Decay Synthesis of Multitritiated Compounds Using CT_4 as a Natural Generator of CT_3^+ Cations

Sir:

Owing to their unusual, and in several respects unique, molecular and nuclear properties, multiply tritiated compounds, containing two or more tritium atoms *in the same molecule*, have been used in recent years in a variety of mass spectrometric,[1] spectroscopic,[2] and gas chromatographic[3] investigations, and especially in kinetic studies as the precursors of labeled carbocations of precisely defined structure.[4]

Unfortunately, the variety of multitritiated molecules available, and consequently the scope of their promising applications to chemistry and radiobiology, has been severely restricted by the formidable problems associated with the synthesis, the purification, and the conservation of these highly radioactive substances, whose specific activity necessarily exceeds ca. 58,000 Ci mol^{-1}.

As a matter of fact, so far only ethane-*1,2-t*$_2$,[5] propane-*1,2-t*$_2$,[6] butane-*1,4-t*$_4$,[7] cyclobutane-*t*$_x$,[1] and cyclopentane-*1,2-t*$_2$[8] have been prepared with a general one-step procedure, involving reduction of the corresponding olefins with an excess of T_2 over a suitable catalyst. The particularly difficult problem of binding several T atoms to one carbon atom has been solved only in the case of CT_4,[9] whose preparation has been recently scaled-up to activities of several curies.[10]

In this communication we wish to report on a new synthetic approach to multitritiated compounds, in particular to those containing the $-CT_3$ group, based on the spontaneous β^- decay of CT_4, which makes the compound a natural generator of fully tritiated methyl cations. In fact, the decay of CT_4 is known[11,12] to give, irrespective of the environment, nearly quantitative (>82%) yields of methyl ions, whose subsequent attack on practically all nucleophiles, including methane itself, leads to the formation of tritiated products which generally[12,13] retain the radioactive atoms exclusively in the $-CT_3$ group.

$$CT_4 \xrightarrow[\text{decay}]{\beta} CT_3^+ + {}^3He + \beta^- \qquad (1)$$

At first sight, the low rate of T decay (ca. 0.46% per month) makes its application to preparative purposes quite unattractive. However, a closer examination reveals that, given the relatively high CT_4 activities now available,[10] this admittedly lazy synthetic approach can provide quite respectable activities of multiply tritiated products, largely sufficient for most applications, within reasonable periods of time. For instance, since the CT_3^+ daughter ions contain approximately three times the decayed activity, storage of 1 Ci of CT_4 for 1 month yields tritiated methyl cations containing the considerable activity of ca. 14 mCi.

As the first example of application the preparation of CT_3OH is illustrated. Tritiated methane (ca. 0.6 Ci, activity distribution: $CT_4 = 60.4 \pm 5\%$, $CHT_3 = 29.4\%$, $CH_2T_2 = 8.1\%$, $CH_3T = 2.0\%$), diluted with CH_4 to a pressure of 11.0 Torr, was allowed to decay in a 2.5-l. Pyrex bulb containing water vapor (153 Torr) and O_2 (5 Torr) for 14.5 days at 60.5°.

Flow counting of products separated by GLC[14] demonstrated that the reaction sequence

$$CT_3^+ + H_2O \longrightarrow CT_3OH_2^+ \xrightarrow{-H^+} CT_3OH \qquad (2)$$

gave tritiated methanol with a yield of approximately 90%, together with traces of HT and HTO. Addition of a known amount of inactive methanol as a carrier, followed by its acetylation, purification of the ester by preparative GLC,[15] and determination of its activity by liquid scintillation counting, led to a more accurate yield value of 86.1%, based on the total activity of methyl ions from CT_4.

These results support the mechanistic conclusions of Nefedov and coworkers[13] on the course of reactions (2) and confirm the lack of isotopic scrambling among their products. In conclusion, storing ca. 0.6 Ci of CT_4 for 14.5 days gave 2.8 mCi of methanol *labeled exclusively in the methyl group*. Another example is afforded by the simultaneous preparation of tritiated MeBr and EtBr from the decay of 0.6 Ci of CT_4 (having the activity distribution previously reported) in a 1-l. pyrex bulb containing CH_4 (137 Torr), O_2 (10 Torr), and HBr (600 Torr), for 43 days at 25°. Radio GLC[16] revealed two major products, tritiated MeBr (4.4 mCi) and EtBr (2.3 mCi), whose formation can be traced to the reaction sequences

$$CT_3^+ \xrightarrow{+HBr} CT_3BrH^+ \xrightarrow{-H^+} CT_3Br \qquad (3)$$

$$CT_3^+ \xrightarrow{+CH_4} C_2{}^*H_5^+ + {}^*H_2 \qquad (4)$$

$$C_2{}^*H_5^+ + HBr \longrightarrow C_2{}^*H_5BrH^+ \xrightarrow{-H^+} C_2{}^*H_5Br \qquad (5)$$

and whose yields account, respectively, for 47 and 24% of the total activity of the methyl ions from CT_4.

