ Hz $CHCH(CH_3)_2$), 6.40 (2H, d, $J_m = 2.5$ Hz, 2 3-H), 6.48 (2H, dd, $J_o = 8.5$ Hz and $J_m = 2.5$ Hz, 2 5-H), 7.30 (2H, d, $J_o = 8.5$ Hz, 2 6-H).

### 1-(2,5-Dimethoxyphenyl)-1-(2,5-[dimethoxy-$^2H_6$]phenyl)-2-methylpropane (12)

Compound **12** was synthesized as **8** using 1,4-hexadeuteriodimethoxybenzene[9] instead of 1,4-dimethoxybenzene as white crystals from ethanol, m.p. 83 °C (yield 60%) (degree of complete D incorporation, 98%). $^1$H NMR ($CDCl_3$), $\delta$: 0.88 (6H, d, $J = 6.8$ Hz, $CH(CH_3)_2$), 2.50 (1H, m, $CH(CH_3)_2$), 3.70 (6H, s, 2 $OCH_3$), 4.35 (1H, d, $J = 11.0$ Hz, $CHCH(CH_3)_2$), 6.63 (2H, d, $J_m = 2.5$ Hz, 4,4′-H), 6.66 (2H, s, 3.3′-H), 6.93 (2H, d, $J_m = 2.5$ Hz, 6.6′-H).

### 1-(2,4-[Dimethoxy-$^{13}C_2$]phenyl)-1-(3,4-dimethoxyphenyl)-2-methylpropane (13)

This was synthesized as **7** using 1,3-[$^{13}$C]dimethoxybenzene instead of 1,3-dimethoxybenzene as white crystals from diethyl ether–light petroleum (b.p. 40–60 °C), m.p. 60 °C (yield 50%) (degree of complete $^{13}$C incorporation, 98%). $^1$H NMR ($CDCl_3$), $\delta$: 0.88 (6H, d, $J = 6.8$ Hz, $CH(CH_3)_2$), 2.40 (1H, m, $CH(CH_3)_2$), 3.63 (6H, d, $J_{H-C} = 144.0$ Hz, 2 $O^{13}CH_3$), 3.66 (3H, s, $OCH_3$), 4.35 (1H, d, $J = 11.0$ Hz, $CHCH(CH_3)_2$), 6.63 $CHCH(CH_3)_2$), 6.36 (1H, d, $J_m = 2.5$ Hz, 3-H), 6.44 (1H, dd, $J_o = 8.5$ Hz and $J_m = 2.5$ Hz, 5-H), 6.70–6.90 (3H, m, 2′-H, 5′-H and 6′-H), 7.20 (1H, d, $J_o = 8.5$ Hz, 6-H).

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