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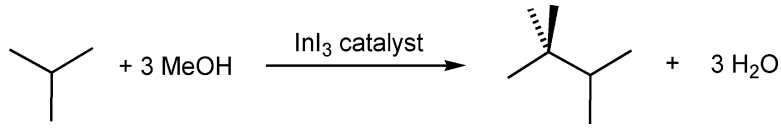

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Selective Methylative Homologation: An Alternate Route to Alkane Upgrading

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Abstract: InI_3 catalyzes the reaction of branched alkanes with methanol to produce heavier and more highly branched alkanes, which are more valuable fuels. The reaction of 2,3-dimethylbutane with methanol in the presence of InI_3 at 180−200 °C affords the maximally branched C_7 alkane, 2,2,3-trimethylbutane (triptane). With the addition of catalytic amounts of adamantane the selectivity of this transformation can be increased up to 60%. The lighter branched alkanes isobutane and isopentane also react with methanol to generate triptane, while 2-methylpentane is converted into 2,3-dimethylpentane and other more highly branched species. Observations implicate a chain mechanism in which InI_3 activates branched alkanes to produce tertiary carbocations which are in equilibrium with olefins. The latter react with a methylating species generated from methanol and InI_3 to give the next-higher carbocation, which accepts a hydride from the starting alkane to form the homologated alkane and regenerate the original carbocation. Adamantane functions as a hydride transfer agent and thus helps to minimize competing side reactions, such as isomerization and cracking, that are detrimental to selectivity.

Introduction

The catalytic conversion of abundant but relatively inert alkanes into higher value chemicals has been a longstanding challenge for chemists and the petrochemical industry. While there have been significant advances in our understanding of C−H activation reactions over the last three decades, they have not yet led to practical methods for alkane functionalization, because of limitations imposed by unfavorable thermodynamics, low selectivity, and/or economic factors.[1] In principle one could avoid these difficult functionalization problems by simply converting a given alkane into another alkane of higher value. Well-known examples, which are extensively utilized by the petrochemical industry, include isomerization of linear to branched alkanes[2] and the alkylation of isobutane with olefins.[3] On a research scale, alkanes may be coupled by mercury-photosensitized dehydrodimerization, although selectivity is limited by the radical mechanism involved.[4] More recently the so-called alkane metathesis reaction has been proposed as a potential method for upgrading light hydrocarbons such as *n*-hexane to diesel-range linear alkanes.[5,6]

The dehydrative condensation of methanol to hydrocarbons has attracted a good deal of interest over the years. Most often this involves reaction over shape-selective solid acids, as in the MTG (methanol-to-gasoline) and MTO (methanol-to-olefins) processes.[7] In contrast, Kim et al. reported that the reaction of MeOH with zinc iodide at 200 °C led to formation of an alkane-rich hydrocarbon mixture, with surprising selectivity to one particular alkane, 2,2,3-trimethylbutane (triptane), in overall yields of up to 20% (based on moles of carbon), corresponding to as much as half of the gasoline-range fraction (eq 1).[8,9] An efficient synthetic route to triptane (research octane number =

[‡] Caltech.
[#] BP.

(1) See, for example,(a) Crabtree, R. H. *J. Chem. Soc., Dalton Trans.* **2001**, *17*, 2437–2450. (b) Labinger, J. A.; Bercaw, J. E. *Nature* **2002**, *417*, 507–514. (c) Goldman, A., Goldberg, K. I., Eds. *Activation and Functionalization of C-H Bonds*, American Chemical Society: Washington, DC, 2004. (d) Fekl, U.; Goldberg, K. I. *Adv. Inorg. Chem.* **2003**, *54*, 259–320.
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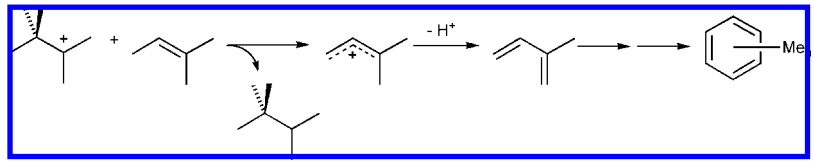
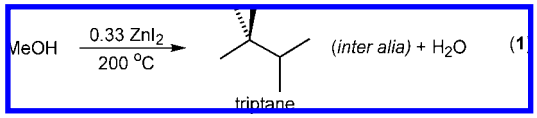
(8) Kim, L.; Wald, M. M.; Brandenburger, S. G. *J. Org. Chem.* **1978**, *43*, 3432–3433.
(9) The reaction can also be carried out by reacting methyl iodide with $Zn(OMe)_2$ (Diaconescu, P. L., unpublished results) or ZnO (Walspurger, S.; Prakash, G. K. S.; Olah, G. A. *Appl. Catal., A* **2008**, *336*, 48–53) with similar outcomes, indicating that the various species readily interconvert under reaction conditions.

10.1021/ja803029s CCC: $40.75

Scheme 1



112) would provide access to a valuable fuel component and gasoline additive.



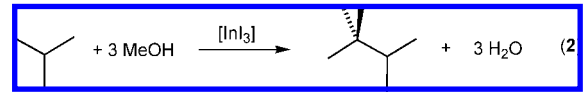
Our mechanistic studies on this complex reaction[10] implicate a carbocation-based route, wherein hydrocarbon growth proceeds by successive olefin methylation and deprotonation, always favoring the most highly substituted carbocations and olefins respectively. Direct C−C bond formation from methanol (and/or dimethyl ether; partial dehydration of MeOH to DME is rapid under reaction conditions) apparently takes place only when solids are present; for a completely homogeneous reaction mixture an initiator is required, typically an olefin or a higher alcohol. Alkanes are generated via hydride transfer from an unsaturated hydrocarbon to a carbocation, with the resulting multiply unsaturated intermediates eventually resulting in the formation of arenes, as illustrated in Scheme 1.

