On the Mechanism of the Conversion of Methanol to 2,2,3-Trimethylbutane (Triptane) over Zinc Iodide

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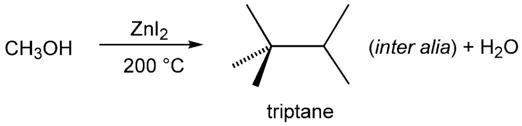

Methanol is converted to a mixture of hydrocarbons by reaction with zinc iodide at 200 °C with one highly branched alkane, 2,2,3-trimethylbutane (triptane), being obtained in surprisingly high selectivity. Mechanistic studies implicate a two-stage process, the first involving heterogeneously catalyzed formation of a carbon−carbon-bonded species, probably ethylene, that undergoes homogeneously catalyzed sequential cationic methylation to higher hydrocarbons. The first stage can be bypassed by addition of olefins, higher alcohols, or arenes, which act as initiators. Rationales for the particular activity of zinc iodide and for the selectivity to triptane are proposed.

Introduction

With the forecast depletion of oil reserves, methanol is likely to play an increasingly important role for both energy and petrochemical feedstocks.[1] One approach that has received considerable attention over the years is the dehydrative conversion of methanol to hydrocarbons over acidic catalysts, which has a very long history (dating back to 1880![2]). Different classes of hydrocarbons can be obtained (usually not very selectively) depending on the nature of the catalyst and the temperature (typically 200−450 °C).[3] The best known are the methanol-to-gasoline (MTG) and methanol-to-olefins (MTO) processes, which operate at temperatures above 300 °C to produce aromatic-rich and light olefin-rich products respectively; selectivity is ascribed to the shape-selective zeolitic and aluminophosphate catalysts. In contrast, reaction of methanol with polyphosphoric acid proceeds at considerably lower temperatures (190−200 °C) to give a complex, alkane-rich mix of hydrocarbons, of which C_7 comprises the largest fraction (27%), primarily mono- and dibranched isomers.[4]

Against this background, a 1978 discovery stands out: at 200 °C methanol reacts with zinc iodide—not normally considered to have strongly acidic properties, unlike polyphosphoric acid—to give an alkane-rich hydrocarbon mix with distribution again peaking at C_7. However, in this case one highly branched alkane, 2,2,3-trimethylbutane (common name triptane), was by far the major product obtained in overall yields up to 20% (moles carbon basis). Triptane was reported to constitute as much as one-half of the gasoline-range fraction. Similar chemistry was found for zinc bromide at slightly higher temperatures but not for zinc chloride.[5] Earlier patents report conversion of methanol to hydrocarbons over molten $ZnCl_2$ at higher temperatures (325−425 °C) with 20−25% selectivity to isobutane along with substantial amounts of hexamethylbenzene (HMB) and coke.[6]

These observations are of significant interest. On the practical side, such a highly branched alkane, with an octane number of

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(1) Olah, G. A. *Angew. Chem., Int. Ed. Engl.* **2005**, *44*, 2636−2639.

(2) LeBel, J. A.; Greene, W. H. *Am. Chem. J.* **1880**, *2*, 20 (cited in ref 3a).

(3) a) Chang, C. D. *Catal. Rev.*—Sci. Eng. **1983**, *25*, 1−118. (b) Olah, G. A.; Molnár, Á. *Hydrocarbon Chemistry*, 2nd ed.; John Wiley& Sons: Hoboken, NJ, 2003; pp 117−122 and references therein.

(4) Pearson, D. E. *J. Chem. Soc., Chem. Commun.* **1974**, 397.

(5) Kim, L.; Wald, M. M.; Brandenburger, S. G. *J. Org. Chem.* **1978**, *43*, 3432−3433. Also see U.S. Patents 4,059,646, 4,059,647, 4,126,642, 4,126,643, 4,151,214, 4,166,189, and 4,249,031.

(6) Grosse, A. V.; Snyder, J. C. U.S. Patent 2,492,984, 1950. Bell, W. K.; Chang, C. D. U.S. Patent 3,969,427, 1976.

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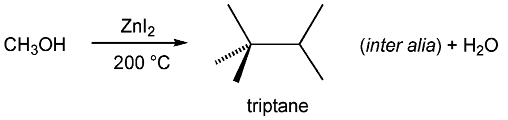

(1)

112, would be a valuable fuel component if it could be produced cheaply and efficiently. Several selective routes to triptane have been previously reported,[7] but all involve precursors and/or reagents that would be prohibitively expensive for large-scale fuel production. However, they are perhaps even more intriguing from a fundamental viewpoint: what mechanism(s) could account for such high selectivity to a single product out of the (literally) hundreds that are formed in detectable quantities?

This issue takes on added importance in light of the fact that there is to date no consensus mechanistic explanation for *any* of the methanol-to-hydrocarbon conversions alluded to above. Methylation/alkylation of intermediate olefinic species via carbocationic intermediates may reasonably be invoked to account for growth of the first-formed light hydrocarbons given the acidic nature of all the catalysts that effect such reactions; however, how might the *first* carbon−carbon bond form? Most proposals center on some form of [$-O-CH_2$:] center produced by deprotonating a surface-bound methanol or methoxy group (or perhaps the trimethyloxonium ion), which reacts with a "methyl cation equivalent", i.e., some [CH_3-O-X] species activated for nucleophilic attack by coordination to the catalyst surface. The plausibility of such a deprotonated intermediate under acidic conditions has been questioned.[3]

Haw put forth a quite different model wherein C−C bond formation takes place via methylation of aromatic intermediates in a "carbon pool" and there is no "first" C−C bond formation, at least not from methanol: organic impurities, always present at some levels, are responsible for the initial formation (during an induction period) of the carbon pool, which then serves as a "scaffold" on which subsequent chemistry takes place. Experimental support for this proposal was obtained for reactions over HZSM-5 and HSAPO-34.[8]

Kim et al. argued that a carbocation-based route could not account for the selective formation of triptane over ZnI_2 and proposed instead a carbene-based route with a carbenoid organozinc intermediate analogous to the Simmons−Smith reagent.[5,9] Such a route may offer a more attractive explanation for the first C−C bond formation—via coupling of two carbenes—and might explain the selectivity for triptane, at least in some aspects (see below). On the other hand, it seems difficult to reconcile stability of any organozinc species with the protic medium in which the reaction takes place.

We report here the results of some recent studies. While we are not yet in a position to formulate a complete detailed mechanism, we have been able to shed some light on a number of questions. These include the existence of a first C−C bond-forming step, the carbocation-based route for hydrocarbon growth, and the properties of ZnI_2 that account for its particular ability to effect this reaction. We hope that these findings can help point the way toward an eventual full understanding of this fascinating system.

Results and Discussion

Toward a Reproducible Experimental Protocol. In a "typical" experiment, a mixture of MeOH and ZnI_2, in molar ratios ranging from 2:1 to 3:1, is heated in a closed vessel at 200 °C for several hours. After cooling to room temperature, three phases are observed: an upper hydrocarbon layer, a lower aqueous layer, and some solid. Analysis of the organic layer by a variety of techniques (GC, GC/MS, ^1H and ^{13}C NMR) reveals the presence of a very large number of components (several hundred by GC; see Figure 1 for a typical chromatogram) with the largest being triptane. Some 2,3,3-trimethylbut-1-ene (triptene) is also present; its GC signal is not always well separated from that of triptane, but its presence is readily seen in the ^{13}C NMR spectra (Figure 2). There is always much more triptane than triptene. The next most prominent single component is hexamethylbenzene (HMB); there are also significant amounts of branched lighter alkanes isobutane, 2-methylbutane, and 2,3-dimethylbutane (signals identified in Figure 2). The combined yield of "triptyls" (triptane plus triptene), on the basis of moles carbon charged as methanol, is generally found to be around 17 ± 3%.

However, it can be difficult to achieve such "typical" results as reproducibility can be affected by several factors: the source of the reagents used (less-pure samples of ZnI_2 sometimes work better); the nature and size of the reaction vessels (autoclaves, glass tubes); the presence of small amounts of various organic additives; and, most disconcertingly, whether or not the mixture is agitated during reaction. The latter can have a dramatic effect: in two otherwise identical reactions carried out in glass tubes, one with stirring (or shaking) and the other quiescent, the former is found to give *no triptyls at all*—indeed, no visible hydrocarbon layer forms—while the latter gives the standard results summarized above. This contrast in behavior is quite reproducible. On the other hand, in the presence of small amounts of additives such as higher alcohols, olefins, and aromatics, stirred and unstirred reactions behave identically.

