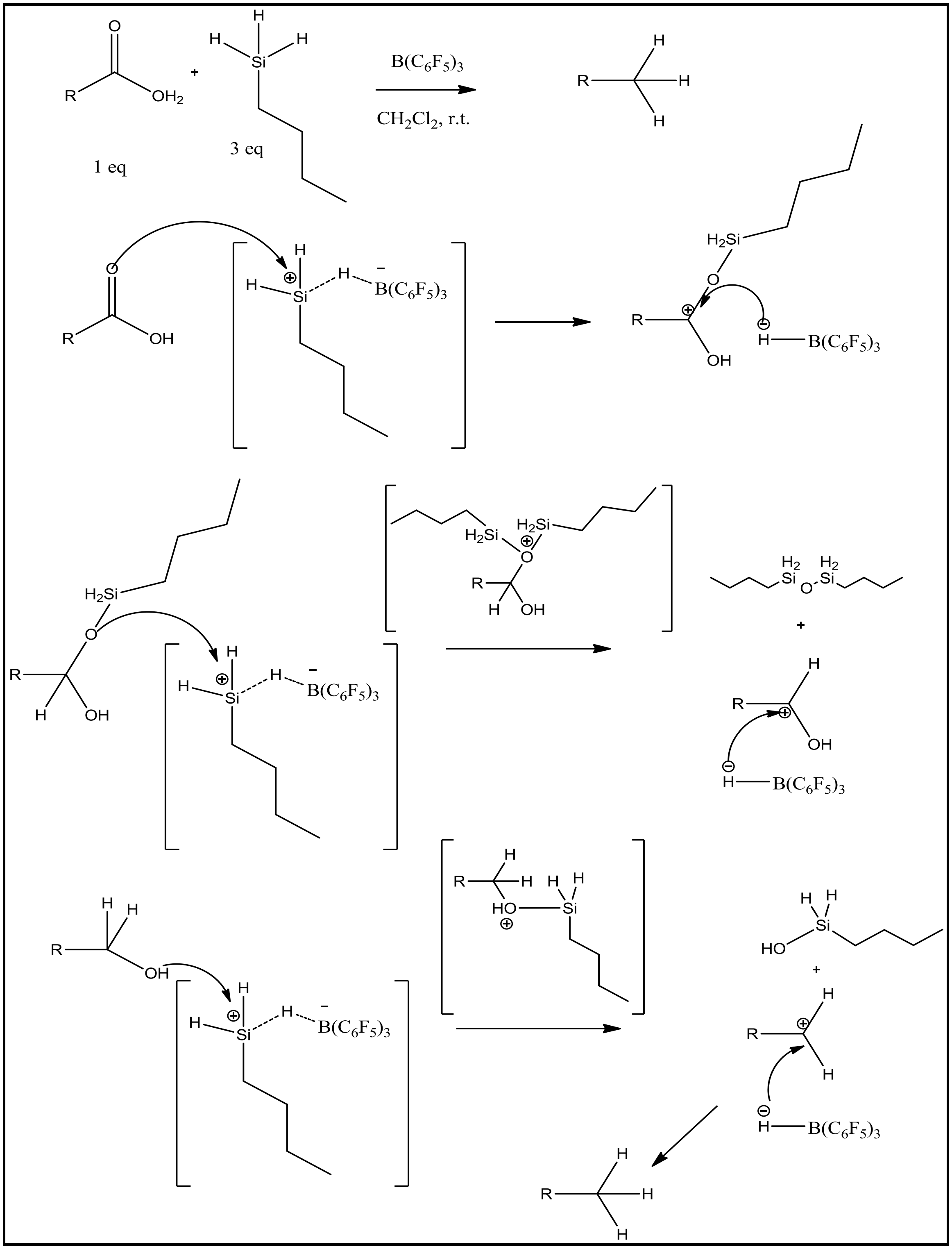

Figure S1. Chemical reduction mechanism as published in Nimmagadda and McRae (*1*)

