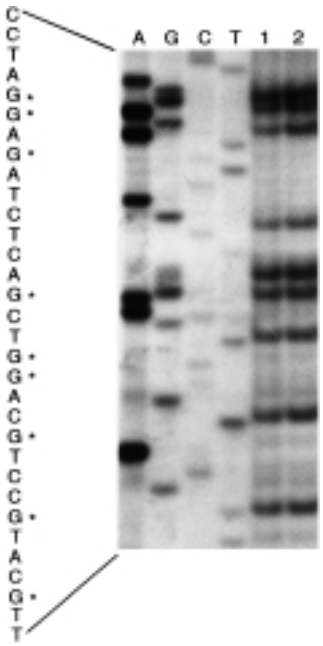

Figure 2. Autoradiogram of polyacrylamide/urea (12%/8M) slab gel electrophoresis for sequence analysis. The 5′-end-labeled M13mp18 DNA was cleaved by the hybrids at pH 7.5 and 25 °C for 2 h under irradiation, as described in Figure 1. Bases 48–79 are shown: lanes A, G, C, and T; Sanger A, G, C, and T reactions, respectively; lanes 1 and 2; **1** and **2** (500 μM), respectively.

cleavage site selectivity of **1** and **2** was different from that of natural neocarzinostatin chromophore.[3]

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Alkane Carbonylation with Carbon Monoxide on Sulfated Zirconia: NMR Observation of Ketone and Carboxylic Acid Formation from Isobutane and CO**

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Direct conversion of inert alkanes into carbonyl-containing organic compounds is an important goal for industrial organic chemistry. Alkanes can be carbonylated into carboxylic acids or aldehydes in superacidic HF/SbF_5 or CF_3SO_3H/SbF_5 systems.[1] However, environmental concerns require the use of more environmentally friendly solid catalysts. The strong acidity and exceptionally high activity of sulfated zirconia[2] (SZ) means it has received much attention as a potential catalyst for hydrocarbon conversion,[3] and especially for overcoming the chemical inertness of alkanes. The direct carbonylation of benzene with CO using a pure SZ as the solid acid catalyst has been reported recently.[4] However, saturated hydrocarbons were never reported to be involved in carbonylation reactions on SZ, only the inhibiting effect of carbon monoxide on linear alkane isomerization with SZ has been demonstrated.[5] Herein we report direct ^{13}C solid-state NMR spectroscopic measurements of the carbonylation of isobutane with CO, using a pure SZ as the solid acid catalyst.

Figure 1 displays the ^{13}C cross-polarization magic-angle spinning (CP/MAS) NMR spectra obtained after coadsorption of isobutane and CO on SZ and subsequent heating of the sample at 70 °C for 1 h. We rationalize these spectra in terms of selective formation of methyl isopropyl ketone (**5**) by pathways a), d), g) and/or b), c), g) in Scheme 1. If 2-^{13}C-labeled isobutane ([2-^{13}C]iC_4H_{10}, that is, isobutane labeled at the quaternary carbon atom) and unlabeled CO are coadsorbed, the following spectral features are observed (Figure 1A): the intense signal at $\delta = 47.0$ arises from the labeled CH group of the isopropyl fragment of **5**, the weak signal at $\delta = 19.6$ is assigned to the unlabeled CH_3 group of the isopropyl fragment, while the signal at $\delta = 25.5$ arises from residual isobutane. The resonance signal of the other unlabeled methyl group of **5** is not seen because of its very low intensity. If unlabeled isobutane and ^{13}C-labeled carbon monoxide are coadsorbed (Figure 1B), the resonance signal