In order to understand this highly unusual behavior and ensure that reliable, reproducible baseline data can be obtained, we developed a standard experimental protocol as follows. A 790 mg amount of MeOH and 2.4 g of ZnI_2 (3.3:1 molar ratio) are loaded into a thick-walled glass tube equipped with a Teflon valve, and the mixture is agitated and/or gently warmed until complete dissolution has occurred. The tube is then immersed up to the Teflon valve in a 200 °C oil bath behind a blast shield, where it is maintained for a desired period of time, then removed and allowed to cool to room temperature. At this point the mixture remains a completely homogeneous solution with no trace of any visible hydrocarbon layer; analysis of the mixture indicates that no reaction has occurred, other than partial dehydration of methanol to dimethyl ether (DME) along with formation of small amounts of MeI, even for heating times as long as 24 h.

If, on the other hand, an identically charged tube is directly immersed in the oil bath, *without* trying to dissolve all the ZnI_2, separation of an organic layer can be observed after an hour or less. After cooling two liquid phases along with a substantial

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[7] See, for example: (a) Ford, T. A.; Jacobson, H. W.; McGrew, F. C. *J. Am. Chem. Soc.* **1948**, *70*, 3793−3795. (b) Howard, T. R.; Lee, J. B.; Grubbs, R. H. *J. Am. Chem. Soc.* **1980**, *102*, 6876−6878. (c) Reetz, M. T.; Westermann, J.; Steinbach, R. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 900−901.

[8] a) Haw, J. F.; Song, W.; Marcus, D. M.; Nicholas, J. B. *Acc. Chem. Res.* **2003**, *36*, 317−326. (b) Olsbye, U.; Bjørgen, M.; Svelle, S.; Lillerud, K.-P.; Kolboe, S. *Catal. Today* **2005**, *106*, 108−111.

[9] The 1978 paper promises "supporting evidence for carbenoid and organozinc intermediates and a detailed mechanism consistent with the high triptane yield" in "subsequent publications"; however, no such publications have appeared.

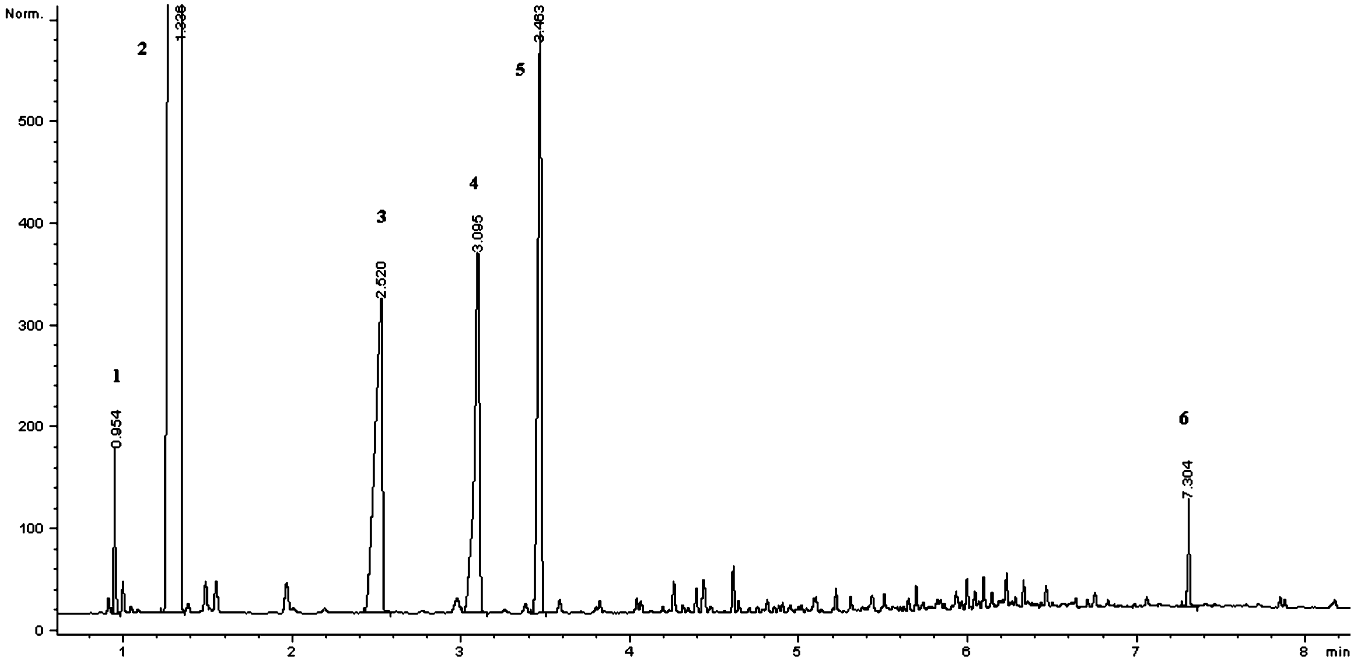

FIGURE 1. GC trace of typical reaction product mixture. Labeled peaks: **1**, dimethyl ether; **2**, acetone (added as solvent); **3**, chloroform (used to extract organic layer); **4**, triptene and triptane (not resolved in standard analysis); **5**, cyclohexane (added as internal reference standard); **6**, hexamethylbenzene.

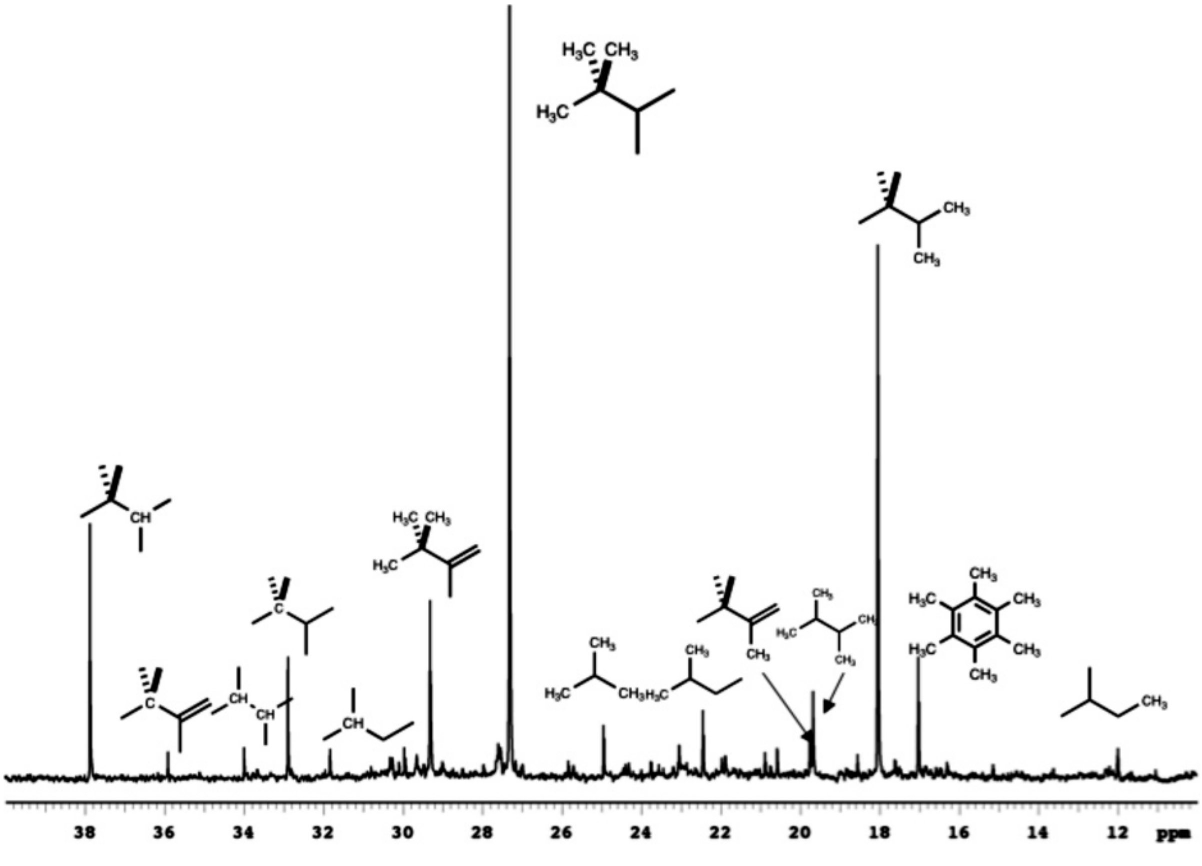

FIGURE 2. Part of the ^{13}C NMR spectrum of a typical product mixture, showing the sp^3 carbon signals for triptane, triptene, HMB, and several minor components.

amount of solid are present, and the organic layer contains substantial amounts of triptyls, as above. The solid is predominantly unchanged ZnI_2, as demonstrated by powder-pattern XRD.