Comprehensive GCxGC-TOF-MS. The distribution of hydrocarbon standards and reduced model compounds in GCxGC space (Figure 2, main text) mapped a chemical landscape that enabled preliminary assignment of broad functionality to an unknown compound based on its 1st and 2nd dimension retention time (^{1}RT and ^{2}RT respectively). Separation in the 2nd dimension is very strongly driven by chemical affinity to the non-polar phase, such that the least polar compounds elute with later ^{2}RTs. Of the standards analyzed in this study, the n-alkane series grouped at the top of the chromatogram, effectively delineating the boundary between saturated and unsaturated hydrocarbons. Accordingly, aromatic hydrocarbons have small ^{2}RTs, and thus group at the bottom of the chromatogram. A wide range of $C_{12}H_{18}$ (aromatic) isomers with different alkane substituents (boxed compounds in Figure 2) were analyzed to further refine the GCxGC landscape. It is assumed that there is no aromatic isomer of $C_{12}H_{18}$ that would produce a significantly longer ^{2}RT than observed in Figure 2, allowing the boundary between aliphatic and aromatic compounds in GCxGC space to be established. An important advantage of GC techniques is that many stereoisomers (cis and trans decahydronapthalene, for example) and positional isomers can be separated without the use of chiral columns. In summary, the ^{1}RT and ^{2}RT spatial distribution of standards shown in Figure 1 lays the foundation for enabling robust assignment of detected peaks to compound classes, and complements and confirms structural assignments based on TOF mass spectra when NIST EI-MS data are not available.

Validation of proposed structures as reduction products of Deoxycholic Acid:

It has been observed that multiple products are formed during the reduction of Deoxycholic Acid **1j**. The following experiment tested the effect of varying catalyst concentration on the products that are formed during the reduction. The exact structure of products was not determined, as it was not critical to the overall analysis.

Experimental: Deoxycholic Acid **1j** was reduced as outlined in the main text under materials and methods. Specific substrate and catalyst amounts used were as follows: **Low Lewis Acid Catalyst**: 8 mg **1j**, 8 mg. Trispentafluorophenylborane, 100uL nBS. **High Lewis Acid Catalyst**: 8 mg **1j**, 16 mg. Trispentafluorophenylborane, 100uL nBS. Work-up for NMR and GC-MS/FID followed experimental protocols described in the main text. For NMR, samples were dried under N_2 and resuspended in $CDCl_3$ before analysis

NMR experiments were performed on a Varian Inova™ 500 MHz spectrometer with a 5 mm inverse detect probe. For ^1H 1D experiments, 64 scans were acquired with 30k time domain points. For ^{13}C 1D experiments, 100000 scans were acquired with 58K time domain points and a recycle delay of 2 s. For heteronuclear single quantum coherence (HSQC) experiment, 80 scans were acquired with 2k data points in the F2 dimension and 128 increments in the F1. The ^1J ^1H-^{13}C value was set to 140 Hz and the relaxation delay was 2.5 s.

Results/Discussion:

1. Observed peaks represent actual isomers (as opposed to chromatographic artifacts) produced during reaction

   In Figure S.2 both high and low catalyst reduction conditions produce varying amounts of peaks 1 and 2, and similar amounts of peak 3(as quantified with GC-FID). Electron impact mass spectra of these peaks (Fig S.3) indicate that peaks 1 and 2 represent unsaturated versions of the expected product, while peak 3 represents a fully saturated product (based on molecular ion). Unreduced **1j** contains 2 hydroxyl groups, located at C-3 and C-12. Peaks 1 and 2 result from the elimination of one of these hydroxyl groups, producing a double bond. To verify that peaks 1 and 2 are in fact isomers, ^{1}H NMR spectra were collected on both reduction mixtures. The overlaid spectra (Fig. S.4) are very similar, but show different relative intensities of peaks, which is expected since the two mixtures contain different amounts of peaks 1 and 2.

2. In each isomer the double bond is located between two tertiary carbons (i.e. there are no olefinic protons)

When either the C-3 or C-12 hydroxyl group is eliminated the double bond located at either site will contain at least one olefinic proton. However, ^{1}H NMR spectra show resonances at 2.7 and 2.9 ppm, which are more upfield than would be expected for an olefinic proton. However, we did not rely on this fact alone to rule out this possibility. The ^{13}C NMR (Fig S.5 f1 axis) spectrum of the Low Catalyst reduction shows 4 peaks between 120-150 ppm, which are within the range of sp^2 hybridized carbons. Heteronuclear single quantum coherence (HSQC) spectroscopy (Fig S.5) shows direct H-C coupling indicated as either blue (CH and CH_3) or red (CH_2). The two previously mentioned ^{1}H NMR resonances (2.65, 2.9 ppm) correlate to sp^3 hybridized carbons further upfield, and the 4 downfield carbons (124, 136, 138.5, 139.5 ppm) do not show any correlations to ^{1}H NMR resonances. These 4 downfield carbon resonances confirm that peaks 1 and 2 each contain one double bond, and that each is positioned between two tertiary carbons (total of 4 peaks).

