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^{199}Hg NMR: a tool for direct detection of the products from acetoxymercuration of alkynes[†]

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Regio- and stereo-isomers formed in the acetoxymercuration of 2-aryl-2-propyn-1-ols were detected and identified by ^{199}Hg NMR spectra, without any need to isolate them. The technique was easy and reliable, and made it possible to find out that the stereochemistry of the addition depends on the ratio of initial concentration of mercuric acetate to that of the alkyne. Copyright © 2000 John Wiley & Sons, Ltd.

Keywords: ^{199}Hg NMR; acetoxymercuration; alkynes; electrophilic addition

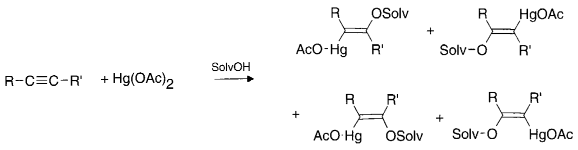
INTRODUCTION

Organomercurio compounds in organic synthesis are intermediate species, which are generally not isolated as such. Instead, reductive demercuration is currently used to yield functionalized organic compounds.[1] However, the latter reaction, performed under basic conditions, may give side products, which complicate product analysis.[2] The problem is particularly important for mercurated compounds derived from oxymercuration of alkynes (Scheme 1): regio- and stereo-isomers are possible, but usual spectroscopic methods (^{1}H, ^{13}C NMR) are of no use in the assignment of the structure.

These compounds cannot be eluted by column chromatography, nor are they detectable by gas chromatography. They are often non-crystalline materials, thus making X-ray analysis rarely practicable. Moreover, they do not usually burn well and therefore elemental analysis seldom gives reliable results. Therefore we deal with mixtures of products, which are difficult to identify.

Thus, it is desirable to have a method for direct identification of mercurated species: the study of the mercuration of alkynes could be greatly improved by the use of a technique that would make it possible to follow the progress of the reaction *in situ*. ^{199}Hg NMR is an ideal tool for such a purpose of the two magnetically active isotopes of Mercury, ^{201}Hg and ^{199}Hg, the latter has nuclear spin $I = 1/2$ and its natural abundance (16.84%) and receptivity (5.42 with respect to ^{13}C) make its detection easy by NMR. Also, relaxation rates are very high, so that a large number of transients can be acquired in a very short time. Chemical shifts are spread over a very large range and, as a consequence, are very sensitive to the electronic environment and geometry at the mercury centre.[3]

Recently, we investigated the acetoxymercuration of aryl(hydroxymethyl)ethynes, ArC≡C-CH_2OH, obtaining one or two regioisomers, depending on the substituent in the aryl ring, on the basis of reductive demercuration.[4] We report here the results of an investigation by ^{199}Hg NMR of the same reaction. In principle, four different compounds may form: two geometric stereoisomers for each of the two regioisomers. On standing (and/or after the work-up), acid-catalysed cleavage of vinyl acetates may occur, leading to α-acetoxymercurio ketones. The structures are shown in Scheme 2, where the Markownikov and anti-Markownikov regioisomers are indicated with M and aM, respectively.