According to this scheme, triptane yields are limited by two constraints. First, the aliphatic pool contains both lighter and heavier highly branched alkanes (and some olefins), along with smaller amounts of less branched isomers; the selectivity for triptane within that pool appears to be governed by the relative rates of methylation and hydride transfer at the various stages of product growth. Second, some fraction of the methanol feed must be diverted to the aromatic pool to satisfy the stoichiometry in hydrogen. The latter factor accounts for the observation that the triptane yield is enhanced by additives containing P−H bonds (phosphorus or hypophosphorous acid), which serve as alternate hydride sources.[11]

More recently we have found that InI_3 also functions as a catalyst for this transformation.[12,13] While many of the features, including reaction conditions and typical triptane yields, are quite similar for ZnI_2 and InI_3, suggesting that the mechanism for the conversion of MeOH to triptane is basically the same for the two systems, there are some significant differences, especially in the detailed product distributions. Much of the difference in behavior can be accounted for by the fact that InI_3—unlike ZnI_2—is able to activate (some) alkanes easily at 200 °C. In particular, alkanes that contain at least one tertiary center are readily isomerized by the InI_3 system, and are also able to function as initiators for triptane synthesis.[13] In contrast, olefins (or olefin precursors such as higher alcohols) are required to initiate ZnI_2-catalyzed reactions at ≤200 °C.[10]

Both the isomerization of and initiation by alkanes implies that they react with InI_3 and thus enter the carbocation/olefin pool, even if only in very low concentrations. This conclusion was supported by an isotopic labeling study. Analysis of the products from a reaction of ^{13}C-MeOH, unlabeled 2,3-dimethylbutane (as an initiator) and InI_3 by GC/MS showed that the two major triptane isotopologues were singly labeled and fully labeled (with much more of the latter). Fully labeled triptane presumably arose via *de novo* synthesis from MeOH, but a singly labeled triptane molecule must have come from the addition of a single methanol-derived CH_2 group to the C_6 olefin generated by the activation of unlabeled 2,3-dimethylbutane.[13]

It should be noted that this *methylative homologation* does not suffer from the hydrogen deficiency of the original methanol-to-triptane conversion; there is no requirement for the formation of arenes or any unsaturated hydrocarbons, removing one limitation on selectivity. If it were possible to convert large quantities of light alkanes in this manner, using MeOH as a methylating agent, it would constitute a route for the selective conversion of relatively low value and abundant alkanes to more valuable fuels by reactions such as eq 2. Isobutane and 2-methylbutane (isopentane) are produced on a large scale in refinery operations;[14] they are also significant byproducts from methanol transformations such as MTG.[7a] While the latter compound is used directly as a gasoline component, its homologation to a higher octane, less volatile C_6 or C_7 branched alkane would represent a significant upgrading of value. We report here on work aimed at exploring this unprecedented and potentially useful approach.



Results and Discussion

Homologation of 2,3-Dimethylbutane. The first series of experiments were performed using reaction mixtures of InI_3 (4.13 mmol), MeOH (12.4 mmol) and varying amounts of 2,3-dimethylbutane (DMB), which were heated at 200 °C for 2 h. The control experiment (with no DMB present) contained isopropanol as an initiator. The results of analysis by gas chromatography (GC) are shown in Table 1. In all experiments conversion of DMB was between 20 and 35%, while all the MeOH/DME was consumed. Both the yield of triptane (in milligrams) and the selectivity to triptane (stated as moles of carbon in triptane per mole of total converted carbon) increase with the amount of DMB added; the latter parameter is plotted in Figure 1.[15] It is noteworthy that the absolute triptane yield is increased more than 3-fold by the addition of one molar equivalent of DMB.

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(15) Detailed analytical results are shown in the Supporting Information.

Table 1. Yields of Triptane and Polymethylbenzenes (Pentamethylbenzene (PMB) and Hexamethylbenzene (HMB)) As a Function of 2,3-Dimethylbutane (DMB) Added[a]

InI_3 (mmol)	MeOH (mmol)	DMB (mmol)	DMB recovered (%)	triptane yield (mg)	triptane selectivity (%)[c]	PMB (mg)	HMB (mg)	triptane: (PMB + HMB)
4.13	12.4	0[b]	–	23	12	12	7	1.2
4.13	12.4	0.76	80	32	14	1	17	1.8
4.13	12.4	1.52	65	33	15	4	9	2.5
4.13	12.4	3.04	71	40	16	4	15	2.1
4.13	12.4	6.2	68	60	17	6	14	3.0
4.13	12.4	12.4	79	75	19	14	9	3.3

[a] All reactions were heated for 2 h at 200 °C. [b] Isopropanol (50 μL, 39 mg, 0.65 mmol) was added as an initiator. [c] Based on total converted carbon.

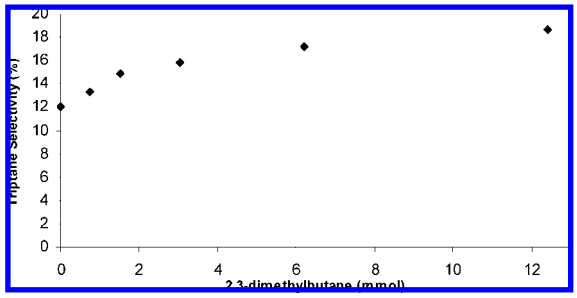


Figure 1. Triptane selectivity against number of mmol 2,3-dimethylbutane.

Because it is conceivable that addition of DMB might increase the efficiency of the direct conversion of MeOH to triptane, this trend does not by itself conclusively establish homologation of DMB to triptane. Two additional lines of evidence do provide support for homologation. First, a labeling experiment analogous to that reported previously[13] but with substantially more added DMB was performed. A reaction mixture containing DMB (1.52 mmol), InI_3 (4.13 mmol), and ^{13}C-labeled MeOH (12.4 mmol) was heated at 200 °C for 2 h, and products were analyzed by GC/MS. Figures 2 and 3 show the MS patterns for the GC fractions of DMB and triptane, respectively. For the former, the major set of peaks from $m/z = 71-76$ correspond to the $(P\text{-}Me)^+$ fragment ions. Of these, by far the largest is at 71 ($^{12}C_5H_{11}$) and the next-largest at 72 ($^{12}C_4{}^{13}CH_{11}$), with weaker peaks resulting from mixed isotopologues and the fully labeled isotopologue 76 ($^{13}C_5H_{11}$). There is also a P^+ peak at 86 m/z for unlabeled DMB; the concentrations of other isotopologues are too low for their parent ions to be observed. The observed isotopologue distribution clearly demonstrates that activation of DMB has taken place, leading to exchange of carbons with the methanol-derived methylating species, as previously documented.[10,13]

