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Superacid-Catalyzed Selective Formylation–Rearrangement of Isoalkanes with Carbon Monoxide to Branched Ketones[**]

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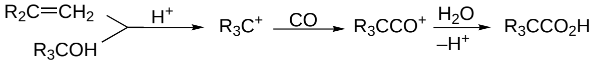
The acid-catalyzed carbonylation of olefins or alcohols to branched aliphatic acids (neo-acids) is known as the Koch–Haaf reaction.[1] It involves the intermediate formation of a trivalent alkyl cation (carbenium ion) which then alkylates CO to the corresponding acyl cation to produce, upon hydrolysis, the branched carboxylic acid (Scheme 1).



Scheme 1. Koch–Haaf reaction of alkenes and alcohols, $R = CH_3$.

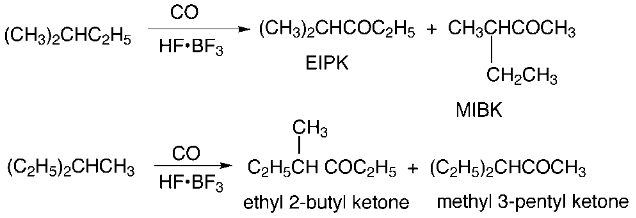
Hopff and Nenitzescu et al.[2a] reported in 1936 that when carbon monoxide was treated with isobutane in the presence of an excess of $AlCl_3$, a mixture of products was obtained, including 31 % of methyl isopropyl ketone (MIPK) besides some *tert*-butyl isopropyl ketone and pivalic acid. Nenitzescu subsequently suggested that MIPK was formed by reaction of CO with the intermediately formed *tert*-butyl cation, followed by hydride transfer from the pivaloyl cation to give pivalaldehyde, which then rearranged to MIPK.[2b] The aluminum halide-catalyzed conversion of saturated hydrocarbons with carbon monoxide, however, as reported by Nenitzescu et al., usually gives complex mixtures of products, containing carboxylic acids and ketones.[3]

In contrast, Sommer et al.[4] treated CO with alkanes with superacidic $HF \cdot SbF_5$ as a catalyst and obtained exclusively Koch–Haaf carboxylic acid products. After studying the superelectrophilic activation of carbon monoxide and its reaction with adamantane, we reported[5] in 1988 that both the Koch type carboxylation as well as a distinctly different direct formylation to give 1-formyladamantane take place. Whereas the Koch-carboxylation involves initial formation of the 1-adamantyl cation, the formylation reaction proceeds by the activated formyl cation inserting into the tertiary C–H bond via a five-coordinate carbocation.

We now report the superelectrophilic formylation of isoalkanes, such as isobutane or isopentane (and their higher homologues), giving selectively and in high yield the corresponding rearranged branched ketones with no detectable (or minimal) branched acids, that is Koch products.[6] To achieve this remarkably efficient conversion superacids weaker than $HF \cdot SbF_5$ or $FSO_3H \cdot SbF_5$, such as $HF \cdot BF_3$ or $HF \cdot CF_3SO_3H \cdot BF_3$, are used, which do not readily oxidatively ionize isoalkanes to the corresponding alkyl cations (which would consequently lead predominantly to Koch carboxylation). They are, however, still strong enough to activate carbon monoxide to an efficient electrophilic formylating agent (that is the formyl cation protosolvated by the acid, $HCO^+ \cdots H^+A^-$). $HF \cdot BF_3$ was found to be particularly suitable to bring about the reaction. Illustrative of this in the experimental section is the example of the conversion of isobutane into MIPK (Scheme 2).

Scheme 2. Carbonylation-rearrangement of isobutane.

Other isoalkanes containing tertiary CH groups, such as isopentane, isohexanes, or isoheptanes, react under related superacidic carbonylation conditions in a similar way to give the corresponding branched ketones (Scheme 3).



Scheme 3. Carbonylation-rearrangement of isopentane and 3-methyl pentane.

Isopentane for example is converted into methyl isobutyl ketone (MIBK) and ethyl isopropyl ketone (EIPK) in a ratio of 1:3. 3-Methylpentane gives ethyl 2-butyl ketone and methyl 3-pentyl ketone, respectively (4:1), as major products. The reaction is considered to involve electrophilic formylation of the tertiary CH bond of isobutane forming pivalaldehyde, which under the superacidic conditions rearranges to MIPK (Scheme 4).