Scheme 1

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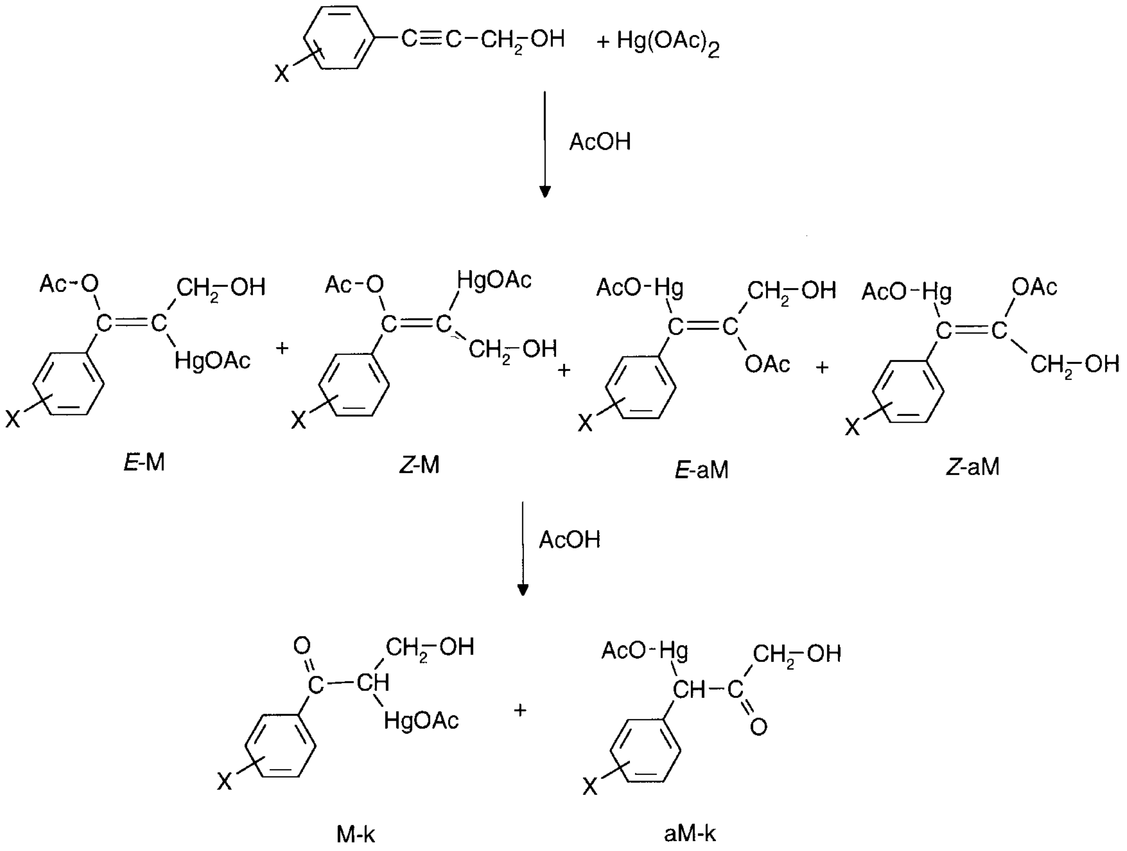


X = H, *p*-OMe, *m*-Me, *p*-Me, *p*-Cl, *m*-Me, *m*-F, *m*-NO_2, *p*-NO_2

Scheme 2

RESULTS AND DISCUSSION

Figure 1(a) shows, as a representative example, the ^{199}Hg NMR spectrum of the reaction mixture between 3-(3-fluorophenyl)-2-propyn-1-ol and $Hg(OAc)_2$ in AcOH/AcOD (1:1), and Fig. 1(b) shows the spectrum of the mixture of products obtained after work-up of the reaction in the same solvent. The resonances of α-acetoxymercurio ketones can be identified at -1645.0 ppm (M-k isomer) and -1243.5 ppm (αM-k isomer).

Three resonances are present in spectrum (a): a singlet at -1549.3 ppm and two doublets of doublets centred at -1488.4 and -1619.4 ppm. Each signal in both spectra is transformed into a singlet by proton decoupling, demonstrating that all the resonances are due to a single mercury-containing species.

The values of coupling constants between Hg

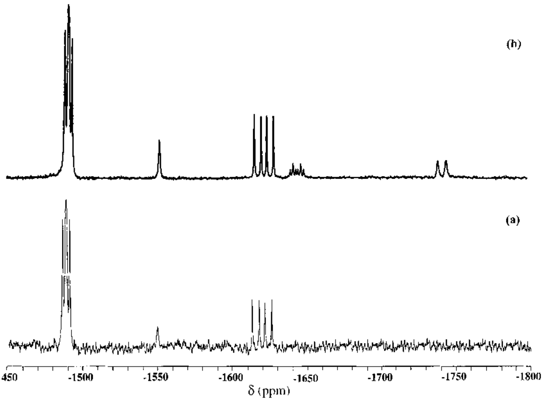
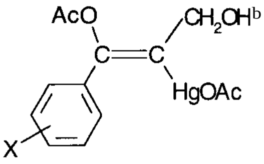
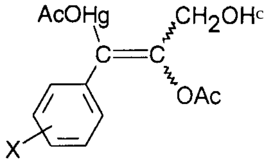
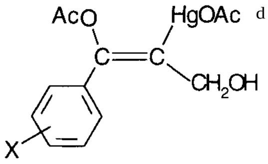