For the triptane fraction, the main signals again correspond to $(P\text{-}Me)^+$ ions; there is barely any detectable signal in the P^+ region. The largest signal at 91 m/z is due to fully labeled $^{13}C_6H_{13}$, while the next largest, at 86 m/z, is due to singly labeled $^{12}C_5{}^{13}C_1H_{13}$; weaker peaks are observed at intermediate values. Table 2 shows the relative percentage of the different isotopologues, as well as the values that would be expected for complete statistical scrambling of carbon atoms in the reaction mixture (in which 59.5% of the carbon atoms are unlabeled and 40.5% are labeled). It is clear that the fraction of singly labeled triptane, which would result from homologation of DMB, is far in excess of the statistical value and conversion of DMB to triptane is occurring. (The intensity of the $^{12}C_1{}^{13}C_5$ signal, which could arise from triptane isotopologues with one and/or two unlabeled carbons, further demonstrates that some scrambling has occurred.)

The quantity of aromatic products generated (Table 1) provides further evidence for conversion of DMB into triptane. Stoichiometrically, when DMB and MeOH react to form triptane, the only byproduct is water. In contrast, direct conversion of MeOH into triptane requires the equivalent of one molecule of H_2 (presumably delivered stepwise, as H^+ and H^-), which is provided by formation of hydrogen-deficient arenes.[10] Thus, if some of the triptane being formed comes from the homologation of MeOH with DMB, a reduction in the amount of aromatics relative to triptane would be expected, compared with a reaction in which there is only direct conversion of MeOH into triptane. In nearly all reactions the major aromatic compounds observed are pentamethylbenzene (PMB) and hexamethylbenzene (HMB), so these two species are used as the indicator for the total amount of aromatics present.

The yields of triptane, PMB, and HMB and the ratio of triptane to PMB + HMB for a series of experiments with varying amounts of DMB are shown above in Table 1. Clearly the ratio of triptane to aromatics increases as the amount of DMB present increases, supporting the conclusion that triptane arises from two competitive processes: direct conversion of MeOH to triptane (which results in aromatic byproducts) and the homologation of DMB (which does not). Some reduction of arene yield is observed even at the lowest DMB levels, indicating some homologation of the alkane to triptane.

Increasing the InI_3 loading appears to reduce the contribution of direct conversion of MeOH to triptane still further. A reaction with equimolar MeOH and DMB but with twice as much In (InI_3:MeOH:DMB = 1:1.5:1.5) gives the same overall triptane yield, but the ratio of triptane to aromatic products (which in this experiment include some tetramethylbenzenes) is 12.8, compared to the value of 3.26 for the experiment shown as the last entry in Table 1 (InI_3:MeOH:DMB = 1:3:3). The analogous experiment using ^{13}C-labeled MeOH in the same proportions showed much more singly labeled than fully labeled product:[15] the triptane $(P\text{-}Me)^+$ signals at 91 and 86 m/z respectively accounted for 3% and 50% of the total, indicating that under these conditions homologation of DMB is the predominant route to triptane. The cause of this effect is unclear; it may be significant that at the higher indium loading some InI_3 remains undissolved at the reaction temperature, whereas solutions are completely homogeneous at the lower indium level.

Variation of Reaction Conditions. The effects of changing reaction time and temperature have been investigated using the standard mixture of InI_3 (4.13 mmol), DMB (6.2 mmol), and MeOH (6.2 mmol). The triptane selectivities for reaction times ranging from 15 min to 2 h at 200 °C are shown graphically in Figure 4. For this (and all future) tables selectivity has been redefined as moles of triptane formed per mole of DMB converted—i.e., the putative selectivity of the homologation of DMB assuming it to be the only triptane-producing process—which is a more useful figure of merit. The high triptane to aromatic ratios observed in these reactions indicates that this assumption is appropriate. Reaction times less than 15 min gave yields and selectivities similar to those at 15 min, but the DMB conversion was lower, as shown in Table 3. Even after only 5 min no unreacted MeOH/DME was detected (although it should be noted that is difficult to detect very small quantities of the highly volatile DME).

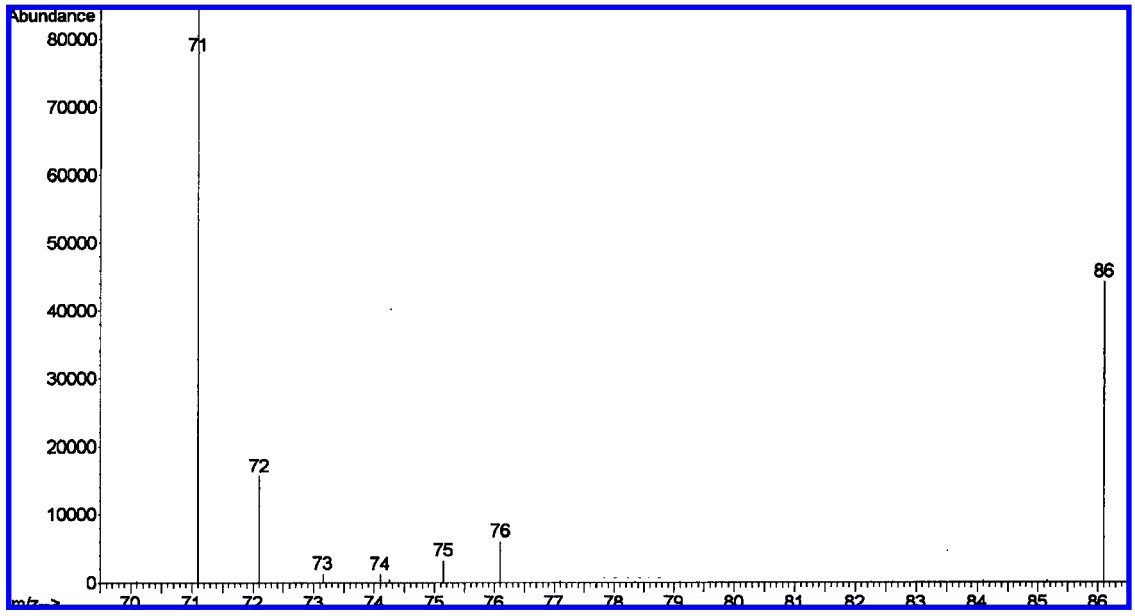


Figure 2. MS of DMB fraction from reaction between InI_3, ^{13}C-labeled MeOH and DMB.