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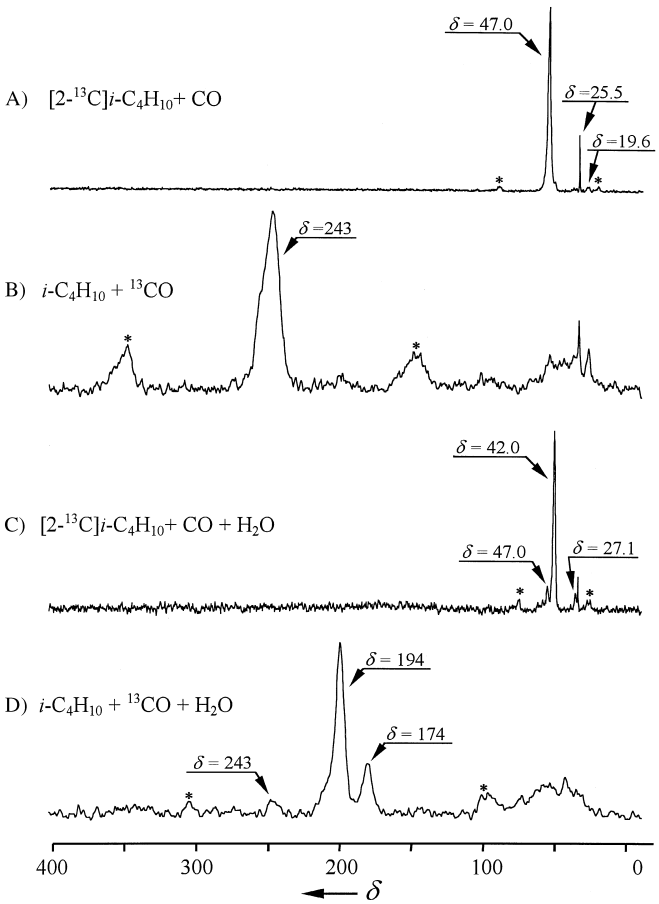
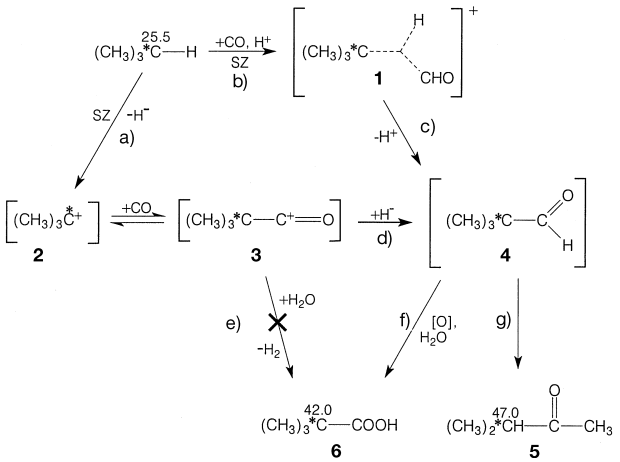


Figure 1. The ^{13}C CP/MAS NMR spectra of the products formed from isobutane and CO and water on SZ at 70 °C: a) coadsorption of the [2-^{13}C]iC_4H_{10} (82 % ^{13}C enrichment) and unlabeled CO; b) coadsorption of ^{13}CO (90 % ^{13}C enrichment) and unlabeled iC_4H_{10}; c) coadsorption of [2-^{13}C]iC_4H_{10}, (82 % ^{13}C enrichment), CO, and H_2O; d) coadsorption of ^{13}CO (90 % ^{13}C enrichment), iC_4H_{10}, and H_2O. * denotes spinning side band.



Scheme 1. Mechanism of isobutane carbonylation on SZ. *C denotes a ^{13}C-labeled carbon atom. Above each of the ^{13}C-labeled carbon atoms the corresponding ^{13}C NMR chemical shifts are given (δ).

of the carbonyl group of **5** becomes clearly visible at $\delta = 243$. We further confirmed the formation of **5** by both GC-MS and high-resolution ^{13}C NMR spectroscopy of the product extracted from the catalyst with Et_2O. The ^{13}C NMR spectrum of the product in $CDCl_3$ exhibits resonance signals at $\delta = 18.1$ $(CH_3)_2$, 41.65 (CH), 27.5 (CH_3), 212.6 (C=O), which are in good agreement with those reported for methyl isopropyl ketone.[6] However, the resonance signal of the carbonyl group of **5** adsorbed on SZ is shifted downfield by $\Delta\delta = 30$ ppm relative to that in $CDCl_3$. This may be related to the strong protonation[7a] or complexation[7b,c, 8] of the ketone carbonyl group by the Brønsted acid sites.

We have not observed the formation of pivalic aldehyde (**4**), which is expected to be the most probable product of isobutane carbonylation. This observation is in a good agreement with earlier findings on the rearrangement of **4** into **5** in the presence of strong acids.[1b, 9]

When the reaction was carried out in the presence of water, the other carbonylation route was utilized (Scheme 1, pathways a), d), f) and/or b), c), f). Upon interaction with CO and H_2O, isobutane converts primarily into pivalic acid (**6**) (see Figures 1 C, D). Resonance signals at $\delta = 42.0$ and 27.1 arise from the ^{13}C-labeled quaternary carbon atom and unlabeled methyl groups of **6**,[8] respectively. Upon reaction with ^{13}CO, we observe a signal at $\delta = 194$ from the COOH group of **6**[8] (Figure 1 D). Low intensity signals at $\delta = 47.0$ and 243 in Figures 1 C and D, respectively, are from compound **5** and indicate that, in the presence of water, a conversion of the alkane into the acid **6** represents the main route of isobutane carbonylation, while in the absence of water **6** is formed only in a trace amount (see Figure 1 A, the low intensity signal at $\delta = 42.0$, which is seen as the shoulder to the intense signal at $\delta = 47.0$ from **5**, arises from **6**).

The conversion of isobutane was 36 % at 70 °C in the absence of water, with **5** and **6** being formed with 97 % and 3 % selectivity, respectively. In the presence of water at 70 °C, only 21 % of the isobutane was converted and the selectivity for **5** and **6** being 29 and 71 %, respectively.