Role of Additives. Unreactive homogeneous (predissolved) mixtures can be "turned on" by the addition of a small amount of a higher alcohol. In the presence of as little as 1% (by weight, relative to MeOH) added isopropanol or *tert*-butanol, reaction

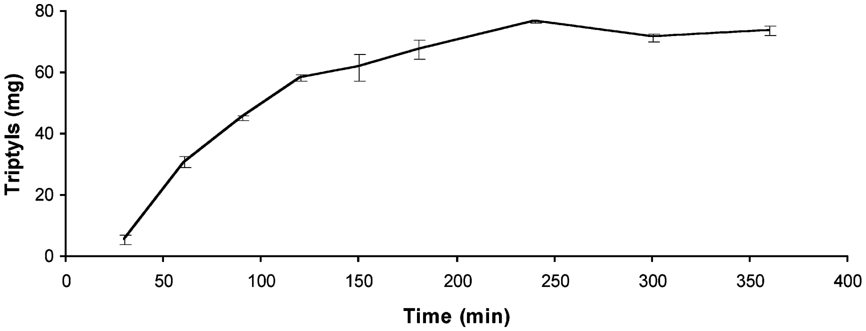

FIGURE 3. Yield of triptyls as a function of time for standard reactions with 1.5 wt % added *i*-PrOH.

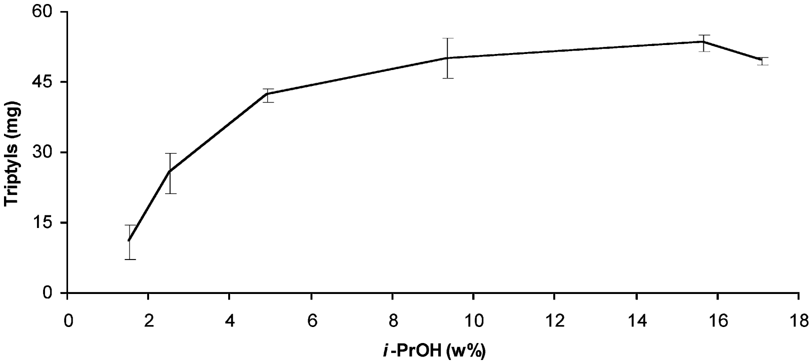

FIGURE 4. Yield of triptyls as a function of wt % added *i*-PrOH for standard reactions carried out for 2 h.

proceeds as in the non-predissolved case, although no solid appears during reaction or after cooling at its conclusion. Formation of triptyls as a function of time (determined by a series of parallel experiments as we have no convenient way to monitor progress in situ) is shown for *i*-PrOH as additive in Figure 3. At an intermediate additive level (1.5%) triptyls are detectable at an early stage, with little induction period, and build to a maximum level over approximately 3 h; no detectable change takes place if heating is continued beyond that point, up to 24 h. The maximum yield, around 70 mg, corresponds to about 20% on the basis of MeOH charged or 18% on the basis of total carbon (including *i*-PrOH).

A "complete" analysis of the hydrocarbon layer obtained from the reaction described above, using a standard refinery GC routine ("PIANO", for paraffin/isoparaffin/aromatic/naphthene/olefin), indicated that the distribution as a function of carbon number peaks at C_7 with lesser amounts of C_{8-11} and much less of the lighter fractions. Isoparaffins dominate, as can be seen by NMR as well (see above); amounts of olefins, naphthenes, and aromatics are considerably smaller, and hardly any normal paraffins are found. This distribution should not be considered quantitatively accurate, however, as many of the assignments, which rely solely on retention time, are probably not reliable, especially for the heavier components that elute at longer times. In particular, hexamethylbenzene, known by NMR to be a major component, was not detected in the PIANO analysis at all; probably it eluted after the run was terminated.

Figure 4 shows triptyl yield as a function of the amount of added *i*-PrOH after 2 h reaction. The yield increases steadily with additive amount up to about 3% and then levels off. Reactions with lower additive levels continue to form triptyls, up to the same maximum yield as above, if allowed to react for longer times (except, as noted above, for the zero-additive point). Also, the (qualitative) composition of the organic layer looks very similar for all these experiments, and reactions with lower triptyl yields contain substantial amounts of unreacted MeOH/DME. Hence, it appears the additive effect has to do with the overall rate of conversion to hydrocarbons rather than any significant alteration of the mechanism of conversion.

Furthermore, the selectivity for triptyls is established from the earliest appearance of hydrocarbons, as opposed to initial formation of lighter hydrocarbons that grow as reaction proceeds. In confirmation of this conclusion, two experiments under standard conditions, with 1.5% *i*-PrOH added, were carried out for 2 and 3 h, and the amounts of unreacted MeOH and DME in the organic and aqueous layers were determined by NMR. The results were as follows: triptyl yield (based on MeOH charged), 12% and 19%, respectively; unconverted MeOH (including DME), 37% and 5%, respectively. The triptyl yield on the basis of *converted* MeOH is the same (19−20%) within experimental accuracy.

Fairly good mass balances can be obtained. A mixture containing 770 mg of MeOH, 40 mg of *i*-PrOH, and 2.27 g of ZnI_2 was heated for 3 h following the standard protocol. In addition to the two liquid layers, about 90 mg of volatiles were produced, estimated by weighing the tube before and after opening. These were shown to consist primarily of light hydrocarbons, particularly isobutane, isobutene, and propene, along with some methyl iodide. The organic and aqueous layers were separated and found to weigh 315 mg and 2.68 g, respectively; the aqueous layer contained about 60 mg of MeOH and 35 mg of DME. Subtracting the latter and the initial weight of ZnI_2 gives 310 mg of water.[10] Correcting for the amount of unconverted MeOH/DME, the reaction should have produced

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(10) This does not take into account iodide lost as MeI, for which we as yet do not have good quantitation, so the actual yield of water is somewhat higher.

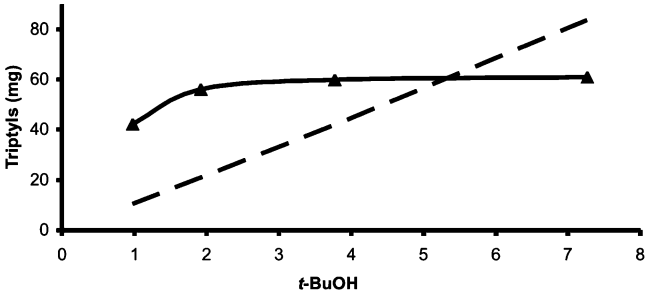
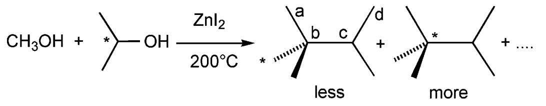


FIGURE 5. Yield of triptyls as a function of wt % added *t*-BuOH for standard reactions carried out for 2 h. The dotted line shows the theoretical maximum yield if triptane were formed solely by alkylating *t*-BuOH.

about 315 mg of hydrocarbon and 380 mg of water, in reasonable agreement with observation.

The role of *i*-PrOH may be probed with the use of ^{13}C-labeled reagents. (Use of deuterium labeling was found to be uninformative as H/D exchange among all positions of all products is rapid and complete under reaction conditions.) When $(^{12}CH_3)_2{}^{13}CHOH$ is used as promoter in the reaction of unlabeled MeOH, relative intensities in the ^{13}C NMR spectrum show that the label is found in the internal ($C_{b,c}$) positions of triptane to a far greater extent than in the methyl ($C_{a,d}$) groups (eq 2). The gas-phase components from the converse experiment—reaction of $^{13}CH_3OH$ promoted with unlabeled *i*-PrOH—include (by NMR) MeI (completely labeled), large amounts of propene (mostly unlabeled), and smaller amounts of isobutene, which is almost completely labeled in the terminal positions but only partially (∼85%) labeled in the central position. These findings suggest that the alcohol is readily dehydrated under these acidic conditions to the olefin, which serves as the actual promoter. Under the particular conditions of these experiments (relatively little promoter added), some of the isobutene comes from direct methylation of propene, but most of it is built up entirely out of MeOH. The fact that little ^{12}C remains in terminal positions further suggests that they are able to exchange with MeOH-derived methyl groups (see below and Supporting Information for more detailed discussion).



(2)

The behavior with *t*-BuOH as additive is similar, although smaller amounts are able to produce the same degree of acceleration (Figure 5). In several of these experiments the number of moles of triptyls obtained is substantially higher than the number of moles of *t*-BuOH added, which demonstrates that these additives act as true initiators, as opposed to being simply frameworks on which triptyls are assembled.