3. Lewis Acid catalyst supports double-bond migration as well as methyl shifts, resulting in backbone rearrangement.

   The presence of double bonds that are not at the position of OH elimination following the reduction suggests that double bonds are migrating in the ring system. It has been shown that BF_3-OEt, a lewis acid of similar strength to the $B(C_6F_5)_3$ catalyst used in the current reaction, catalyzes double bond migration as well as methyl shifts in similar steroid systems[2]. The mass fragmentation patterns helped to further limit where the location of the double bond. Published fragmentations patterns of similar steroids indicate that a double bond located on either the a, b, or c ring of a steroid structure will yield a characteristic 215 m/z fragment ion[3,4]. This fragment ion was not abundant in the spectra of either Peak 1 or 2, suggesting that the double bond is on the d ring. Similar unsaturated steroids with the double bond on the d ring (between either C-13 and C-17, C-14 and C-15, or C-17 and C-20) have 257 m/z as the base peak[2,5]. Peaks 1 and 2 both have 257 m/z as their base peak, and have no olefinic protons. Structures provided in Fig. S.2 satisfy both GC-MS and NMR constraints.

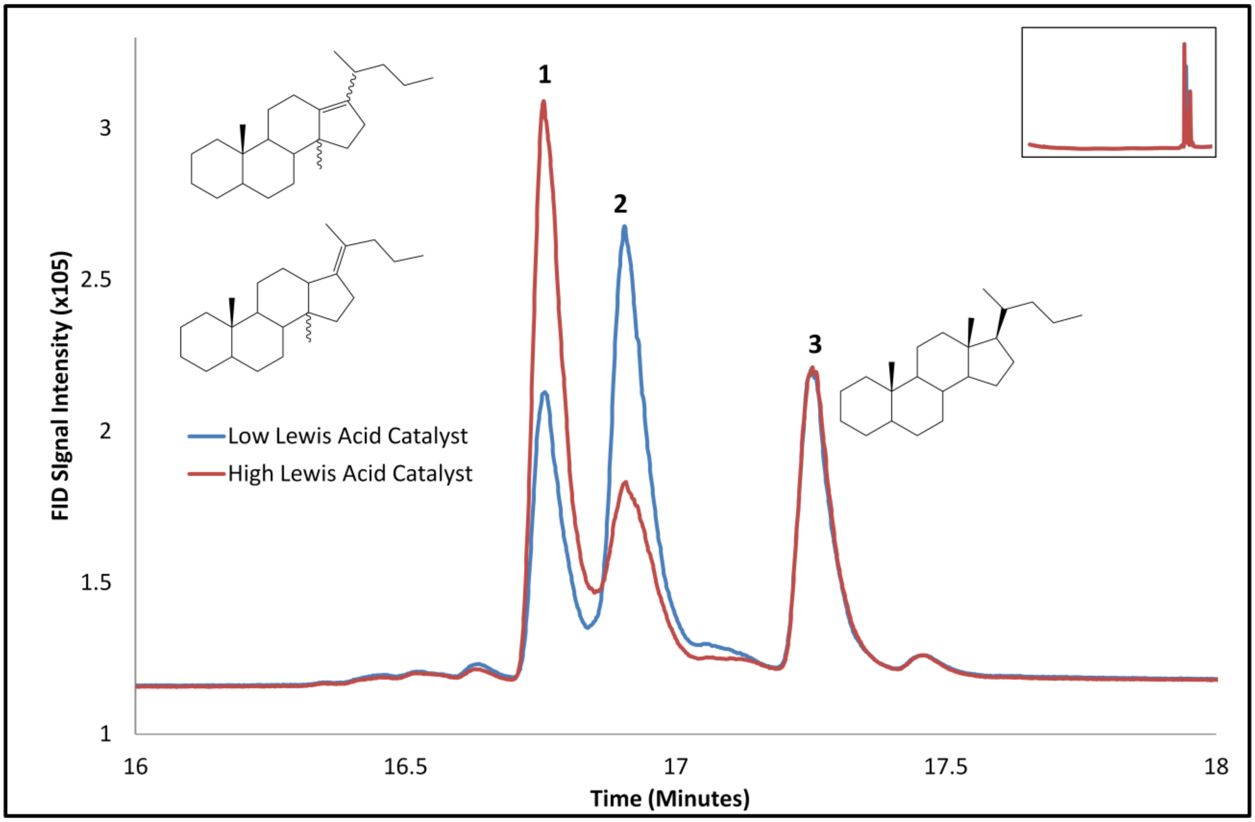

Figure S2. Overlaid GC-FID chromatograms of concurrent reductions with varying catalyst concentrations. Possible structures for peaks 1 and 2 are depicted on left. Structure of peak 3 is depicted on right.

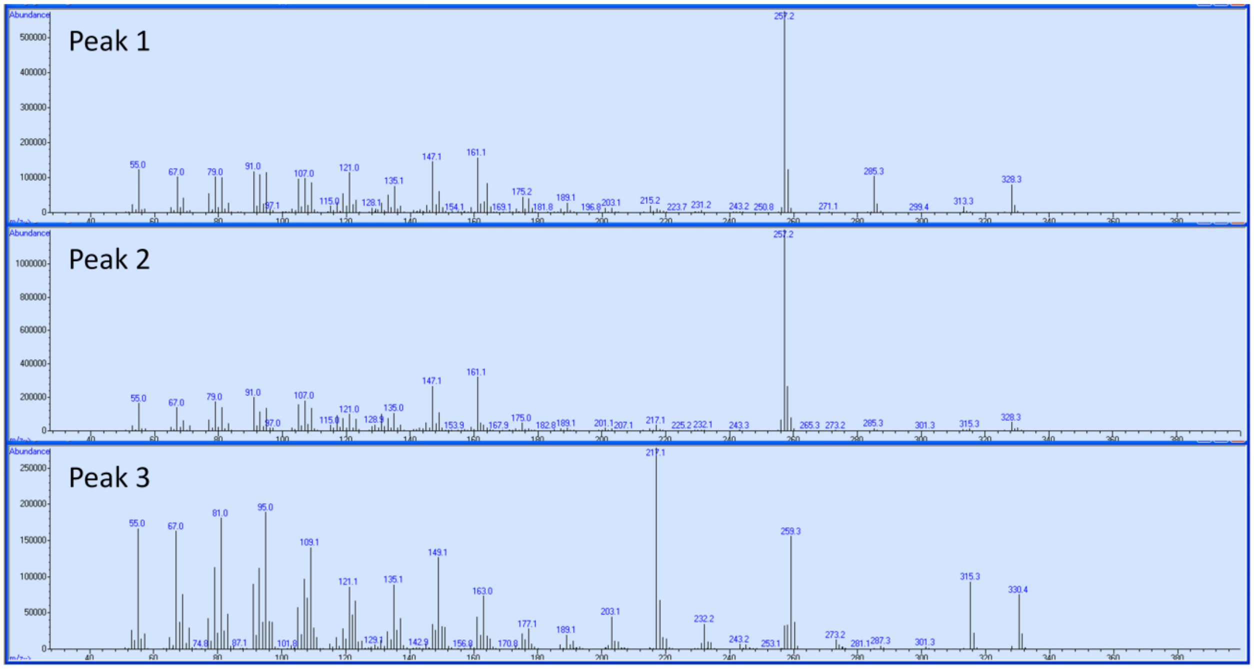

Figure S.3 GC-MS spectra of peaks 1, 2, and 3 from Fig. S.2.