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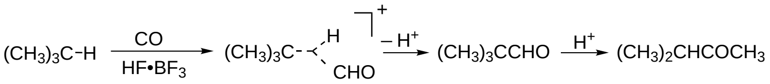
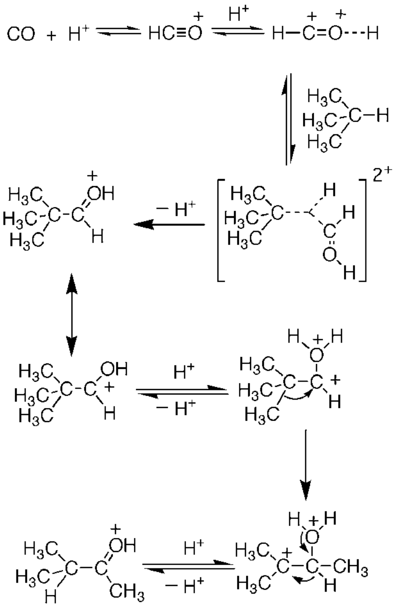


Scheme 4. Formylation of isobutane, followed by rearrangement.

The formyl cation itself is a linear carboxonium ion $HC\equiv O^+$ in which the charge is substantially localized on the oxygen atom. The carbocationic nature is enhanced by protosolvation that results in the decrease of neighboring oxygen participation ($HCO^+\cdots H^+A^-$, in the limiting case $HC^+{=}O^+H$) and renders the formylating species reactive enough (that is superelectrophilic) to attack the C–H bond via a five-coordinate carbocation.[7]

The rearrangement of pivalaldehyde again involves O protonation and protosolvation, rendering the carbonyl carbon a carbocation-like center, facilitating rearrangement (Scheme 5).



Scheme 5. Proposed mechanism for the direct formylation and rearrangement.

We indeed found that pivalaldehyde rearranges quantitatively to MIPK when treated with HF or $HF\cdot BF_3$ (Scheme 6).

The reported carbonylation rearrangement of isoalkanes to branched ketones, but not acids is fundamentally different from the Koch–Haaf type of carbonylative carboxylation which exclusively gives branched carboxylic acids. Branched aliphatic ketones, such as MIPK, EIPK, MIBK, and the like are efficient high octane (>100) oxygenate additives for gasoline, without many of the detrimental effects of the methyl *tert*-butyl ether (MTBE) and, thus, have also practical significance.

$$(CH_3)_3CCHO \xrightarrow{HF\ \mathrm{or}\ HF\bullet BF_3} (CH_3)_2CHCOCH_3$$

Scheme 6. Superacid-induced rearrangement of pivalaldehyde.

Experimetal Section

Anhydrous HF (56 g, 2.80 mol) was added to a precooled (–78 °C) autoclave. Subsequently isobutane (22.04 g, 0.38 mol) was condensed into the autoclave and 5.17×10^6 Pa (750 psi) of BF_3 (170 g, 2.5 mol) was slowly introduced with thorough stirring, followed by CO (47 g, 1.7 mol) while the temperature was raised to 0 °C and the pressure to 10.34×10^6 Pa (1500 psi). The temperature of the reaction mixture increased gradually to 35 °C (pressure rose to 14.82×10^6 Pa (2150 psi)), and the reaction mixture was stirred for 14 h during which a pressure drop of 2.41×10^6 Pa (350 psi) was observed. The autoclave was cooled to –78 °C and slowly depressurized through two traps kept in an acetone/dry ice bath. The vessel was subsequently warmed to 0 °C, and after complete depressurization the liquid reaction mixture was quenched by adding in small portions of ice (400 g in total) in a polyolefin flask. The mixture was neutralized with sodium bicarbonate and extracted three times with diethyl ether (total volume 500 mL). The combined diethyl ether extracts were dried with anhydrous $MgSO_4$, filtered, and worked up by distillation in the usual way. The yield of isopropyl methyl ketone was 91 % with 93 % selectivity (GC, GC-MS, and NMR analysis). No isobutane was detected by GC in the condensate of the traps. At the same time the aqueous layer did not show the presence of any pivalic acid.

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