Other additives have been shown to function as initiators. Olefins ranging from light, such as ethylene and propylene, up to some heavier than C_7, such as di-isobutylene (2,4,4-trimethylpent-2-ene), act similarly to the above-described alcohols as do aromatics, up to and including hexamethylbenzene, a reaction product. Benzene itself is a less effective initiator: under standard conditions with benzene as initiator the only new hydrocarbon observed after 3 h is toluene. After more prolonged reaction triptyls begin to form, along with more highly methylated benzenes. Paraffins appear to be completely ineffective. EtOH does not initiate reaction following the standard protocol but does under some other conditions (different reactor types/sizes); running the standard reaction under an ethylene atmosphere *does* initiate. We believe this is a consequence of the lower solubility of ethylene compared to propene or isobutene; whether there is enough dissolved ethylene to effectively initiate will then depend on factors such as headspace volume.

From these observations we infer that the unpromoted conversion of methanol to hydrocarbon involves two separate stages: an initiation stage, involving formation of one (or more) reactive C−C-bonded species, probably ethylene, and a growth stage, involving elaboration of these species by successive methylation, leading ultimately to triptyls and other hydrocarbons. The stirring/predissolution effects strongly suggest that the first stage is not only relatively slow, taking place during a moderately lengthy induction period, but also catalyzed *heterogeneously*, as it does not take place at all in the absence of undissolved solid. The second stage, in contrast, proceeds equally well whether or not there is any solid phase. The initiation stage can be completely bypassed by addition of a suitable additive, either an unsaturated compound (olefin, arene) or an alcohol, which presumably functions as a facile precursor to an olefin.

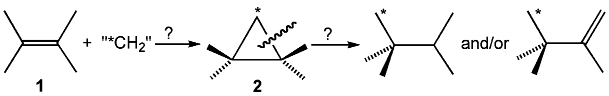
The observation that less-pure ZnI_2 samples are often more effective catalysts might be due to the presence of insoluble impurities that catalyze initiation. Another possibility is that the impurities themselves are sources of initiator, as in Haw's proposed mechanism for MTO. For example, some samples appear to be contaminated with alkylammonium salts, which could generate olefins via Hoffmann elimination.

At least some of the triptane appears to form by direct sequential buildup on the initiator, as suggested by the experiment with labeled *i*-PrOH: carbon atoms that are part of the olefinic backbone of the (presumed) intermediate propene preferentially end up in the backbone (internal) positions of triptane. The fact that triptane is produced in (molar) excess of the amount of added initiator implies that other processes are going on as well. This issue is addressed in more detail below.

It is of interest to compare this picture to Haw's proposal for MTO. Our findings strongly suggest that formation of C−C-bonded species from methanol alone is difficult—much more so than the growth steps—but *does* take place under the right conditions. One *could* argue that even in the absence of deliberately added initiator there are impurities present that are responsible for initiating growth. However, these would have to be species that only function effectively as initiators in the presence of solids, whereas the reaction works perfectly well with a wide variety of deliberately added initiators in the absence of solid. Such an interpretation seems to us quite improbable.

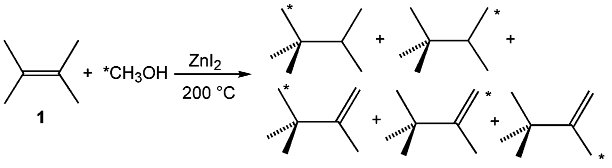
It would be harder, at this point, to say whether the growth stage involves (in part or exclusively) a carbon pool of substituted aromatics as opposed to buildup of increasingly substituted olefins. The observations with benzene as initiator suggest that Haw's mechanism *can* serve as a source for light olefins as no triptane formation is observed until after methylated benzenes have begun to appear. A labeling experiment is also suggestive: reaction of $^{13}CH_3OH$ with unlabeled hexamethylbenzene as initiator affords triptane with a substantial amount of ^{12}C in all positions. However, the recovered hexamethylbenzene contains a good deal of ^{13}C in methyl positions, indicating that those positions exchange with MeOH, so any conclusion from this experiment is open to question. Additional experiments bearing on this point will be described in the following section.

Attempts To Test a Carbene-Based Mechanism. The proposed carbene-based route that could explain selectivity for triptane was not spelled out in detail,[5,9] but it seems likely that any such mechanism would involve successive olefin cyclopropanation and ring-opening steps. In such a scheme the conclusion of a sequence leading to the triptane framework would be cyclopropanation of 2,3-dimethylbut-2-ene (**1**) to give 1,1,2,2-tetramethylcyclopropane (**2**), which would ring open at one of the less-substituted C−C bonds; this hypothetical sequence is represented by eq 3. Possible precedent may be found in the Cu-catalyzed hydrogenolysis of **2**, which under certain conditions (admittedly, quite different from those of the present study) gives triptane nearly quantitatively.[11]



(3)

To test whether this sequence is at all plausible, we added **1** and **2**, respectively, to ZnI_2/MeOH reaction mixtures. In both cases reaction was observed even at 160 °C (at which temperature conversion of MeOH to hydrocarbons does not normally proceed at all). Cyclopropane **2** readily ring opens to a mixture of triptane and triptene along with much smaller amounts of a number of additional components (by NMR). Similarly, **1** reacts under these conditions to give triptyls. At early stages the latter consist primarily of triptene; the triptane/triptene ratio gradually increases over time. Side products, all in lower amounts, include isomerized olefin (2,3-dimethylbut-1-ene) and oligomers. When the reaction is carried out using $^{13}CH_3OH$, label is found in *all* methyl/methylene positions of triptane and triptene but not the internal positions; GC/MS shows that each triptyl contains exactly one $^{13}CH_3$ group (eq 4).

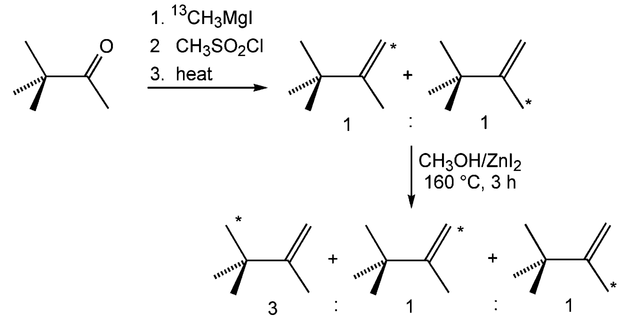


(4)

These results are necessary, but not sufficient, to show that **2** is an intermediate in the ZnI_2-catalyzed conversion of MeOH to triptyls. Equation 3 suggests a further diagnostic test: label introduced from the cyclopropanating species should wind up exclusively in the *tert*-butyl group (C_a), not at C_d, but the reaction of **1** with $^{13}CH_3OH$ puts label in all terminal positions (eq 4). If the ring opening of **2** labeled at the 3-position is regiospecific as shown, that would rule out this mechanism for the methylation of **1** to triptyls.

However, such a conclusion would require that we know label does not scramble among the terminal positions under reaction conditions. In fact, it does: a ^{13}C label in the methylene/adjacent methyl positions of triptene undergoes complete statistical scrambling to all peripheral positions under the above conditions (160 °C, 3 h) (Scheme 1). Hence, the labeling experiment cannot be used to determine whether the carbene/cyclopropane mechanism is viable.

SCHEME 1



Carbene or Carbocation? A Further Labeling Experiment. The facile rearrangement of label in Scheme 1 strongly implicates a carbocation-based mechanism; it is possible, however, that the rearrangement and growth process involve two distinct mechanisms. We can distinguish between the two alternatives, carbene-based and carbocation-based, by examining the labeling pattern of triptane synthesized from ordinary MeOH and dilabeled EtOH. Although EtOH is not a reliable initiator as discussed above, the reaction can be carried out by not predissolving the ZnI_2; ^{13}C NMR of the product mixture obtained is shown in Figure 6.

There are two key informative features. First, as in the previous experiment with labeled *i*-PrOH, the signals corresponding to internal carbons (b, c) are considerably enhanced relative to those for the methyl carbons (a, d). Second, for all four carbons the signals appear as approximate 1:3:1 “triplets”, attributable to superimposed singlet and doublet signals (corresponding to ^{13}C with no or one adjacent ^{13}C, respectively) in about 60:40 ratio. The signals for the internal carbons exhibit weak outer peaks as well, indicating an additional triplet signal arising from two adjacent ^{13}C nuclei.

The complete analysis of the spectral results and their mechanistic implications is complex and, hence, provided in the Supporting Information. Briefly summarized, the carbene mechanism is not viable as the symmetry of the initial cyclopropane intermediate precludes any outcome where internal positions are more enriched in label than methyls. A carbocation route, in contrast, can satisfy the observations, both qualitatively and quantitatively, if (and only if) the growth sequence—methylation of olefins by a methyl cation equivalent—is at least partly reversible, that is, that the resulting carbocation can lose a methyl cation to revert to the precursor olefin in competition with the normal growth step of losing a proton to give the next higher olefin. That such a process does in fact operate is demonstrated by the labeling pattern found for isobutene derived from labeled methanol plus unlabeled isopropanol (see above).

