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Isomerization of Substituted Biphenyls by Superacid. A Remarkable Confluence of Experiment and Theory

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Acid-catalyzed isomerization of dimethylbiphenyls is determined by the relative stability of intermediate carbocations, rather than the neutral products, and may be predicted by a simple semiempirical method (AM1). A general kinetic model for such isomerizations is suggested in which the rearrangement of an intermediate cation is the rate-limiting step. Control of regiochemistry of dialkylbiphenyls provides a useful entry into high-purity monomers for high-polymer synthesis.

Introduction and Background

Our interest in facile synthesis of disubstituted biphenyls was prompted by the use of the biphenyl moiety as a well-known building block for high-temperature, high-modulus polymers as well as liquid crystals.[1] While the 4,4′-bibenzoic acid monomer has been demonstrated to produce thermotropic liquid crystalline polyesters,[2−7] copolyesteramides,[8] and high-performance copolyester-ether elastomers,[9−10] its commercial use has been hindered by the absence of a rational, moderate cost synthetic route to polymer purity monomer. Other isomers, e.g., 3,4′-substituted biphenyls, for such applications have only been briefly described,[11] but by analogy to the meta-substituted arylenes[12] could be expected to produce materials of significant interest. Thus, the synthetic strategy of (1) oxidative dimerization of toluene to dimethylbiphenyl and (2) oxidation of dimethylbiphenyl (dmbp) to bibenzoic acid (BBA) or oxidation/esterification to dimethyl bibenzoate (DMBBA) was undertaken as a potentially viable method for producing the desired monomer(s) from low cost, readily available starting materials. Unfortunately, all possible isomers were found when toluene was coupled by conventional technology, and the predominant species [2,X'- ($X = 2$, 3, 4) and 3,3′-dmbp] were of little commercial utility.[13] Thus, we concentrated our efforts on changing the distribution of isomers after the coupling reaction.

Pd-catalyzed oxidative coupling of toluene[14] in the presence of $HClO_4$ favored the 3,4′- and 4,4′-dmbp isomers. In the presence of trifluoromethanesulfonic acid (triflic acid, HOTf), the distribution of the dmbps was rich in 3,4′-dmbp.[15] Variation of electronic and steric factors (ligand environment on Pd) did not improve the regioselectivity of the reaction, but a strong acid, such as HOTf, immediately showed some unusual formation of 3,4′-dmbp in large excess (up to 56%). Since the most stable isomer among the dmbp isomers is the 4,4′ isomer, we speculated that this augmentation of the relative amount of 3,4′-isomer in the reaction mixture was the result of acid-catalyzed isomerization of dmbps in which the major product was controlled not by the stability of the hydrocarbon, but by the most stable intermediate cation.

Olah and Molnar discussed the use of superacids in hydrocarbon isomerizations.[23] They commented that superacids permitted alkane isomerizations at lower temperatures and thus the products showed much skel-

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etal branching. The product distribution was dictated by the thermodynamic equilibrium of the carbocations when excess acid was used and when the system was quenched. In this chapter, the authors described a mechanism for isomerization that uses a carbocation intermediate. Reaction mechanisms are described for isomerization of cycloalkanes, side chain isomerization in arylalkanes and positional isomerization of substituted arenes. McCaulay and Lien[16] showed that the equilibrium distribution of xylenes could be varied from (15%/64%/22%: *o*-/*m*-/*p*-xylene) to exclusively *m*-xylene at 80 °C by introducing increasing amounts of BF_3 to a mixture of HF and the substrate (HF/substrate = 6). The calculated[17] equilibrium compositions of these three isomers were 18%/58%/24%: *o*-/*m*-/*p*-xylene. They explained these results by a theory in which a complex equilibrium existed among neutral species in the organic phase and carbocation species in the acid phase. When the ratio of BF_3/substrate exceeded unity, the acid-phase equilibrium dominated the system. This same phenomenon was observed for other substrates such as trimethylbenzenes and tetramethylbenzenes.