Noteworthy is the absence of molecular hydrogen (H_2) evolution in the carboxylic acid formation. Evolution of H_2, readily detectable by in situ ^1H MAS NMR spectroscopy as a narrow signal, expected at $\delta \approx 4$,[10] would provide evidence for a protolytic step in isobutane activation to form a pentacoordinate carbonium ion,[11] which further evolves H_2 to give the *tert*-butyl carbenium ion **2** (Scheme 1). The cation **2** is trapped with CO and H_2O to form the carboxylic acid by pathway e) in Scheme 1. The absence of H_2 suggests another route for isobutane conversion into the acid. We conclude that oxidation of the intermediate aldehyde[12] **4** by the SZ sulfate groups[4] (noncatalytic pathway f)), rather than quenching of **3** with water (pathway e)), represents the main route for isobutane conversion into the acid in the presence of water.

It should be noted that for the reaction of ^{13}CO with isobutane in the presence of water (Figure 1 D), as well as for the interaction of only CO and H_2O at 70 °C, an additional signal is observed at $\delta = 174$ arising from a formate species.[13] To date, we have no additional experimental data which could help us to show if a formate compound plays some role in the activation step of the alkane on SZ. One can suggest that the formyl cation [HC^+O] is formed from formate as an equilibriated species, producing **4** by direct formylation of isobutane by pathways b) and c) with the formation of a three-center two-electron-bonded pentacoordinate carbonium ion **1**

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as the transition state, similar to superacidic solutions.[1b] At the same time, according to literature data both parallel pathways a), d) and b), c) are possible for the formation of pivalic aldehyde (**4**) by the direct formylation of the C–H bond in isobutane with the [HC$^+$O] cation[1b] and by reduction of pivaloyl cation **3** with hydride ion.[1b, 14] Thus, we are not able to demonstrate by which pathway (a) and d) or b) and c)) the intermediate pivalic aldehyde (**4**) preferentially forms.

The observed alkane carbonylation provides new insight into the negative influence of CO on the alkane isomerization over SZ. The data obtained imply that suppression of the alkane isomerization by CO may result not only from the blocking of Lewis acid sites with CO[5] or from the reversible formation of **3** from **2**,[15, 16] but that carbon monoxide can also change the reaction route from isomerization towards carbonylation, thus contributing to the inhibiting effect on the alkane isomerization rate.

In conclusion, the present work represents the first small-alkane carbonylation on a SZ catalyst. The valuable chemical products (carboxylic acids and ketones) have been shown to be selectively produced over SZ at low temperature. This finding opens up a new possibility for the use of SZ-based catalysts for direct carbonylation of alkanes with CO.

Experimental Section

A sample of SZ of the low-temperature tetragonal phase with a surface area of 60 $m^2 g^{-1}$ and 9.9 wt % SO_3 content was prepared by a procedure described earlier.[17] The sample of SZ was calcined at 600 °C in air for 1 h and at 400 °C in vacuum (10^{-5} Torr) for 2 h. Equal amounts of isobutane (ca. 300 μmol g^{-1}) and CO (or isobutane, CO and H_2O) were frozen out on the SZ under vacuum at liquid nitrogen temperature. After sealing the SZ sample inside a glass tube (volume 0.2 cm^3) it was heated at 70 °C for 1 h; the pressure of CO was 8 atm under these conditions. Reaction products were analyzed in situ in the sealed glass tubes by ^{13}C CP/MAS NMR spectroscopy.

The ^{13}C CP/MAS NMR and ^{13}C high-resolution NMR spectra in $CDCl_3$ solution were recorded on a Bruker MSL-400 NMR spectrometer at room temperature (~23 °C). The conditions used for CP experiments are described in refs. [7c, 8], spinning rate was 3–10 kHz. A few thousand scans were collected for each spectrum. Chemical shifts (δ) of the organic compounds adsorbed and in $CDCl_3$ were measured with respect to TMS as external reference.

GC-MS analysis of the reaction products extracted with Et_2O from the SZ sample was made with VG 70–70 mass spectrometer. The fused silica capillary column of 35 m × 0.3 mm internal diameter with SE 30 as the active phase, forming a film of 0.3 μm thickness, was used for the separation of the organic products.

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Nucleoglycoconjugates: Design and Synthesis of a New Class of DNA–Carbohydrate Conjugates**

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Solid-phase DNA synthesis, based upon phosphorus(III) coupling chemistry,[1] has revolutionized the study of nucleic acids. In addition to providing synthetic DNA for molecular biological investigations, these solid-phase strategies have facilitated the synthesis of chemically modified oligonucleotides,[2] which have been used as probes of DNA structure and function[3] and as tools for mechanistic studies in nucleic acid biochemistry.[4] The synthesis of modified DNA also has fueled antisense therapeutics[5] and provided insight into the chemical evolution of nucleic acid structure.[6] The phosphoramidite method offers a general strategy for the conjugation of molecules such as biotin and fluorescein to DNA through

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