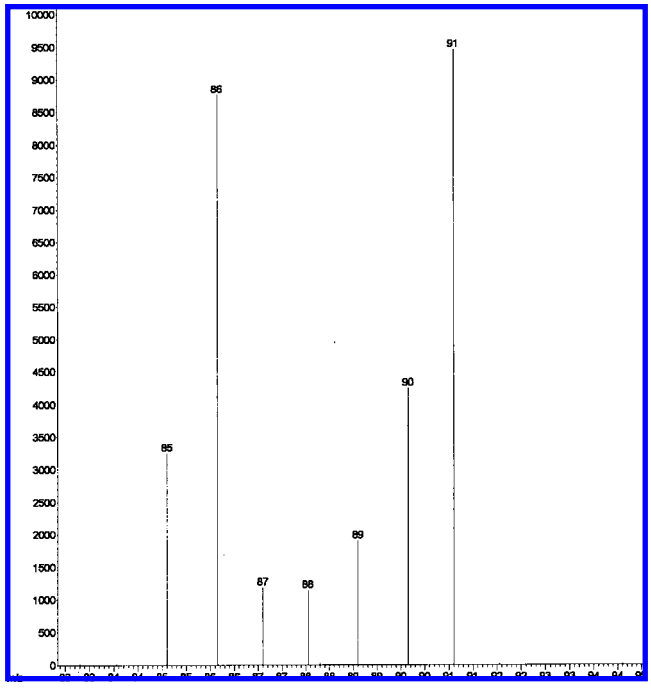


Figure 3. MS of triptane fraction from reaction between InI_3, ^{13}C-labeled MeOH and DMB.

Table 2. Relative Statistical and Observed Percentages of Isotopologues of $(P\text{-}Me)^+$ for Triptane

molecular formula	statistical distribution (%)	observed distribution (%)
$^{12}C_6H_{13}$	4.43	9.5
$^{12}C_5{}^{13}C_1H_{13}$	18.12	31.6
$^{12}C_4{}^{13}C_2H_{13}$	30.84	2.6
$^{12}C_3{}^{13}C_3H_{13}$	27.98	3.5
$^{12}C_2{}^{13}C_4H_{13}$	14.28	5.2
$^{12}C_1{}^{13}C_5H_{13}$	3.89	15.5
$^{13}C_6H_{13}$	0.44	32.5

The decrease in triptane selectivity beyond 15 min corresponds to a decrease in the recovered DMB at longer reaction times, along with a much smaller decrease in the total quantity

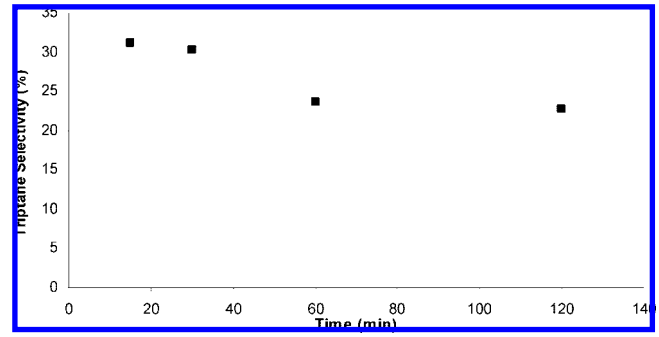


Figure 4. Triptane selectivity against time.

Table 3. Effect of Time on Triptane Yield and Selectivity[a]

time (min)	DMB recovered (%)	triptane yield (mmol)	triptane selectivity (%)[b]	triptane: (PMB + HMB)
5	73	0.51	30	>100
10	70	0.56	31	40
15	67	0.62	31	28
30	66	0.64	30	28
60	58	0.62	24	29[c]
120	56	0.59	23	19[c]

[a] Reactions were performed at 200 °C and used InI_3 (4.13 mmol), MeOH (6.2 mmol), and DMB (6.2 mmol). [b] Percentage of converted DMB which becomes triptane. [c] Some tetramethylbenzene (TMB) was observed in these reactions and has been included so the quoted figure is the ratio of triptane to (TMB + PMB + HMB).

of triptane produced. This is a consequence of side reactions of DMB. We have previously demonstrated that both isomerization into other C_6 alkanes and cracking into lighter alkanes such as isobutane and isopentane are catalyzed by InI_3, and further that the presence of MeOH slows down InI_3-catalyzed alkane isomerization and cracking.[13] Because MeOH undergoes processes other than providing methylating equivalents for DMB conversion, such as direct conversion of MeOH to triptane and the methylation of aromatic species, MeOH/DME is completely consumed long before DMB (as noted above), so that no further homologation can occur, but the isomerization and cracking processes continue. (Triptane isomerization and cracking also take place, but at a slower rate, as previously demonstrated.[13])

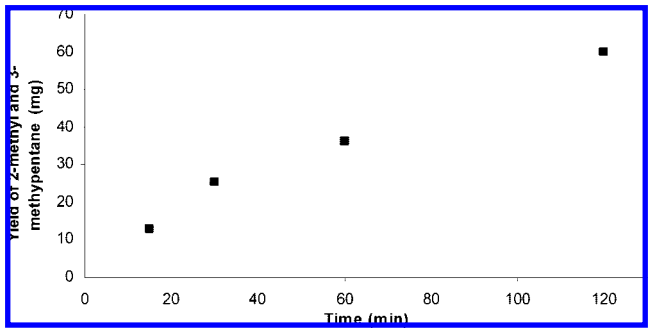


Figure 5. Combined yield of 2-methyl and 3-methylpentane against time.