The thermodynamic mixture of isomeric diisopropylbenzenes following $AlCl_3$ catalyzed isomerization contained only about 66% of the meta isomer, as was shown by Olah, Meyer, and Overchuck.[18] Later, Olah[19] showed that a mixture of diisopropylbenzene isomers equilibrated to form the meta isomer exclusively in the presence of excess HF or a perfluorinated alkanesulfonic acid (e.g., trifluoromethane sulfonic acid) and a Lewis acid fluoride (BF_3, PF_5, etc.). The result was the formation of practically pure (98−100%) *meta*-diisopropylbenzene, consistent with control of the reaction by the most stable Wheland intermediate, the 1,5-diisopropylphenonium ion.

Carbocation intermediates have been proposed in the isomerization of hexanes[24] and the coupling of methylcyclopentane[25] to form the isomers of dimethylspirodecane and dimethyldecahydronaphthalene. The reactivity of these alkanes and cycloalkanes in trifluoromethanesulfonic acid is relevant in considering their use as solvents for other organic substrates.

With these results in mind, we explored the superacid-catalyzed isomerization of related type of substituted aromatic compounds—dimethylbiphenyls. Pure samples of 3,3′-dmbp and 4,4′-dmbp were treated with HOTf in different reaction conditions at room temperature and elevated temperatures (100 °C) to demonstrate the effect of changing acid/substrate ratio without a solvent. In subsequent tests, the effect of several solvents upon the reactivity and isomer distribution were examined.

Experimental Section

Calculations. AM1 calculations were performed on a personal computer with Titan software suite (Wavefunction, Inc., Schrödinger, Inc.). Isomer distributions were obtained by calculation of the heats of formation of all cations leading to each isomer and statistically corrected to free energies.

Materials. Trifluoromethanesulfonic acid and 3,3′- and 4,4′-dimethylbiphenyl were obtained from Aldrich, as well as the solvents (benzene, toluene, octane, *o*-, *m*-, *p*-xylene, cumene, *p*-cymene, and mesitylene), which were used without further purification. Other dimethylbiphenyls were prepared by independent synthesis in small quantities for the purpose of their identification by GC/MS according to published methods.

Procedures: Chemical Conversions. All reactions were carried out under Ar using standard Schlenk techniques. Care was exercised in transferring the triflic acid to minimize exposure to the atmosphere. Typically, 5−10 mL of triflic acid was taken with the required volume of substrate in a 25 mL glass vial affixed with a rubber stopper. The contents were stirred so that the observed concentration versus time data were not a function of the stirring speed, thus ensuring that the kinetic reaction rates were controlling the overall reaction process. An inert diluent, e.g., hexane, was added so that the substrate or acid amounts could be changed individually. The reactors were immersed in the appropriate bath to control the reaction temperature. Small aliquots of the reaction mixture were withdrawn at frequent intervals (15−30 min) to establish the reaction kinetics. Samples were introduced into ice−water to quench the reaction.

The effect of acid/substrate ratio was demonstrated for the reaction of 4,4′-dmbp at room temperature using the following proportions of acid/substrate: 10, 20, and 50 mol/mol. No added solvent was used in these experiments. The reaction temperature for all tests was 25 °C. The reactions were completed in a Pyrex glass reactor of 25−50 mL in volume. Products were withdrawn at 2, 18, 43, and 67 h for analysis by GC/MS. The products were prepared for analysis by pouring into water, separating the organic layer and treating with aqueous sodium bicarbonate.

Analysis. All samples were diluted with acetone (100 μL per 1.75 mL of acetone) and analyzed on a Hewlett-Packard HP 5890 Series II GC/HP 5972 MS. The partitioning agent was a Supelco SPB-5 column (30 m × 0.25 mm × 0.5 μm).