With that feature included, both the enrichment of label at the internal positions and the relative intensities of the apparent multiplets for each signal can be accurately modeled, as shown in the Supporting Information; the latter agreement is illustrated in Figure 7. The proposed mechanism is spelled out in the last section below along with a proposed explanation of how it can account for selectivity to triptane.

Hydrogen Transfer. Formation of alkanes, such as triptane, by dehydrative condensation of MeOH ($= CH_2 + H_2O$) requires that an equivalent of H_2 be supplied at some point with corresponding formation of hydrogen-deficient species. As noted above, the latter are primarily aromatics, especially HMB. How does this process occur?

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[11] Bartók, M.; Pálinkó, I.; Molnár, Á. *J. Chem. Soc., Chem. Commun.* **1987**, 953−954.

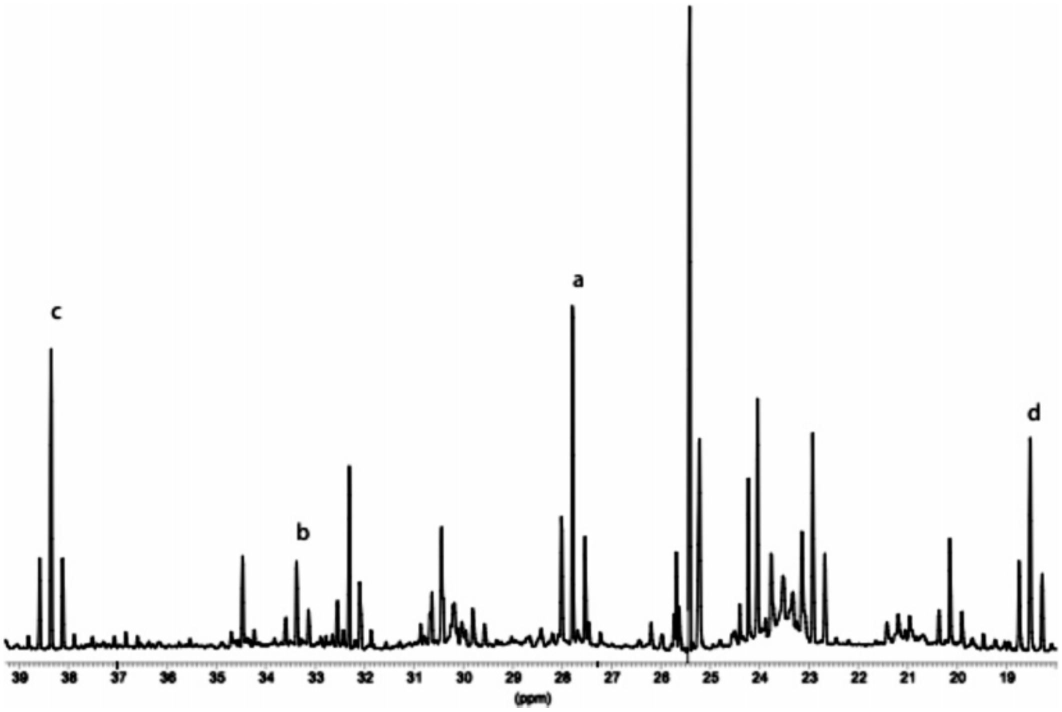

FIGURE 6. Part of ^{13}C NMR spectrum showing triptane signals for reaction of unlabeled MeOH with $^{13}C_2H_5OH$. (Position labeling shown in eq 2.)

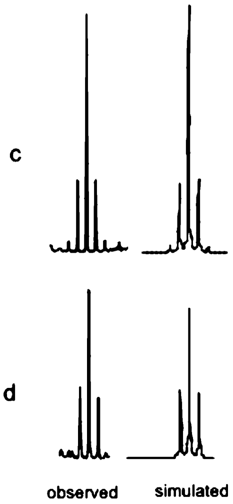

FIGURE 7. Observed and simulated ^{13}C NMR patterns for the c and d positions of triptane formed from unlabeled MeOH and doubly labeled EtOH. (See Supporting Information for details of simulation.)

One possibility would be direct transfer from MeOH to olefin, giving alkane plus formaldehyde; the latter could be a precursor to aromatics via condensation. Triptene is partially reduced to triptane by heating with MeOH/ZnI_2 even at 160 °C but only if the mixture is unstirred and not predissolved. A fully predissolved reaction mixture shows no hydrogenation of added triptene to triptane over 3 h at 200 °C. On the other hand, triptane *is* formed by ring opening of **2** or methylation of **1** under the same conditions (see above), implying that intermediate hydrocarbons are the immediate source of the requisite hydrogen.

Stoichiometrically, then, this amounts to transfer of H_2 from one olefinic hydrocarbon to another, resulting in an alkane and a multiply unsaturated species; the latter would eventually end up as an arene, which would be further methylated to HMB. Under standard reaction conditions, the growth of HMB correlates closely with that of triptane (Figure 8), supporting the proposed link.[12] The molar ratio of HMB:triptane is considerably lower than 1:3, the ratio required for *all* the excess hydrogen in triptane (not even considering other alkanes) to be accounted for by HMB (eq 5). Presumably the deficit is explained by formation of other aromatics, of which a number are detected, even though no single one is obtained in high yield.

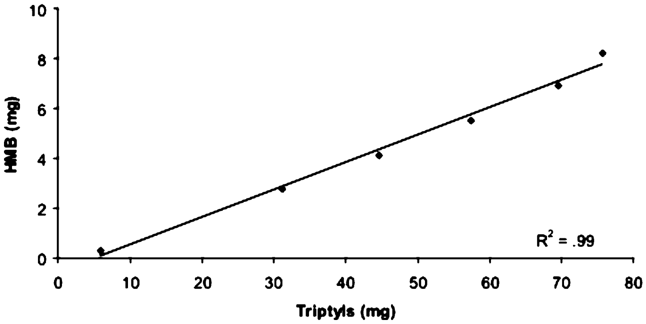

FIGURE 8. Correlation between yields of triptyls and HMB for standard reactions carried out to varying degrees of completion.

$$33CH_3OH \rightarrow 3C_7H_{16} + C_6(CH_3)_6 + 33H_2O \qquad (5)$$

As a test, a standard reaction mixture containing added triptene and cyclohexa-1,4-diene, a model arene precursor, was heated at 150 °C for 2 h. Both triptane and benzene were formed as major products along with a small amount of methylated

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[12] The ratio of HMB/triptyls does vary under different reaction conditions, especially in reactions starting with DME carried out at lower temperatures (see below). We believe this reflects increased yields of less-substituted benzenes at the expense of HMB but do not yet have sufficiently complete analytical data to confirm that.

benzenes. No hydrogenation of triptene was observed under these conditions in the absence of the diene.

On the Role of ZnI_2. In a standard run the ratio of MeOH:ZnI_2 is about 3.3:1; since the maximum yield of triptane is around 20%, less than one MeOH per Zn is actually converted to triptane. On the other hand, the MeOH (and its initial dehydration product DME) can be essentially entirely converted to hydrocarbon under these conditions, which suggests at least the possibility that ZnI_2 acts as a catalyst. Kim et al. reported that ZnI_2 can be recovered and reused, which again suggests it is a catalyst, but provided no details.[5] We carried out a number of experiments which bear on this question.

If the starting ratio of MeOH:ZnI_2 is increased, similar behavior and triptyl yields are maintained only up to around 4:1. Beyond that yields fall off rapidly; in most such experiments no hydrocarbon formation at all is observed. This suggests that the first, initiation stage of the reaction is inhibited by too much MeOH. Since partial dehydration of MeOH to DME is rapid at any concentration, it seems likely that this is a water effect, which could be offset by using DME instead of MeOH as feed.

A mixture of pure DME with dry ZnI_2 is not reactive, but in the presence of small amounts of water and MeI (typically around 10% and 30%, respectively, relative to DME), reaction proceeds readily. At 160 °C (where MeOH does not react at all, even with initiator), DME reactions proceed at rates close to those for MeOH at 200 °C. With addition of initiator (*i*-PrOH or di-isobutylene) such reactions proceed even faster and can be carried out at temperatures as low as 140 °C to attain ultimate triptyl yields around 20%. This comparison strongly suggests that water inhibits the initiation stage, which is completely shut down if too much water is present.

As the conversion of MeOH/DME to hydrocarbon proceeds, of course, still more water is formed: what is the effect on the growth stage? To test that a mixture of DME and ZnI_2 in 1.1:1 molar ratio, additionally containing small amounts of water, MeI, and di-isobutylene, was heated at 160 °C for 4 h. The reactor was cooled, a small sample removed for analysis, and another charge of DME added; this was repeated for a total of five cycles. Triptyl yields around 25% based on DME + MeI (corresponding to 17% based on total carbon charged, including the initiator) were found for each of the first three cycles, the yield for the fourth cycle fell off to around 16%, and the fifth cycle produced *no* additional triptyls.