Table 4. Effect of Temperature on Triptane Yield and Selectivity[a]

temp (°C)	DMB recovered (%)	triptane yield (mmol)	triptane selectivity (%)[b]	triptane: (PMB + HMB)
200	66	0.64	30	13[c]
190	60	0.79	32	26
180	63	0.90	38	48
170	61	0.80	33	>100
160	78	0.18	13	nr[d]
150	>90	0.01	1	nr[d]
140	>90	0	0	nr[d]

[a] Reactions were performed for 30 min and used InI_3 (4.13 mmol), MeOH (6.2 mmol), and DMB (6.2 mmol). [b] Percentage of converted DMB which becomes triptane. [c] Some tetramethylbenzene (TMB) was observed in this reaction and has been included so the quoted figure is the ratio of triptane to (TMB + PMB + HMB). [d] not recorded.

The combined yield of 2-methylpentane and 3-methylpentane, two of the major isomerization byproducts, as a function of time is shown graphically in Figure 5.

The effect of temperature on the homologation of MeOH with DMB is shown in Table 4. As the temperature is decreased from 200 °C, the extent of isomerization and cracking of DMB and triptane decreases, which results in an increase in the triptane yield and selectivity. At these temperatures the rate of activation of the alkane and methylation of the olefin is sufficiently fast to allow significant amounts of conversion (approximately 40% conversion of DMB), but below 170 °C, conversion slows dramatically and eventually stops altogether. Furthermore, at and below 180 °C almost all of the triptane is formed by homologation of DMB with little or no direct conversion of MeOH to triptane, as shown by the high triptane:arene ratios; a labeling experiment at 180 °C using ^{13}C-MeOH and unlabeled DMB confirms this, as virtually no signal arising from fully labeled triptane is detectable.[15] The maximum selectivity for DMB homologation to triptane, 38%, was achieved at 180 °C.

In an effort to further suppress the direct conversion of MeOH to triptane, several experiments were performed using higher ratios of DMB to MeOH. The results (Table 5) show that this does not significantly affect the triptane:aromatic ratio, but does decrease the triptane selectivity, so that the optimum ratio of MeOH:DMB appears to be 1:1.

The catalyst loading cannot be lowered substantially; for starting ratios of MeOH:InI_3 above 4:1 the yield of triptane drops off sharply, regardless of the amount of DMB. This inhibition is most probably a water effect (since, as noted above, partial dehydration of MeOH to DME is rapid at any concentration), as observed in the direct conversion of MeOH to triptane, where high effective turnover numbers were achieved in cyclic mode by removing water (use of DME instead of MeOH as feedstock for methylative homologation gives essentially identical results[15]).[10,13] The same approach works for homologation: at the end of a reaction all volatiles (including water) were removed and the remaining InI_3 dried under vacuum at 60 °C; a fresh charge of DMB and MeOH was added to the reaction mixture, and the reaction performed again, with no decrease in the triptane yield or selectivity.[15] The reaction can be thus continued for a number of cycles if the volatiles are periodically removed in this manner.

Table 5. Ratio of Triptane to (PMB + HMB) as Concentration of DMB Increases[a]

InI_3 (mmol)	MeOH (mmol)	DMB (mmol)	DMB recovered (%)	triptane selectivity (%)[b]	triptane: (PMB + HMB)
4.13	6.2	6.2	63	38	48
4.13	6.2	9.3	61	29	35
4.13	6.2	12.4	75	27	25
2.07	3.1	7.75	70	25	42
2.07	3.1	9.3	74	25	—[c]

[a] Reactions performed for 30 min at 180 °C. [b] Percentage of converted DMB which becomes triptane. [c] No PMB or HMB was detected.

Table 6. Comparison of Triptane Yield and Selectivity for Homologation[a] in the Presence and Absence of Adamantane

adamantane[b] (mg)	DMB recovered (%)	triptane yield (mmol)	triptane selectivity (%)[c]
0	63	0.90	39
10 (1.2)	30	2.32	55
50 (5.9)	51	2.10	65
100 (12)	44	2.05	59

[a] Reactions were performed at 180 °C for 30 min and used 4.13 mmol of InI_3, 6.2 mmol of DMB, and 6.2 mmol of MeOH. [b] Number in parentheses is mol % of adamantane relative to DMB. [c] Percentage of converted DMB which becomes triptane.

Table 7. Comparison of Ratios of Side Products to Starting Material and Triptane for Homologation in the Presence and Absence of Adamantane[a]

ratio of hydrocarbons	no adamantane	with adamantane[b]
DMB: other C_6 alkanes	40:1	56:1
Triptane: other C_7 alkanes	10:1	17:1
(DMB + triptane): (isobutane + isopentane)	7:1	35:1

[a] Same reaction conditions as Table 5. [b] 50 mg of adamantane added.

Effect of Added Adamantane on Homologation. Adamantane has been shown to suppress cracking and thus enhance alkane isomerization reactions that proceed through a mechanism involving carbocations, presumably by acting as a hydride transfer catalyst.[16] Because cracking represents a major side reaction in the alkane homologation reactions described above, we examined the effect of adding a small amount of adamantane to a reaction between DMB and MeOH catalyzed by InI_3. Table 6 compares the triptane yield and selectivity in the presence and absence of adamantane; there is a dramatic beneficial effect on both, along with a significant increase in the amount of DMB converted. The increase in selectivity occurs because adamantane suppresses the isomerization of both DMB and triptane and also greatly reduces cracking side reactions. Table 7 shows that adamantane suppresses isomerization (of both C_6 and C_7 alkanes) as well as cracking (which leads to isobutane and isopentane, among other products) competing with DMB homologation. The effect involves a catalytic action of adamantane, as 90−100% of added adamantane is recovered (by

(16) Iglesia, E.; Soled, S. L.; Kramer, G. M. *J. Catal.* **1993**, *144*, 238–253.