Results: Isomerization of dmbp

Effect of Acid/Substrate Ratio. A. Room Temperature. The data, Figure 1, showed that the approach to chemical equilibrium depended on the amount of excess acid starting with either neat 3,3′- or 4,4′-dmbp. In Figure 1, we show the concentration versus time behavior when the acid/substrate ratio was 10, 20, or 50 mol/mol for the 4,4′-dmbp and when the acid/substrate ratio was 10 mol/mol for 3,3′-dmbp as the reactant. The equilibrium distribution of isomers contained no 2,*X*′-dmbp isomers (*X* = 2′, 3′, or 4′), and the 3,4′-dmbp composition was the greatest of the remaining three isomers. At the highest acid/substrate ratio, the yield of 4,4′-dmbp was very low (1−3%) with the 3,4′-dmbp showing the highest yield (67%) with the balance 3,3′-dmbp (30%). In contrast to these results, the catalytic coupling of toluene to dimethylbiphenyl in a weakly acidic system (HOAc) showed a distribution of all six isomers.[13] The combined yield of the 2,*X*′-dmbp isomers was 37% whereas the 3,3′- and 3,4′-dmbp isomers showed a combined yield of 53%.

Increasing the amount of acid/substrate changes the trajectory of concentration versus time so that high concentrations of 3,4′-dmbp are formed early in the reaction trajectory when the acid/substrate ratio increases from 10 to 50 mol/mol. The conversion rate also increases with increasing ratio of acid/substrate.

B. 100 °C. The effect of changing the acid-to-substrate ratio was elaborated further for the isomerization of 3,3′-dmbp at 100 °C using the protocol described above. The acid/substrate ratio in these studies was 10 and 25 mol/mol. The results showed that the concentrations of isomers did not change for reaction times greater than 10 min at either acid/substrate ratio. The distribution of

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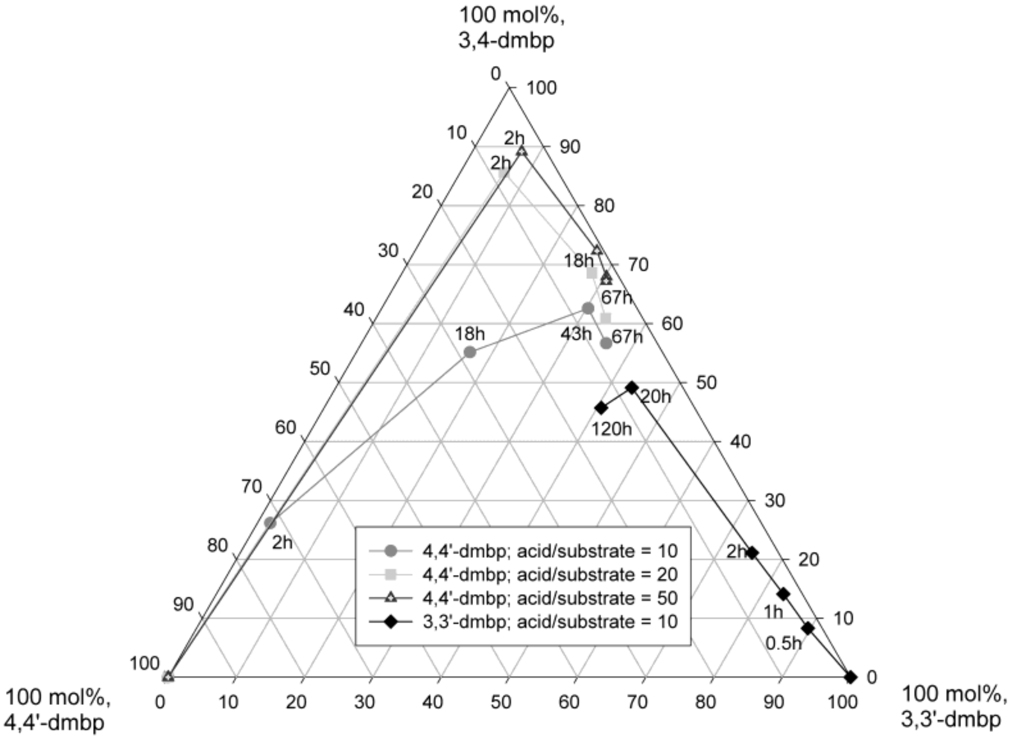


Figure 1. Isomerization of 3,3′- and 4,4′-dmbp at room temperature.