Figure 1 ^{199}Hg NMR spectra of the reaction mixture obtained from 3-(3-fluorophenyl)-2-propyn-1-ol and mercuric acetate: (a), as such; (b), after work-up.

Table 1 ^{199}Hg chemical shifts (δ) of the products of the acetoxymercuration of 3-aryl-2-propyn-1-ols,[a]

X	 [b]	 [c]	 [d]
H	−1487.4 (70)		−1619.7 (30)
p-OMe	−1486.2 (70)		−1623.6 (30)
p-Me	−1486.9 (100)		
p-Cl	−1489.7 (85)		−1622.6 (15)
p-NO_2	−1491.0 (50)	−1559.2 (50)	
m-NO_2	−1494.0 (70)	−1546.9 (30)	
m-Me	−1487.9 (80)		−1618.6 (20)
m-F	−1488.4 (85)	−1549.3	−1619.4 (10)

[a] Relative percentages in parentheses.
[b] All resonances are doublets of doublets [$^3J(^{199}Hg–^1H_a) = 145 \pm 5$ Hz, $^3J(^{199}Hg–^1H_b) = 200 \pm 5$ Hz].
[c] All resonances are singlets.
[d] All resonances are doublets of doublets [$^3J(^{199}Hg–^1H_a) = 335 \pm 5$ Hz, $^3J(^{199}Hg–^1H_b) = 600 \pm 5$ Hz].

and other nuclei are known to vary in the order $^1J \gg {}^3J > {}^2J > {}^4J$.[3,5] In vinylmercurio compounds $^4J(^{199}Hg–^1H)$ has been reported to be very small (5–12 Hz) and has been observed in the ^{1}H NMR spectra.[6]

At field strength $B_o \geq 4.7$ T relaxation arising from chemical shift anisotropy dominates ^{199}Hg spectra and produces broad resonances.[5] The half-height linewidths measured for a series of mercurated arylphenylethenes range between 75 and 100 Hz.[7] No coupling is then expected to be observed between mercury and the methylene group for *E*-aM and *Z*-aM structures, thus indicating that the two doublets of doublets observed are due to *E*-M and *Z*-M compounds.

We have previously reported that a good linear correlation exists between ^{199}Hg chemical shifts and calculated mercury atomic charge: a decrease in the metal atomic charge has been found to cause an increase in shielding.[7] Mercury atomic charge for the series of compunds *E*-M and *Z*-M has been calculated on the optimized geometries obtained by semi-empirical methods (PM3). The values of atomic charge have been obtained with the RHF/LanL2DZ basis set[8,9] by Mulliken population analysis (MPA). Limitations inherent to such calculations have been discussed previously.[7] The values obtained for compounds *E*-M and *Z*-M (X = H) are 0.8093 and 0.8322. Furthermore, the ^{199}Hg δ values reported for the structurally related *E* and *Z* isomers of 2-acetoxy-1-chloromercurio-1-phenylpropene are respectively −1154 and −1191.[10] These results indicate that the most shielded resonance can be attributed to the *E*-M isomer and the one centred around −1600 ppm to the *Z*-M isomer.

The observed coupling patterns indicate the non-equivalence of the hydrogen atoms of the α-methylene group. When the reaction mixture obtained by adding mercuric acetate to a solution of 3-(4-methoxyphenyl)-2-propyn-1-ol in acetic acid was heated to $T = 365$ K, close to the solvent boiling point, the doublet of doublets at $\delta = -1486.2$ ppm become a triplet-shaped resonance (intensity 1:2:1), indicating that for the *E*-M isomer the two methylenic hydrogens became equivalent at that temperature. In contrast, no variation has been observed for the resonance due to isomer *Z*-M at $\delta = -1623.6$ ppm. It is apparent that hindered rotation is different for the two isomers.