Table 8. Summary of Homologation Reactions between MeOH and Isopentane Catalyzed by InI_3[a]

InI_3 (mmol)	MeOH (mmol)	isopentane (mmol)	time (min)	temperature (°C)	isopentane recovered (%)	triptane yield (mmol)	triptane selectivity (%)[b]	triptane + DMB selectivity (%)[c]
4.13	6.2	6.2	60	180	52	0.60	23	41
4.13	12.4[d]	6.2	300	200	56	0.70	26	45
4.13	18.6	6.2	750	200	76	0.36	25	40

[a] All reactions contained 0.367 mmol of adamantane. [b] Percentage of converted isopentane which becomes triptane. [c] Percentage of converted isopentane which becomes either DMB or triptane. [d] A control reaction using InI_3 (4.13 mmol), MeOH (12.4 mmol), adamantane (0.367 mmol), and isopropanol as an initiator, but no isopentane, produced only around 5 mg of triptane.

Table 9. Summary of Homologation Reactions between MeOH and Isobutane Catalyzed by InI_3[a]

InI_3 (mmol)	MeOH (mmol)	isobutane (mmol)	time (min)	isobutane recovered (%)	triptane yield (mmol)	triptane selectivity (%)[b]	triptane + DMB selectivity (%)[c]	triptane + DMB + isopentane selectivity (%)[d]
3.49	5.2	5.2	60	48	0.09	4	5	22
3.49	10.5	5.2	300	53	0.15	6	8	36
3.49	15.8	5.2	720	56	0.17	7[e]	10	42

[a] All reactions were performed at 200 °C and contained 0.367 mmol of adamantane. [b] Percentage of converted isobutane which becomes triptane. [c] Percentage of converted isobutane which becomes either DMB or triptane. [d] Percentage of converted isobutane which becomes either isopentane, DMB, or triptane. [e] This reaction also produced 10 mg of PMB and 7 mg of HMB, indicating that some direct conversion of MeOH to triptane was occurring.

GC) in all cases. Varying the loading of adamantane between 1−12 mol % (relative to DMB) had little effect on triptane yield or selectivity.

The increased DMB conversion does not appear to be a consequence of adamantane increasing the rate of homologation; rather, it suppresses side reactions that use up the methylating agent. As noted earlier, although the synthesis of triptane requires only one equivalent of MeOH per DMB, in nearly all experiments (with or without adamantane) using either a 1:1 or 1:2 ratio of DMB to MeOH, the MeOH is completely consumed, while only a fraction of the DMB has been converted.[15] At very short times, reactions can be stopped and analyzed before all the MeOH was consumed; the results[15] demonstrate that MeOH consumption is *slowed* by the addition of adamantane. This suggests that the increased conversion in the presence of adamantane is achieved by reducing the quantity of MeOH "wasted" by side reactions, such as the homologation of alkanes which are not on the pathway to triptane, and thus allowing the MeOH to be utilized more efficiently for homologating DMB. Furthermore, it has been demonstrated that addition of adamantane greatly suppresses the direct conversion of MeOH to triptane,[17] so under these conditions methylative homologation becomes even more favored.

Homologation of Lighter and Less Branched Alkanes with MeOH. The upgrading of isobutane and isopentane, which are available in much larger quantities, would be significantly more practical than the upgrading of DMB. The results of a series of reactions of isopentane with MeOH in the presence of InI_3 and adamantane are summarized in Table 8. Homologation of isopentane to DMB and triptane is observed, along with products resulting from isomerization and cracking. The ratios of DMB to other C_6 alkanes and triptane to other C_7 alkanes are around 2.5:1 and 5:1 respectively, while the ratio of DMB + triptane to isobutane is approximately 5.5:1, depending on the exact reaction conditions. If adamantane is not present, more isomerization and cracking occurs.[15]

The selectivity (either combined, or to triptane alone) is essentially independent of the starting MeOH:isopentane ratio, although as the amount of MeOH present increases, the rate of reaction decreases significantly, so that higher temperatures and longer reaction times are required. This is consistent with previous results which indicate that as the amount of MeOH present is increased, the activation of alkanes becomes slower, as well as the observation that isopentane is activated more slowly than DMB.[13] No aromatic species are detected by GC in these experiments, which is indicative of almost complete suppression of the direct MeOH to triptane pathway; but MeOH is completely converted in all experiments, which is why the triptane yield decreases while the triptane selectivity remains almost constant (using the definitions given earlier) as the amount of MeOH is increased. Clearly, as in DMB homologation, there are side reactions that use up MeOH without involving isopentane.

In contrast to DMB homologation, there is some consumption of adamantane in these reactions: only about 50% of the starting adamantane is recovered (by GC) at the end, probably because of the somewhat more stringent conditions (higher temperature and/or long reaction time) required. Also, the mass balance achieved in these reactions is not as good as that for DMB homologation: only around 60% of the total carbon present at the start of the reaction is accounted for at the end. This is due in part to the volatility of isopentane.

Similarly, isobutane is homologated to isopentane, DMB, and triptane, with the first being the major product, as shown in Table 9. Here the selectivity for the conversion of isobutane into higher branched alkanes increases with higher MeOH to isobutane ratios; as above, that also requires longer reaction times. The 2:1 ratio of MeOH to isobutane is probably optimal; although the selectivity appears to be higher at 3:1, significant quantities of aromatics are observed for that reaction, indicating some direct conversion of MeOH to triptane. Since the calculated selectivity (as defined previously) assumes no such conversion of MeOH, it somewhat overstates the actual homologation selectivity.

As with isopentane, there were substantial problems with mass balance in all isobutane reactions because of its high volatility. It should be noted that such losses will result in *underestimating* the selectivity for homologation, as the apparent conversion of starting branched alkane will be artificially high. Hence, the selectivities reported in Tables 8 and 9 are lower limits.

The above examples all involve homologation of alkanes that can form olefins that are on the pathway to triptane. Our earlier observation that InI_3 can catalyze isomerization of other alkanes, so long as they contain at least one tertiary center,[13] suggests

(17) See footnote d to Table 8. Additional experiments demonstrating this conclusion will be published in a later paper.