A similar experiment was carried out using DME for the first charge but MeOH for the second, and the full amount of additional triptyls was produced in the second cycle, although MeOH is normally unreactive at 160 °C. In contrast, when an analogous experiment was performed using 3:1 MeOH:ZnI_2 at 200 °C, the second cycle produced little or no additional triptyls.

These results indicate that water plays a limiting role in the growth stage in addition to its inhibitory role in the initiation stage. The latter explains why DME can be made to react at temperatures considerably lower than can MeOH: much less water is present at the outset. In subsequent reaction cycles initiator is already present, so that MeOH reacts perfectly well at the lower temperature. As for the former, it appears that about four molecules of feed per Zn, corresponding to four (starting with MeOH) or eight (starting with DME) CH_2/Zn, can be converted to hydrocarbons. In other words, reaction ceases when four H_2O/Zn have been generated, which suggests that the end point is formation of the fully hydrated salt, $[Zn(H_2O)_4]I_2$. The "aqueous layer" that separates out on cooling is thus perhaps better described as a low-temperature molten salt: the melting point of the tetraaquo salt has been reported to be −7 °C.[13]

If water formation is indeed the limiting factor, then it ought to be possible to continue reaction by removing it. This is in fact the case. Another multicycle DME reaction like the one described above was stopped after the fourth cycle, and all volatiles were removed by vacuum transfer, leaving an off-white solid. This was treated with a fresh charge of DME and MeI, and the next cycle produced the full expected amount of triptyls. No reaction took place if DME but no MeI was added. This pattern can be continued indefinitely: up to 18 CH_2/Zn have been converted over a single initial charge of ZnI_2, as long as water (along with all other volatiles) is periodically removed and lost MeI replaced, with no apparent falloff in reactivity or triptyl yield.

Mechanistic Considerations: Why Triptane? Why Zinc Iodide? While the results discussed above do not establish any mechanism unequivocally, everything seems to us to suggest that the growth stage of the reaction involves an acid-catalyzed carbocation-based mechanism that takes place homogeneously in a very concentrated aqueous/methanolic solution of ZnI_2. This could involve Brønsted acidity, Lewis acidity, or both. Furthermore, ZnI_2 is quite soluble in alcohols, and concentrated aqueous ZnI_2 solutions readily dissolve substantial quantities of organic compounds—a saturated solution can take up an equal weight (or more) of diethyl ether at ambient temperatures[14]—so that as long as the ZnI_2 is completely dissolved before heating, it should stay that way throughout the reaction.

How can we account for the remarkable selectivity to triptane within such a mechanistic framework? It should first be noted that selectivity for triptane cannot be explained on any thermodynamic grounds. From published thermochemical data[15] we calculate that triptane would comprise only 6% of the total C_7 alkane fraction at equilibrium (at 500 K). Furthermore, the values of $\Delta G°$ calculated for the reactions of triptane plus methanol to give 2,2,3-trimethylpentane plus water and the corresponding conversion of 2,3-dimethylbutane plus methanol to triptane plus water are identical (−13.4 kcal/mol at 200 °C). Thus, there is no thermodynamic preference for triptane, relative either to other C_7 alkanes or to highly branched alkanes of different carbon number.

A different, quasi-thermodynamic explanation might be offered: that the distribution of carbocationic intermediates governs that of the alkane products, with the triptyl carbocation being the most stable. However, this also is not the case: Brouwer has shown by ^1H NMR that the triptyl cation is in fact *not* more stable than other C_7H_{15} cations, comprising only about one-fourth of the total tertiary heptyl cations at equilibrium at −20 °C.[16]

Why then do we *not* see the equilibrium distribution of products that might be anticipated once carbocations are invoked? It is important to keep in mind that the conditions here are far from superacidic: the pH of 5 M ZnI_2 is around 1.[17] We would hence not expect carbocations to be at all long-

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[13] Aylett, B. J. In *Comprehensive Inorganic Chemistry*; Trotman-Dickenson, A. F., Ed.; Pergamon Press: Oxford, 1973; Vol. 3, p 215.

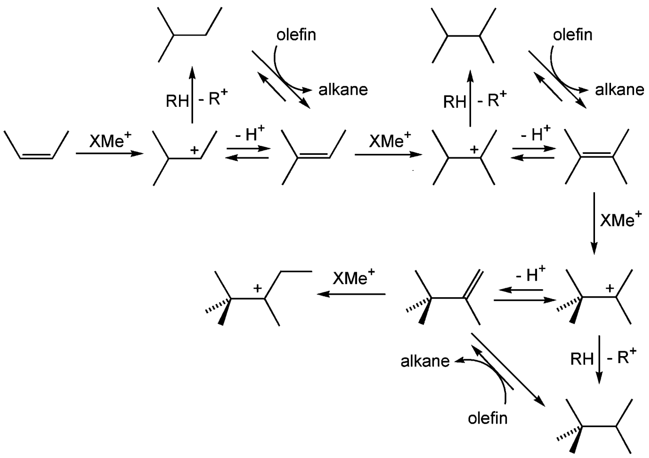
[14] Guempel, O. *Bull. Soc. Chim. Belg.* **1929**, *38*, 443−477.

[15] Rossini, F. D.; Pitzer, K. S.; Arnett, R. L.; Braun, R. M.; Pimentel, G. C. *Selected Values of Physical and Thermodynamic Properties of Hydrocarbons and Related Compounds*; Carnegie Press: Pittsburgh, 1953; pp 467−469, 751−753.

[16] Brouwer, D. M. *Recl. Trav. Chim. Pays-Bas* **1968**, *87*, 210−224.

[17] Reiff, F. *Z. Anorg. Allg. Chem.* **1932**, *208*, 321−347.

SCHEME 2



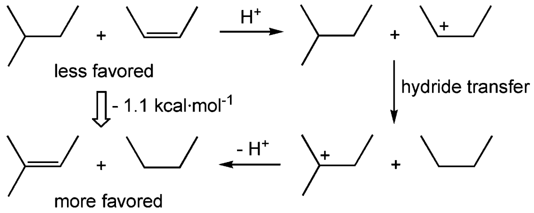
lived, and the reaction would need not to be under thermodynamic control, as it obviously is not.[18] We do not yet have a detailed model that fully accounts for high selectivity to triptane but offer the following sketch that may serve as the nucleus of such an explanatory schema.

First, we need to have one or more light olefins; these (or their precursors, such as alcohols) can be deliberately added or generated directly from MeOH during the initiation stage. The latter appears to take place heterogenously at surface sites; we cannot say any more about its nature at this point. When additives such as *i*-PrOH or *t*-BuOH are used, the amount of triptyls formed exceeds the amount of additive. That implies that there must be a mechanism for continuous regeneration of light olefins as the reaction proceeds. There are many possibilities, including cracking of intermediate or heavier hydrocarbons; the fact that di-isobutylene serves as initiator implies such processes are possible. On the other hand, the observations using benzene as initiator (see above) support Haw's carbon pool proposal[8] as an attractive possibility. Aromatics generated as a consequence of hydrogen transfer would be converted to highly methylated species, such as HMB, that could function as nuclei for side chain C−C bond formation, followed by splitting out light olefin and a dealkylated aromatic that would rapidly remethylate.

Next, we need a methylating species—a methyl cation equivalent. Most probably this is generated by coordination of MeX to a Zn^{2+} center, where MeX might be MeOH, DME, or even MeI. The limiting role of water on conversion suggests that to be thus active Zn^{2+} must have fewer than four waters coordinated. (It also suggests that MeX is activated by coordination rather than protonation.) Reaction of the methylating species with olefin produces a homologous carbocation, which can either lose a proton to give the next higher olefin or accept the equivalent of hydride from a suitable donor (ultimately an arene precursor to satisfy stoichiometry in hydrogen). The ubiquitous participation of proton transfers is consistent with the observation of complete H/D scrambling in all species.

A representative sequence of reactions leading up to triptane is shown in Scheme 2, where XMe^+ is the methylating species and RH the hydride donor; for simplicity it starts at but-2-ene and leaves out (an extremely large number of) alternate pathways. (The reversibility of methylation, which as discussed earlier is required to explain labeling results but has no consequence otherwise, is not shown.) The observed preference for a highly branched product such as triptane is a consequence of both methylation and proton loss taking place so as to afford the most highly substituted carbocation and olefin, respectively, at every stage.

SCHEME 3



Of course, this does not yet explain the selectivity for a C_7 species relative to lighter and heavier branched alkanes. Note though that in this scheme each successive olefin in the sequence is more substituted than its predecessors, *until* we reach triptene, which is the first that is *less* substituted. We propose that this fact is of key importance, as a consequence of the following trends.