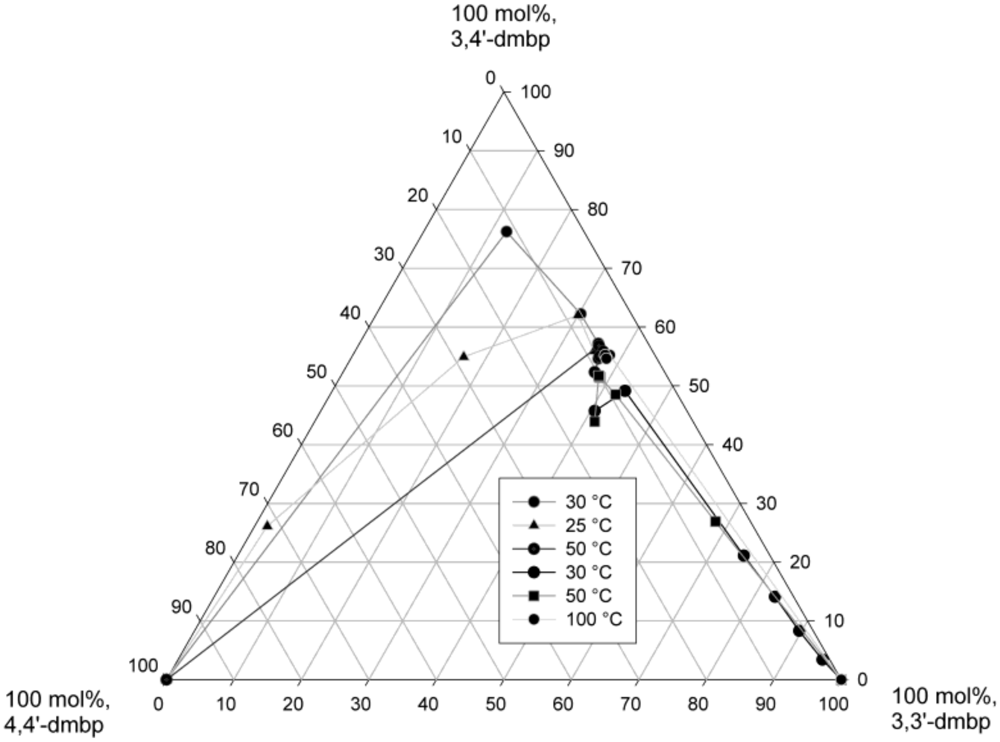


Figure 2. Effect of temperature upon the isomerization of 3,3′- and 4,4′-dmbp at acid/substrate ratio = 10.

isomers was 2,X'-dmbp = 0; 3,3′-dmbp = 39(38)%; 3,4′-dmbp = 49(55)%; and 4,4′-dmbp = 9(5)% (the numbers in parentheses indicate data for acid/substrate ratio = 25; the numbers without parenthesis indicate data for acid/substrate ratio = 10). This distribution of isomers obtained by reacting 3,3′-dmbp was very similar to the distribution (36%/56%/7% for 3,3′-/3,4′-/4,4′-dmbp) obtained from reacting the 4,4′-dmbp at a similar acid/substrate ratio and 25 °C for 67 h.