The restricted rotation appears to be a peculiarity of the alcoholic substrate. If the reaction is carried out on 1-phenylpropyne the ^{199}Hg spectrum of the reaction mixture shows a quartet-shaped resonance centred at −1470 ppm [$^3J(^{199}Hg–^1H) = 200$ Hz] and a singlet at −1530 ppm due to the *E*-M compound. These regioisomers should be of *E* configuration, according to literature data.[12]

Spectral parameters relative to the series of compounds investigated are reported in Table 1.

The assignment of the singlet centred around −1550 ppm is more difficult. Two possible isomers, *E*-aM and *Z*-aM, can be responsible for the

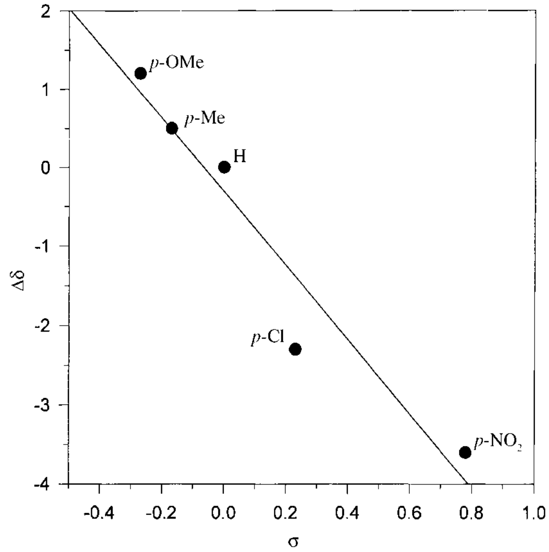


Figure 2 Least-squares fits of ^{199}Hg chemical shift to Hammett σ for the series *E*-M of *para*-substituted compounds; $r^2 = 0.932$.

signal. However, in this case we also can use the correlation between the calculated mercury atomic charge and the ^{199}Hg chemical shifts. The values obtained for compounds *E*-aM and *Z*-aM are 0.8730 and 0.8476 for X = *p*-NO_2, and 0.8670 and 0.8578 for X = *m*-NO_2.

A good correlation exists only for the series of *E*-aM compounds. As previously reported, however, correlations between ^{199}Hg chemical shift values and calculated Hg atomic charge must be limited to a series of structurally homologous compounds.[7] Thus, for the series of *E*-aM *para*-substituted compounds r^2 is 0.972 and and for the series of *E*-aM *meta*-substituted species r^2 is 0.943.

Moreover, the chemical shift of the resonance of the *E*-aM product from 1-phenylpropyne is 60 ppm higher than that of the *E*-M isomer (see above). The same shift between −1490 and −1550 ppm points at an analogous structural relationship.

As expected, the ^{199}Hg chemical shift of *E*-M are sensitive to the electronic effect of the substituents, as shown in Fig. 2. A good correlation is observed between (δ^{199}Hg) and Hammett σ values.[13]

The success of the ^{199}Hg NMR technique, which makes it possible to follow the reaction *in situ*, is well demonstrated by the spectra shown in Fig. 3. A different stereochemical behaviour was observed when the ratios of the initial concentrations of the reactants were changed. With a large excess of mercuric acetate, only the *E* stereoisomer was observed, independently of the actual concentration (Figs 3a and 3b). If the alkyne was in a large excess with respect to the mercurating agent, only the *Z* stereoisomer appeared (Fig. 3d). Finally, with comparable initial concentrations of the reagents, both stereoisomers were detected (Fig. 3c).