(1) Alkanes and olefins interconvert (but not so readily as to equilibrate everything) as the reaction proceeds, as indicated in Scheme 2. The more substituted olefin will be favored in any such reaction; for example, the interconversion shown in Scheme 3 is exothermic by about 1.1 kcal mol^{-1}.[19] Such thermodynamic preferences will reflect kinetic preferences for the corresponding elementary steps. As noted above, triptane is the *first* alkane produced by this sequence that must revert to a *less* substituted olefin than the lower hydrocarbons from which it is generated. Hence, it will be more likely to accumulate as the alkane than its precursors: while intermediates such as 2-methylbut-2-ene and 2,3-dimethylbut-2-ene can get temporarily trapped as alkanes along the way, they will be more likely than triptane to revert to highly substituted olefins by hydrogen transfer and become available for further growth.

(2) The rate of olefin methylation generally increases with the degree of substitution of the olefin as it becomes more electron rich. For example, Mayr has shown that of the series isobutene, 2-methyl-2-butene, 2,3-dimethyl-2-butene, and triptene, triptene is the *least* reactive olefin toward the carbon-centered electrophile (p-MeOC_6H_4)(C_6H_5)CH^+. It must be noted that this trend is by no means universal: Mayr found that 2,3-dimethyl-2-butene is apparently less reactive than 2-methyl-2-butene (there is some ambiguity here owing to possible reversibility), although it is more reactive than triptene.[20] In another study 2-methyl-2-butene was shown to be slightly less reactive than isobutene in acid-catalyzed hydration[21] (it was more reactive, by an order of magnitude, in Mayr's study). Nonetheless, it seems reasonable to postulate that triptene would be less

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[18] By way of contrast, in the reaction of methanol with polyphosphoric acid at 190 °C[4] the three largest C_7 components identified were just those that are calculated from the thermochemical data to be thermodynamically most stable (2,3-dimethylpentane, 2-methylhexane, and 3-methylhexane), although the distribution does not precisely match the thermodynamic predictions.

[19] Data from *Handbook of Chemistry and Physics*, 82nd ed.; CRC Press: Boca Raton, FL, 2001, pp 5−26−5−36.

[20] Mayr, H.; Schneider, R.; Irrgang, B.; Schaded, Ch. *J. Am. Chem. Soc.* **1990**, *112*, 4454−4459.

[21] Knittel, P.; Tidwell, T. T. *J. Am. Chem. Soc.* **1977**, *99*, 3408−3414.

susceptible (kinetically) to further methylation and consequent growth beyond C_7 than the lighter olefins from which it arises.[22]

Taken together, these considerations should significantly favor triptane over all the other possible alkanes—lighter, heavier, differently branched—that could be generated by this sequence. However, whether the entire speculative picture might in fact be the basis for a plausible detailed mechanistic explanation will probably need to be addressed by modeling both to test the validity of the two above postulates and to determine whether the kinetics they imply are capable of reproducing the observed distributions. We hope to initiate such studies in the near future.

As for the special[23] ability of ZnI_2 to promote this reaction, we believe its extremely high solubility in aqueous/alcoholic media, along with the Lewis-acidic character of the Zn^{2+} centers and/or the Brønsted acidity of the concentrated solutions, are central. The further ability of concentrated ZnI_2 solutions to dissolve substantial quantities of organics (see above) may also be important as the growth stage of the reaction appears to take place homogeneously. Whether iodide plays an additional role—for example, to convert MeOH into MeI which participates directly at one or more stages of the reaction—is unclear at this point. (MeI certainly *is* formed, but that could be a nonessential side reaction.) The fact that some MeI must be added to reactions of DME may suggest it does play an intimate role in the initiation phase. As noted earlier, $ZnBr_2$ also catalyzes triptane formation, albeit at higher temperatures; this could be consistent with either a parallel role for (less reactive) MeBr or an MeX-independent pathway, with $ZnBr_2$ less potent than ZnI_2. Again, modeling may be the best approach to distinguish between these alternatives.

While we are still well short of complete understanding of this interesting (and potentially useful) transformation, our findings do provide a mechanistic framework that can account for the unexpectedly selective formation of triptane from methanol and may offer useful parallels for important processes such as MTG and MTO, which mechanistically are not yet well understood either.

Experimental Section

General. Zinc iodide, methanol, dimethyl ether, and other organic compounds used as initiators were reagent-grade commercial samples used without further purification. ^1H and ^{13}C NMR spectra were obtained on a Varian 300 MHz instrument; GC analyses were done on an HP model 6890N chromatograph equipped with a 10 m × 0.10 mm × 0.40 um DB-1 column.

Standard Reaction Protocols. Reactions were carried out in thick-walled pressure tubes equipped with Teflon stopcocks (Ace Glassware), rated up to 10 bar. In a typical experiment, the tube was charged with 2.4 g of zinc iodide and a stir bar, closed, evacuated, and refilled with argon. (If reactions are carried out in the presence of air, products are intensely colored owing to formation of some iodine, but there does not appear to be any significant effect on the nature or amounts of organic products.) The stopcock was replaced with a septum, and 1.00 mL (790 mg) of methanol plus 50.0 μL of isopropanol, previously sparged with argon, were injected. The septum was replaced with the stopcock, and the reaction mixture was stirred until all solids dissolved. The pressure tube was placed into an oil bath, behind a blast shield (*CAUTION*), and stirred at 200 °C for the desired period of time, usually 2−3 h. (It is important that the tube be immersed in the bath as close as possible to the bottom of the stopcock. If a significant portion of the tube is above the bath, results become much less reproducible, presumably as a consequence of distillation of reactants/products to the cooler regions. Reactions carried out under different conditions are also much less reproducible than the above protocol.)

After heating the tube was removed from the bath and allowed to cool to ambient temperature. The stopcock was removed, and 1.00 mL of chloroform, containing a known amount of cyclohexane as an internal standard, was pipetted into the reaction mixture followed by 0.5 mL of water. The stopcock was replaced, the mixture was shaken vigorously, and the organic layer was separated. A small aliquot was diluted with acetone for GC analysis. In cases of samples to be used for NMR analysis, chloroform-*d* was used for the extraction.

For reactions of dimethyl ether, all ingredients except DME were loaded into the tube, which was then frozen in liquid nitrogen and degassed, and the desired amount of DME was condensed in; the tube was allowed to warm to room temperature and then heated as usual. DME is only converted to triptane if small amounts of water (5 wt% or more) are added to the reaction mixture along with ZnI_2 and promoter.

For consecutive reactions, a tube containing DME, ZnI_2, H_2O, MeI, di-isobutylene (promoter), and *n*-octane (internal standard) in molar ratio 1.1:1:0.13:0.38:0.16:0.014 was prepared as described above and heated for 4 h at 160 °C. The tube was allowed to cool; a small sample was removed for GC analysis; a fresh charge of DME was condensed in, and the cycle was repeated. In another series, after four cycles all volatiles were removed to give an off-white solid, to which was added a fresh charge of DME and MeI, and the cycle was repeated.

Synthesis of Triptane from $^{12}CH_3OH + (^{12}CH_3)_2{}^{13}CHOH$. A standard reaction was carried out in the presence of added $Me_2{}^{13}CHOH$ (100 μL, 79.8 mg, 99% ^{13}C), and the organic layer was extracted into $CDCl_3$ for analysis by ^{13}C NMR. The triptane signals are identified according to the labels shown in eq 2. The approximate intensity ratios for C_a:C_b:C_c:$C_d \approx 1.5:1:2.5:1$, in contrast to the values observed for an ordinary unlabeled reaction (with the same spectrometer settings): 8.7:1:1.3:7. Quantitative interpretation is not possible since in addition to the common problems associated with reliable quantitation of ^{13}C signal intensities there is no way to assess the relative contributions of added label and natural-abundance ^{13}C. However, it is clear that *much* more label has been incorporated in the two internal positions, C_b and C_c, since their signals are enhanced relative to the methyl signals by 5−10-fold compared to the unlabeled reaction.

Gaseous Products from $^{13}CH_3OH + (CH_3)_2CHOH$. A reaction completely analogous to the preceding one but with the labels reversed was carried out. After cooling the gaseous products were condensed into a liquid-nitrogen-cooled tube and dissolved in $CDCl_3$ for analysis by NMR. The ^1H NMR shows strong signals for (unlabeled) propene. In the ^{13}C NMR, the region corresponding to saturated (sp^3) carbons is complex, but two signals stand out in the olefinic region. The stronger one, centered around 111 ppm, consists of a doublet ($^1J_{CC} \approx 71$ Hz) of triplets ($^2J_{CC} \approx 3$ Hz) along with a much weaker triplet in the middle ($^2J_{CC} \approx 3$ Hz); the relative total intensities are about 85:15. A considerably weaker signal around

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[22] A referee has suggested this trend might have a steric component as well. The results cited immediately above indicate that a steric effect can compete with the positive electronic effect of increasing substitution; perhaps some unfavorable factor specific to methylation of triptene, such as the 1,3-interaction between the incoming methylating species and one of the methyls of the adjacent *tert*-butyl group, could inhibit growth beyond the C_7 stage. We plan to examine this and related questions by means of molecular modeling in the near future.