Effect of Temperature at Constant Acid/Substrate Ratio. The effect of temperature was demonstrated for the isomerization of 3,3′-dmbp using an acid/substrate ratio of 10 mol/mol (Figure 2). The protocol was as before and the temperatures were 30, 50, and 100 °C. The reaction time could be reduced to less than 10 min by using a temperature of 100 °C. The distribution of isomers did not appear to change significantly with increasing temperatures: 2,X'-dmbp = 0%; 3,3′-dmbp =

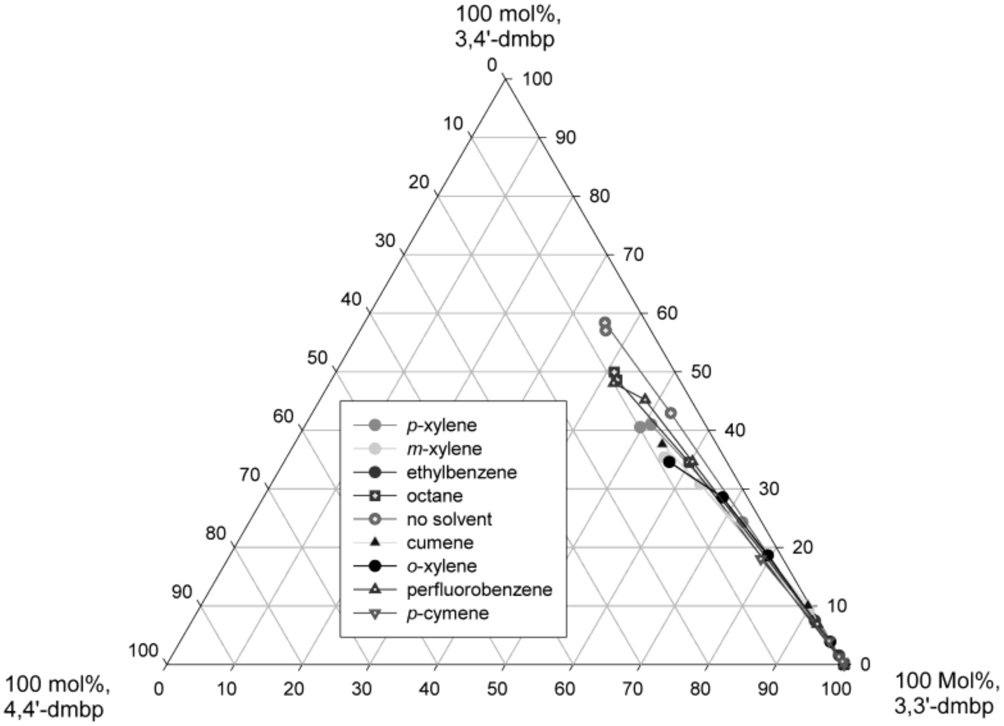


Figure 3. Effect of solvent upon the isomerization of 3,3′-dmbp at 25 °C.

31−39%; 3,4′-dmbp = 49−52%; 4,4′-dmbp = 8−9%. The effect of temperature was confirmed for the isomerization of 4,4′-dmbp using the same protocol and an acid/substrate ratio of 10. The reaction temperatures were 25, 30, and 50 °C. The final concentration of isomers were 31−37%/52−67%/2−8% for 3,3′-/3,4′-/4,4′-dmbp at these conditions. The distribution of isomers (8%/37%/52%) at the longest reaction time, 67 h, and 50 °C was similar to that observed when 3,3′-dmbp was isomerized at 100 °C and for 2 h (9%/39%/49%).

Solvent Effects. The effect of solvent was examined for its impact on the reactivity and composition of the final mixture (Figure 3). For these tests, 3,3′-dmbp was isomerized at 25 °C in a batch reactor. Samples were withdrawn at times of 20 and 94 h. The acid/solvent ratio was 1 mol/mol whereas the substrate/solvent ratio was 0.05 mol/mol. Use of substituted aromatics as solvents such as *o*-, *m*-, *p*-xylene, cumene, cymene, and mesitylene appeared to slow the isomerization rate so that little conversion of substrate was observed after 20 h. Other data for reaction in solvents such as benzene, toluene, and octane showed reactant conversion at 20 h that was similar to that observed for the neat substrate. The data at 94 h showed a definite trend in isomerization activity in these different solvents. The product mixtures of the runs using cumene and *p*-cymene showed evidence of disproportionation reactions between the solvents. This conclusion is based on the fact that di- and triisopropylbenzene were found in the reaction with cumene as the solvent and diisopropyltoluene was found in the reaction with *p*-cymene as the solvent. None of the other experiments showed evidence that the solvent reacted during the isomerization.