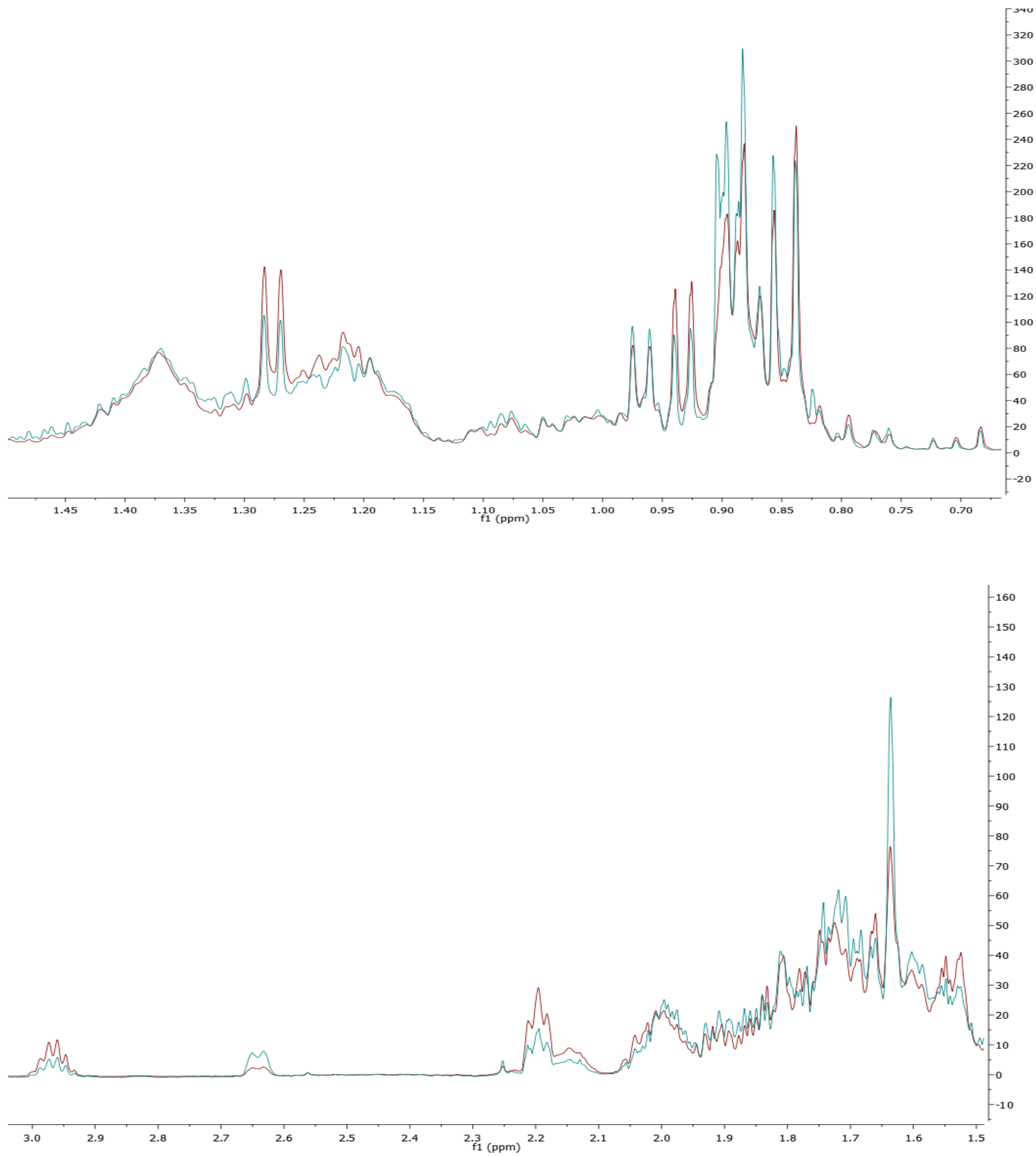

Figure S.4 ^{1}HNMR of low catalyst reduction mixture (blue) and high catalyst reduction mixture (red). Varying abundances of peaks 1 and 2 (Fig. S.2) are expressed as intensity differences in peaks of the same chemical shift.