[23] However, not unique: several other metal iodides can also effect conversion of methanol to triptane under similar conditions, most notably InI_3 (Kay, R. D.; Morris, G. E.; Sunley, J. G. PCT/GB2004/003578, 2005). There is also a much older report of the homologation of 2-methylbut-2-ene to higher olefins, including a substantial amount of triptene (but no alkanes), by treatment with MeCl (or MeI) and stoichiometric amounts of CaO above 200 °C (GB Patent 577,112, 1946). We will report on mechanistic studies for InI_3, and its similarities to/differences from ZnI_2, in a later publication.

143 ppm is a doublet ($^1J_{CC} \approx 72$ Hz) of triplets ($^1J_{CC} \approx 41$ Hz). The shifts and C−C coupling constants agree well with those reported for isobutene,[24] and the specific patterns are only consistent with an 85:15 mixture of $^{13}CH_2{=}^{13}C(^{13}CH_3)_2$ and $^{13}CH_2{=}^{12}C(^{13}CH_3)_2$.

Mass Balance Determination. ZnI_2 (2.27 g, 7.11 mmol), isopropanol (50.0 μL, 0.654 mmol), and methanol (0.772 g, 24.1 mmol) were reacted for 3 h as described above. The cooled tube was weighed, then the stopcock removed to allow volatile products to escape, and the tube re-weighed. A 90.4 mg amount was lost as volatiles. Separate analysis of the volatile fraction identified propene as the major component in addition to DME.

The reaction flask was fitted with a septum, and the organic phase was carefully transferred via cannula into a round-bottom flask previously charged with $MgSO_4$. The organic fraction was dried, and a weighed portion (173.4 mg) was analyzed by GC. The analysis showed triptane and triptene as the major components, combining for 31.2 mg (23% w/w) of the organic layer. The next most abundant compound was hexamethylbenzene at 2.0% w/w. From previous experiments, analyzed as described above, the total yield of triptyls from such a reaction should be 67.6 mg; hence, the actual weight of the organic layer was estimated to be 297 mg.

The bottom layer of the reaction mixture, after removal of the organic layer, weighed 2.68 g, corresponding to 0.41 g of liquids after subtracting the original weight of ZnI_2. ^1H NMR analysis of this fraction, using added nitromethane as an internal standard, identified methanol (14% w/w), DME (9% w/w), and water as the major components. Neglecting the amount of DME lost with the volatiles, the conversion of the reaction is calculated to be 86%.

Methylenation of 2,3-Dimethylbut-2-ene. Reaction mixtures of methanol (2.4 g), 2,3-dimethylbut-2-ene (1.07 g), and ZnI_2 (7.2 g) were heated in glass pressure tubes at 160 °C for varying periods of time, and the organic product layer was analyzed by GC in the usual manner. After 3 h approximately 60% of the starting olefin had been converted, increasing to 90% by 17 h. The main products identified were triptyls, comprising 20−30%, and isomerized olefin 2,3-dimethylbut-1-ene, around 5−10%. Substantial amounts of heavier products were apparent in the GC trace. The triptane:triptene ratio was initially very low, around 1:10, but increased over time.

A similar experiment was performed on a smaller scale, using $^{13}CH_3OH$, and analyzed by both NMR and GC-MS, demonstrating that label appeared in all peripheral positions (methyls, methylene) of triptane and triptene but not in any internal positions and that each product molecule contained exactly one ^{13}C atom, within the accuracy of the GC-MS analysis.

Synthesis and Isomerization of Regiospecifically ^{13}C-Labeled Triptene. A 500 mL three-neck round-bottom flask equipped with a magnetic stirrer, a reflux condenser, and an addition funnel was charged with finely divided magnesium turnings (2.4 g, 99 mmol) and flushed with argon. Dry diethyl ether (10 mL) was placed over the magnesium, and the addition funnel was charged with ^{13}C-labeled methyl iodide (10 g, 70 mmol) and ether (20 mL). The solution was added dropwise to the magnesium suspension and further diluted with ether fractions (2 × 10 mL) 10 min apart. After the addition was complete, the reaction was refluxed for 15 min. The mixture was then cooled in an ice bath, and a solution of pinacolone (7.5 mL, 60 mmol) in ether (20 mL) was added dropwise via the addition funnel. After the addition was complete, the reaction was stirred for additional 30 min at room temperature. The mixture was placed in an ice batch, and a saturated aqueous solution of NH_4Cl (100 mL) was slowly added. The organic layer was separated, and the aqueous layer was further extracted with ether (2 × 20 mL). The combined organic fractions were washed with brine and dried over $MgSO_4$. The ether solution was treated with CaH_2 (2.0 g, 48 mmol) and stirred at room temperature until hydrogen evolution stopped. The mixture was filtered and the solvent removed under reduced pressure to give $(CH_3)_3CC(CH_3)(^{13}CH_3)OH$ (^{13}C-labeled triptanol, 4.3 g, 63%) as a colorless liquid.

A 250 mL round-bottom flask equipped with a magnetic stirrer and an addition funnel was charged with the ^{13}C-labeled triptanol (4.3 g, 37 mmol), 1-methylimidazole (10 mL, 125 mmol), and methylene chloride (40 mL). The mixture was cooled in an ice bath, and a solution of methylsulfonyl chloride (4.4 mL, 56 mmol) in methylene chloride (10 mL) was added dropwise. After the addition was complete, the addition funnel was replaced with a reflux condenser, and the reaction was stirred at reflux overnight. An aqueous HCl solution (1.0 N, 100 mL) was added to the reaction mixture, and the organic layer was separated, washed with a saturated solution of $NaHCO_3$ followed by brine, and dried over $MgSO_4$. Distillation provided ^{13}C-labeled triptene as a clear liquid, shown by NMR to be a 1:1 mixture of isotopomers $(CH_3)_3CC(CH_3)(^{13}CH_2)$ and $(CH_3)_3CC(^{13}CH_3)(CH_2)$. ^1H NMR: δ 4.74 (d, 1H,$^1J_{C-H} = 150$ Hz, $C(CH_3)(^{13}CHH')$), 4.74 (d, 1H,$^3J_{C-H} = 7.5$ Hz, $C(^{13}CH_3)(CHH')$), 4.66 (d, 1H,$^1J_{C-H} = 150$ Hz, $C(CH_3)(^{13}CHH')$), 4.66 (d, 1H,$^3J_{C-H} = 7.5$ Hz, $C(^{13}CH_3)(CHH')$), 1.77 (d, 3H,$^1J_{C-H} = 126$ Hz, $C(^{13}CH_3)(CH_2)$), 1.77 (d, 3H,$^3J_{C-H} = 6$ Hz, $C(CH_3)(^{13}CH_2)$), 1.08 (s, 18H, $(CH_3)_3C$)

A pressure tube was charged with ZnI_2 (294 mg, 0.92 mmol), methanol (130 mg, 4.1 mmol), and ^{13}C-labeled triptene (50 μL, 0.36 mmol). The tube was sealed with a stopcock and placed into an oil bath for 180 min at 160 °C. The vessel was then allowed to cool to room temperature, and the reaction mixture was further diluted with water (0.2 mL) and benzene-d_6 (0.8 mL). NMR analysis of the organic layer showed that the ^{13}C label was statistically distributed among the four methyl and one methylene positions.

Hydrogenation of Triptene by Cyclohexa-1,4-diene. A pressure tube was charged with ZnI_2 (2.40 g), MeOH (1.0 mL, 791 mg), 1,4-cyclohexadiene (42.4 mg, 0.529 mmol), and triptene (52.9 mg, 0.538 mmol). The mixture was stirred to dissolve all solids, and the tube was heated at 150 °C for 2.5 h. After cooling to room temperature, the organic layer was analyzed by GC in the usual manner, using cyclohexane as an internal standard. Triptene was almost completely consumed with formation of triptane and benzene in yields (based on 1,4-cyclohexadiene as a limiting reagent) of 92% and 72%, respectively. The GC chromatograph also indicated the presence of some higher boiling components, probably methylated benzenes. Under these conditions no reduction of triptene to triptane is observed in the absence of cyclohexadiene nor is there any formation of triptyls from methanol and ZnI_2 alone.

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Supporting Information Available: Full analysis and discussion of the experiment involving di-^{13}C-labeled ethanol. This material is available free of charge via the Internet at http://pubs.acs.org.

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[24] Kalinowski, H.-O.; Berger, S.; Braun, S. *Carbon-13 NMR Spectroscopy*; John Wiley & Sons: Chichester, 1988.