Our preparative results are consistent with the conclusions reached in an earlier mechanistic study on the reactivity of CT_3^+ decay ions in gaseous hydrogen halides.[17]

Isolation of tritiated MeBr, after dilution with an excess of inactive carrier, afforded the possibility to demonstrate the actual formation of CT_3Br and to measure its abundance in the product.

The Grignard reagent prepared from MeBr was decomposed with water, and the tritiated methanes formed were separated by low-temperature GSC.[3]

$$CT_3Br \xrightarrow{Mg} CT_3MgBr \xrightarrow{H_2O} CHT_3$$

It was found that CHT_3 accounted for 56 ± 5% of the methanes activity, *and therefore* CT_3Br *must necessarily account for a corresponding fraction of the tritiated MeBr activity.*

Taking into account the activity distribution in the tritiated methane used as a generator of methyl cations, one must conclude that the isotopic composition of the labeled MeBr reflects essentially the composition of the decay methyl ions, thus indicating the lack of significant isotopic scrambling in the reaction sequence (3).

Other synthetic applications of the decay technique, including those to amines, ethers, halides, alkanes, cycloalkanes, arenes, etc., are currently being investigated, while extension to molecules of great biological and genetic interest, e.g., thymine-CT_3, opens intriguing perspectives. It should be pointed out that the decay method provides a direct and convenient route to a number of multitritiated products whose preparation by conventional synthetic techniques is prevented by overwhelming experimental difficulties. In addition, under suitable conditions, the decay synthesis offers the truly remarkable advantage that its multitritiated products are formed in an essentially carrier-free state. Furthermore, the undecayed CT_4 can be used repeatedly, as shown by radio GSC of the CT_4 recovered after the CT_3Br preparation, which failed to show a significant change in the isotopic composition of tritiated methane.

References and Notes

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(14) A 3.5-m glass column, packed with 20% Carbowax on silanized Chromosorb W was used at 80°, in conjunction with a 25-ml internal-flow proportional counter.
(15) The ester was purified using a 4-m glass column, packed with 25% diisodecylphthalate on Chromosorb W at 60°.
(16) Separation was achieved with a 12-m glass column, packed with 25% β,β'-oxydipropionitrile on silanized Chromosorb W at 80°.
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A Novel Tridentate Ligand Formed by the Condensation of Two Benzoyl Isothiocyanate Molecules in the Presence of $RhCl(PPh_3)_3$

Sir:

We wish to describe the preparation and characterization of a novel complex of Rh(III) in which a new tridentate ligand, formed by the condensation of two molecules of benzoyl isothiocyanate, is attached to the metal through S, C, and O linkages.

A mixture of $RhCl(PPh_3)_3$ (0.325 mmol) and excess benzoyl isothiocyanate (2.84 mmol) in a 1:1 benzene-hexane mixture (by volume) was kept at room temperature under nitrogen for 14 hr and then refluxed for 1 hr, giving a yellow-orange powder in 84% yield. Recrystallization of the crude product from mixed solvent (1:1 methylene chloride-diethyl ether) yielded a reddish orange microcrystalline solid, mp 174.5-175.5°, after 1 day. The analysis of these crystals is consistent with the formula, $RhCl(PPh_3)_2(C_6H_5CO\text{-}NCS)_2$: Anal. Calcd: C, 63.13; H, 4.08; N, 2.83. Found: C, 63.28; H, 4.18; N, 2.91. The NMR spectrum in $CDCl_3$ shows no sign of diethyl ether or methylene chloride. However, when the crude complex was recrystallized slowly, over a few days, from methylene chloride-diethyl ether, reddish orange prismatic crystals, mp 176-177°, were obtained which contained incorporated diethyl ether, as seen in the NMR spectrum (τ_{Me} 8.8). NMR and infrared studies of the product did not lead to a ready formulation of the nature of the complex. Accordingly an X-ray diffraction investigation was undertaken.