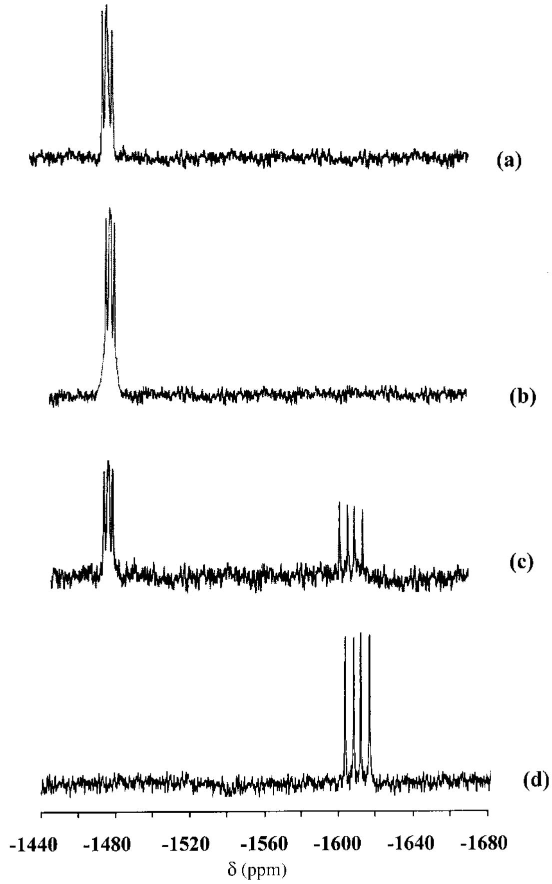


Figure 3 ^{199}Hg NMR spectra of reaction mixture obtained by reaction of 3-(4-methoxyphenyl)-2-propyn-1-ol and mercuric acetate in AcOH/AcOD (1:1 v/v), with different initial concentrations: (a) mercuric acetate:alkyne 10:1, $[Hg(OAc)_2] = 0.05\ mol\ l^{-1}$; (b) mercuric acetate:alkyne 10:1, $[Hg(OAc)_2] = 0.2\ mol\ l^{-1}$; (c) mercuric acetate:alkyne 1:1, $[Hg(OAc)_2] = 0.05\ mol\ l^{-1}$; (d) mercuric acetate:alkyne 1:5.4, $[Hg(OAc)_2] = 0.05\ mol\ l^{-1}$.

A tentative explanation of this finding may be as follows. When mercuric acetate is in excess, the intermediate mercurinium ion, sterically hindered on one side, favours the attack of the nucleophilic acetate from the *anti* side, thus yielding the *E* isomer. However, with an excess of alkyne, only acetate coordinated to the mercury atom of the mercurinium intermediate is available, thus rendering a *syn* attack necessary.

If confirmed with other families of alkynes, this stereochemical pattern may explain why contrasting results were reported in the literature: apparently, different initial concentrations were used.

In conclusion, in this paper we have stressed the utility of the ^{199}Hg NMR technique as a tool for directly identifying mercurated compounds in a simple, reliable and sensible way.

Further studies will be devoted to the aim of identifying the until-now elusive reaction intermediates of acetoxymercuration.

EXPERIMENTAL

Acetoxymercurated derivatives from 3-aryl-2-propyn-1-ols were prepared as previously described.[4]

In the present study the reaction was performed in the NMR tube by treating a 1×10^{-2} M solution of substrate in AcOH/AcOD solvent with $Hg(OAc)_2$ at known concentration.

^{199}Hg NMR spectra were recorded on a Bruker AM 400 spectrometer operating at a frequency of 71.64 MHz with a variable-temperature unit. The temperature was calibrated using the standard Wilmad methanol and ethylene glycol samples. All chemical shifts are given in ppm and referenced to $Hg(OAc)_2$ (1 M in AcOH), the chemical shift of which has been set at -2389.0 ppm relative to the primary standard of neat $HgMe_2$ = 0 ppm.[5] Typical spectra consist of 512 transients of 4096 data points over an 8 kHz bandwidth with a 90 ° pulse of 12.5 μs. Concentration of the reagent samples was in the range 5×10^{-2}–5×10^{-3} M. A 1:2 mixture of deuterated and non-deuterated solvent was used.

MPA analyses have been performed using the Gaussian 94 system of programs.[14]

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