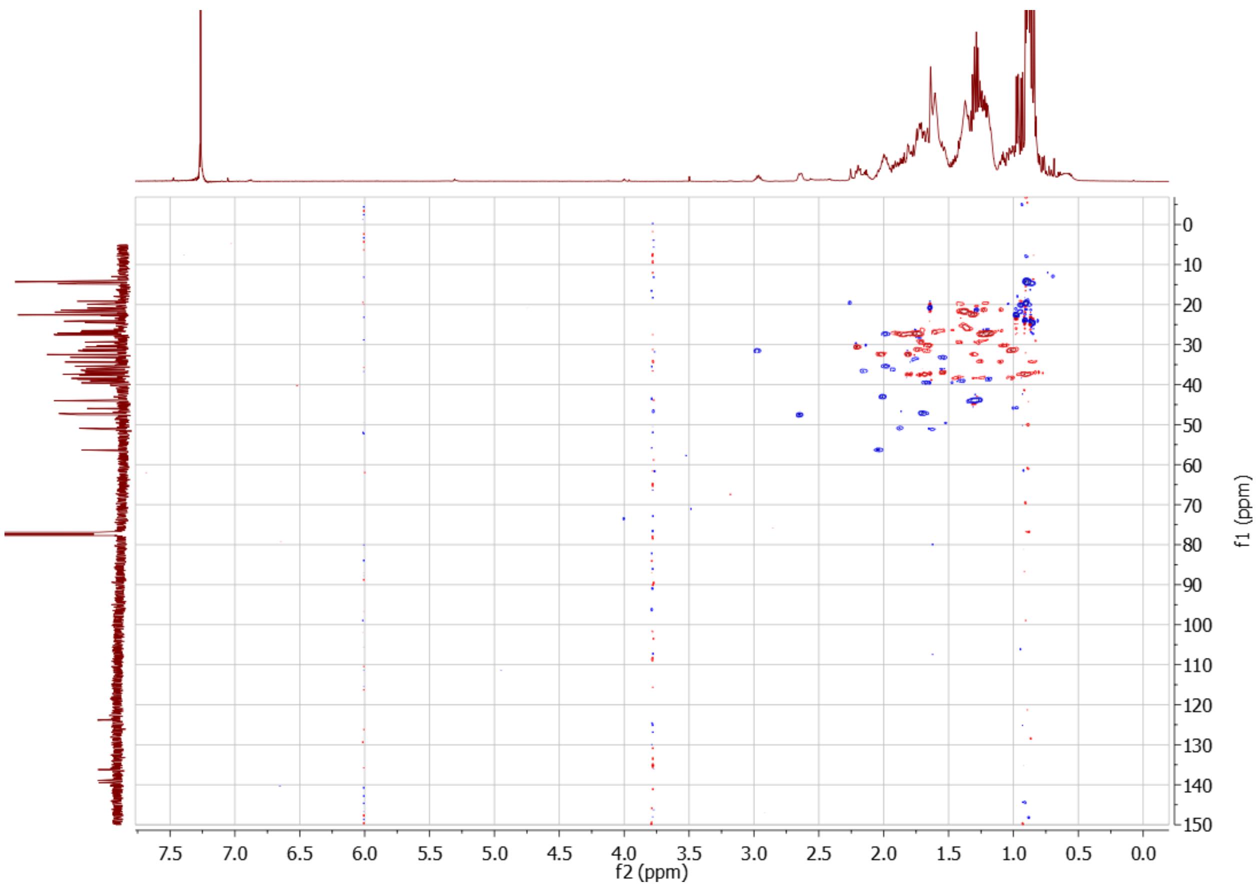

Figure S.5. Heteronuclear Single Quantum Coherence Spectroscopy (HSQC) spectrum of low level catalyst reduction mixture. ^{1}HNMR (Fig S.4) is located on the f2 axis. ^{13}CNMR is located on the f1 axis. Correlations are depicted as either blue (CH, CH_3) or red (CH_2). Note that the 4 downfield carbon peaks (120-140 ppm) do not show correlations with ^{1}HNMR peaks. The two potential olefinic protons (2.7 and 2.9 ppm), correlate to upfield sp^{3} hybridized carbons.

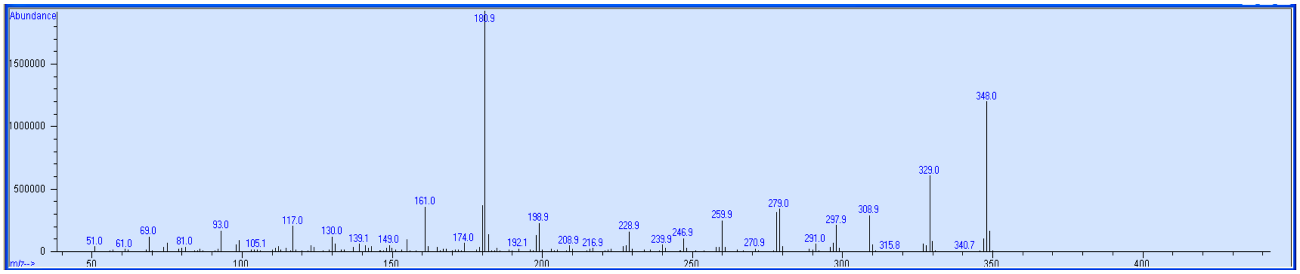

Figure S.6 GC-MS spectrum of catalyst degradation peak

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