Table 10. Products from the Homologation of 2-Methylpentane with MeOH

product	yield (mg)
isobutane	23.5
isopentane	10.7
DMB	1.76
2-methylpentane	267
3-methylpentane	73.0
2,4-dimethypentane	12.1
triptane	5.03
2-methylhexane	5.25
2,3-dimethylpentane	27.4
3-methylhexane	8.48
C_8 alkanes	17.3

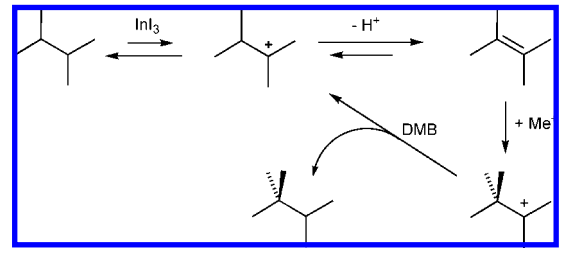
that alkanes such as 2-methylpentane could be homologated as well. A reaction with MeOH (6.2 mmol), 2-methylpentane (6.2 mmol), InI_3 (4.13 mmol), and adamantane (0.367 mmol), heated at 180 °C for 30 min, exhibited the GC analysis shown in Table 10. A quantity of 2,3-dimethylpentane (27.4 mg), the expected primary homologation product, was formed, and 267 mg (3.1 mmol, 50%) of 2-methylpentane was recovered, corresponding to a selectivity for homologation of about 9%. The low selectivity corresponds to a considerably higher level of isomerization and cracking than that found in reactions of DMB; we have observed that both 2-methylpentane and 2,3-dimethylpentane (which can undergo isomerization without a change in the length of the main carbon backbone) are more reactive for these transformations than DMB or triptane.[13]

Despite these side reactions, 2,3-dimethylpentane comprises approximately 50% of the C_7 fraction and highly branched C_7 alkanes (2,3-dimethylpentane, 2,4-dimethylpentane and triptane) comprise approximately 75% of the C_7 fraction. Furthermore, we observe C_8 products in the homologation of 2-methylpentane (in contrast to the homologation of DMB), indicating that further methylation of C_7 species has occurred. Our original explanation for high triptane selectivity was based in part on the expectation that methylation of a more substituted (and hence more electron-rich) olefin will be faster.[18] Hence, since 2,3-dimethyl-2-pentene (the olefin in equilibrium with 2,3-dimethylpentane) is trisubstituted, whereas triptene (the olefin in equilibrium with triptane) is only disubstituted, further methylation of 2,3-dimethylpentane (the major C_7 product from 2-methylpentane) should be more extensive than methylation of triptane (the major C_7 product from DMB), as observed.

Attempts to homologate hexane resulted in only small quantities of C_7 products; even that required extremely long reaction times.[15] We believe this is because there are only *primary* and *secondary* C−H bonds in hexane, which are more difficult to activate than *tertiary* C−H bonds; also even if hexane is activated, it will only form a disubstituted olefin, so the rate of methylation is expected to be slow.

Mechanism. The mechanism proposed for the homologation of DMB with MeOH begins with the activation of DMB by InI_3 to give the 2,3-dimethylbutyl carbocation, the same as the first step in alkane isomerization catalyzed by InI_3.[13] The 2,3-dimethylbutyl carbocation will be in equilibrium with 2,3-dimethyl-2-butene, which is methylated to give the triptyl carbocation. The latter presumably obtains a hydride from another alkane to give triptane; most often that will come from DMB, which is in greatest abundance, resulting in the chain

Scheme 2



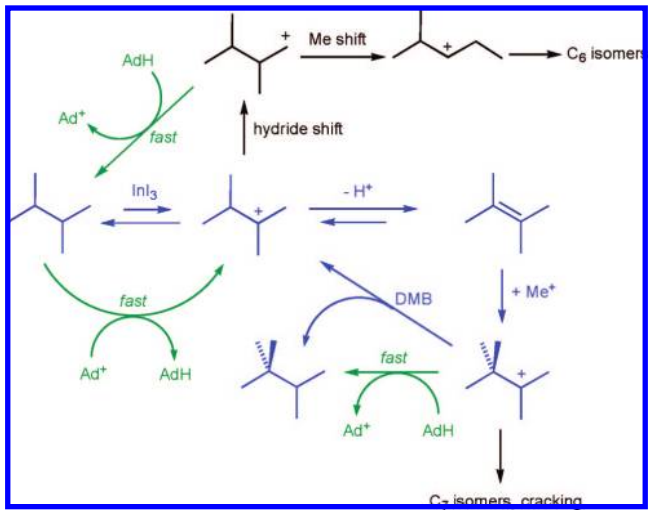
process shown in Scheme 2. The carbocation intermediates will undergo competitive skeletal rearrangements (which lead to isomerization) and scissions (which lead to cracking); the resulting side products and the carbocations and olefins derived therefrom will participate in similar chemistry, using up the MeOH that does not participate in the direct homologation route.

The facile transfer of H^- between alkanes and carbocations is a key feature of this chain mechanism, which must be operating (or something very similar) to permit homologation to proceed efficiently even though the steady-state concentration of olefins, produced via alkane activation by InI_3 followed by deprotonation, must be very low indeed. It is notable that ZnI_2 does *not* catalyze alkane homologation at these temperatures; carbocations are formed as intermediates in the ZnI_2-catalyzed conversion of MeOH to triptane,[10] so a chain process would seem possible in principle, once reaction has been initiated. Nonetheless, reactions in which a small amount of an olefin (2,3-dimethyl-2-butene) as initiator was added to a solution containing DMB, MeOH, and ZnI_2 showed no conversion of DMB to triptane at all. Our explanation for this observation is related to the presence or absence of olefins. Transfer of H^- from an olefin to a carbocation is particularly favorable as it generates an allylic carbocation (ultimately leading to arenes).[10] In ZnI_2-catalyzed reactions, a macroscopic amount of olefin is required to generate the initial carbocation at 200 °C, and olefin concentrations remain significant throughout, so that transfer of H^- from alkane never competes effectively, and no chain process can take place. In contrast, with InI_3-catalyzed homologation olefin concentrations are always extremely low, allowing transfer from the large excess of DMB to dominate and the chain process to proceed efficiently.