$RhCl(PPh_3)_2(PhCONCS)_2 \cdot Et_2O$ (Ph = C_6H_5, Et = C_2H_5) crystallizes in the space group $C^5{}_{2h}\text{-}P2_1/n$ with four formula units of the complex and four solvent molecules in a cell of dimensions $a = 21.184$ (3) Å, $b = 19.963$ (2) Å, $c = 12.226$ (2) Å, $\beta = 100.03$ (1)°, and $V = 5091.56$ Å^3. The experimental and calculated densities are 1.39 (1) and 1.387 g cm^{-3}, respectively.

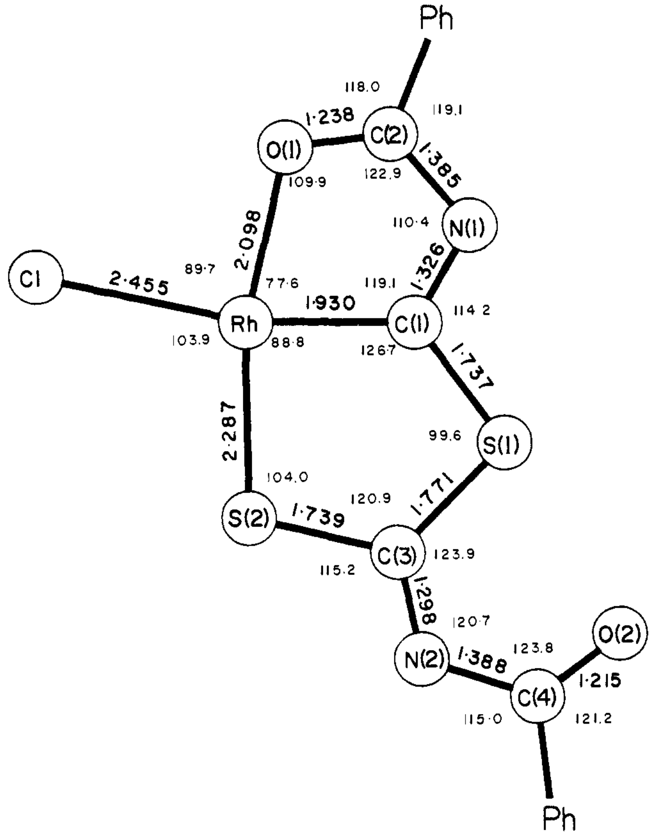

Figure 1. A drawing of $RhCl(PPh_3)_2(PhCONCS)_2$ viewed in the isothiocyanate ligand plane, showing important bond distances and angles. PPh_3 groups, approximately perpendicular to this plane, are omitted for clarity. Standard deviations in the bond lengths (in Å × 10^3) are: Rh-Cl, 2; Rh-O, 2; Rh-C, 6; Rh-S, 2; C-O, 8; C-N, 8; S-C, 7.

Data were collected on a Picker X-ray diffractometer, using nickel-filtered Cu Kα radiation. Of the 8248 unique reflections measured, 6266 were significantly above background ($F_o{}^2 > 3\sigma(F_o{}^2)$). The absorption-corrected data have been refined by full-matrix least-squares methods to an R of 0.061 and R_w of 0.079. The diethyl ether molecule was found to be severely disordered.

Fractional coordinates for the individual atoms and positional parameters for the rigid groups appear in Tables I and II in the microfilm edition.[1]

The Rh atom has a slightly distorted octahedral coordination with trans PPh_3 groups in the axial positions. The four equatorial sites are occupied by a chloro ligand and the tridentate ligand $(PhCONCS)_2$. Figure 1 shows the molecule viewed in the isothiocyanate ligand plane, with relevant bond lengths and angles shown. The PPh_3 groups, approximately perpendicular to this plane, are omitted for the sake of clarity.

This tridentate ligand is an interesting and unexpected consequence of the aforementioned reaction. Although the five-membered ring formed by Rh, O(1), C(2), N(1), and C(1) is not surprising, on the basis of the previous work on benzoyl and thiobenzoyl isocyanates,[2] the condensation of the two ligands at C(3)-S(1) is without precedent. This sulfur-carbon bond joining the two ligands is a regular S-C single bond agreeing well with the distance of 1.77 Å based on the sums of the C and S covalent radii.[3,4]

The Rh-C(1) bond is believed to be the shortest Rh(III)-C(carbene) bond yet observed, being, for example, signifi-