We attribute the beneficial effect of adamantane to its ability to act as an efficient hydride transfer agent, analogous to the interpretation of previous observations.[16] Reactions shown in Scheme 3 effectively catalyze the transfer of hydride between the triptyl carbocation and DMB, thus improving the efficiency of the chain process that is central to homologation, while suppressing side reactions by partially quenching the carbocations that lead to them. The primary carbocation derived from DMB, which leads to isomerization via methyl shifts, is rapidly trapped by adamantane (AdH) to reform DMB and generate the adamantyl cation (Ad^+). Of course, AdH can also transfer hydride to the tertiary DMB-derived cation, which at first would seem to be chain-inhibitory, but that is reversible: the predominant fate of the resulting Ad^+ (which does not appear to undergo any side reactions of its own, under these conditions) will be to take H^- back from another molecule of DMB and start a new chain. Also, of course, the driving force for transfer of H from AdH to a (less stable) primary carbocation is greater than that for transfer to the tertiary carbocation; the latter process is

(18) Mayr, H.; Schneider, R.; Irrgang, B.; Schade, C. *J. Am. Chem. Soc.* **1990**, *112*, 4454–4459.

Scheme 3



approximately thermoneutral (in the gas phase).[19] One function of adamantane is thus basically a "repair" mechanism, capturing the isomeric carbocation before it can undergo skeletal rearrangement and returning it to the parent DMB pool. Furthermore, by decreasing the lifetime of the triptyl carbocation (and others) adamantane will lower the rate of cracking. On both counts, then, the addition of adamantane inhibits the rates of side reactions relative to methylative homologation.

The mechanism for the homologations of isopentane and isobutane would look much the same, starting from an earlier point in the growth sequence. In each case, methylation of the olefin derived from the starting alkane takes place so as to generate the most substituted carbocation; thus, DMB is a significant product, along with triptane, from the homologation of isopentane, and likewise isopentane is one of the products from isobutane.

Conclusions

The results presented above demonstrate that lighter branched alkanes can be converted to more valuable products through a novel process involving methylative homologation. Product distributions, as well as the observation that homologation yields are substantially improved by the addition of adamantane as hydride transfer agent, are consistent with a mechanism in which InI_3 activates branched alkanes to produce tertiary carbocations. The latter are in equilibrium with olefins which undergo chain growth by reacting with methylating species generated from methanol and InI_3, as previously shown for the direct conversion of methanol to triptane.[13] Although carbocationic mechanisms are not usually associated with highly selective transformations, selectivities as high as 65% based on converted alkane were achieved for the homologation of DMB to triptane. Selectivities in homologations of the abundant branched alkanes isopentane and isobutane are not quite so high, but even for the most difficult case, the combined selectivity to higher branched alkanes from homologation of isobutane exceeds 40%; a process involving separation and recycle of the intermediate products might be effectively applied. Methylative homologation also affords product mixtures with much lower aromatic content than most processes for direct conversion of methanol to hydrocarbons over zeolites or other catalysts, another highly desirable feature. This route thus offers considerable promise for upgrading relatively low-value, lighter branched alkanes to species that are both less volatile and higher octane, and hence significantly more valuable fuels.

(19) (a) Solomon, J. J.; Field, F. H. *J. Am. Chem. Soc.* **1975**, *97*, 2625–2628. (b) Meot-Ner, M; Solomon, J. J.; Field, F. H. *J. Am. Chem. Soc.* **1976**, *98*, 1025–1026. (c) Kruppa, J. H.; Beauchamp, J. E. *J. Am. Chem. Soc.* **1986**, *108*, 2162–2169.

Experimental Section

General. InI_3 (purchased from Alfa Aesar), ZnI_2 (purchased from Sigma-Aldrich), MeOH and other organic compounds were reagent-grade commercial samples used without further purification. GC analyses were performed on an HP model 6890N chromatograph equipped with a 10 m × 0.10 mm × 0.40 μm DB-1 column. GC/MS analyses were performed on an HP model 6890N chromatograph equipped with a 30 m × 25 mm × 0.40 μm HP5-1 column and equipped with an HP 5973 mass selective EI detector.

Standard Reaction Protocols. All reactions were performed in thick-walled pressure tubes equipped with Teflon stopcocks (Kontes valves), rated up to 10 bar. The procedure for alkane homologation reactions is based on the procedure reported earlier for MeOH to hydrocarbon conversions using ZnI_2 and InI_3.[10,13] In a typical experiment, the tube was equipped with a stir bar and charged with InI_3 (2.05 g, 4.1 mmol), MeOH (0.25 mL, 6.2 mmol), and DMB (0.807 mL, 6.2 mmol). (The InI_3 was weighed out in a glovebox due to its hygroscopic nature; however the reactions were carried out under an atmosphere of air.) If adamantane was utilized, it was added at this stage. The pressure tube was then placed in a preheated oil bath behind a blast shield and stirred at the appropriate temperature for the desired period of time. After heating, the tube was removed from the bath and allowed to cool to room temperature and then placed in an ice bath. The stopcock was removed, and chloroform (1.0 mL), containing a known amount of cyclohexane as an internal standard, was pipetted into the reaction mixture followed by water (0.5 mL). The stopcock was replaced, the mixture was shaken vigorously and the organic layer separated. A small aliquot was diluted with acetone or tetradecane for GC analysis.

In reactions involving isobutane, all reagents except isobutane were loaded into the tube. The tube was then degassed using three consecutive freeze−pump−thaw cycles and frozen in liquid nitrogen. The desired amount of isobutane was condensed into the tube using a calibrated gas bulb, and the tube was allowed to warm to room temperature and then heated as described above. For reactions involving isopentane all components were cooled at 0 °C to minimize evaporation, and the isopentane was then added.

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Supporting Information Available: A complete listing of experimental results (in Excel format), along with an explanatory guide to the Excel tables and details of a labeling experiment. This material is available free of charge via the Internet at http://pubs.acs.org.

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