Results: Isomerization of Mixtures

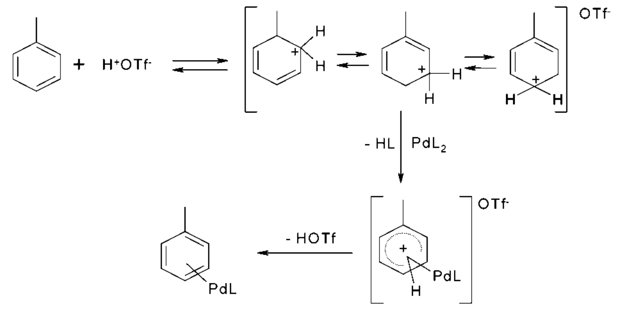
The remaining reactions were completed using, as the substrate, a mixture of the dmbp isomers that were the products of the Pd-catalyzed coupling of toluene.[13] This product mixture was purified to remove the unreacted toluene and the Pd catalyst. Thereafter, the mixture of dmbp isomers was handled as described above.

Effect of Acid/Substrate Ratio. A. 25 °C. The effect of varying the acid/substrate ratio from 3.6 to 183 mol/mol in the presence of toluene as a solvent is shown in Table S1 (Supporting Information). The reaction temperature was 25 °C, and samples were withdrawn at 20 and 140 h. At low values of the acid/substrate ratio (3.6 mol/mol), the isomerized product distribution changed only slightly from that of the substrate, even after 140 h of reaction. However, for very large values of the acid/substrate ratio (91 and 183 mol/mol) the isomerized products contained only the 3,3′- and 3,4′-dmbp isomers (26.3 and 73.8%, respectively). Quite remarkable was the complete absence of the 2,*X*′-dmbp isomers where *X*′ = 2′, 3′, or 4′.

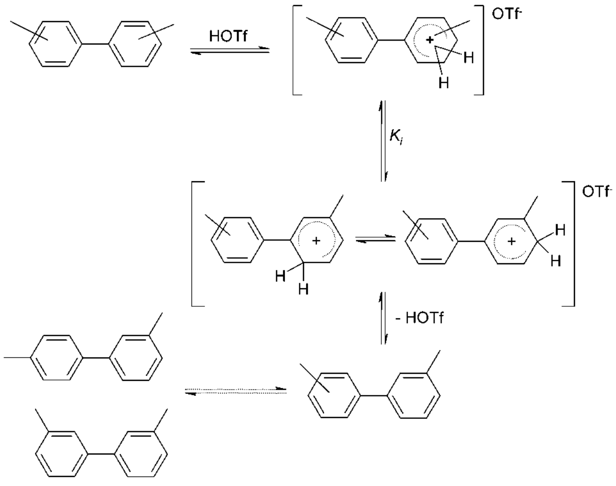
B. 100 °C. The reaction was completed in 10 min for acid/substrate ratios of 5 or 10 mol/mol. The isomerized product distribution (39%/52%/8% = 3−3′-/3,4′-/4,4′-dmbp) was nearly the same as the results (39%/49%/9%) obtained from a pure substrate when the acid/substrate ratio was 5 or 10 mol/mol (Tables S2 and S3, Supporting Information). At these reaction conditions, the combined yields of 2,X′-dmbp isomers was less than 3%, whereas the substrate showed a combined yield of 37% for the 2,*X*′-dmbp isomers.

All these data suggest that all possible isomers, in the presence of HOTf, were converted into a mixture of 3,3′-, 3,4′-, and 4,4′-dmbps. These three isomers define the thermodynamic equilibrium that depends only slightly upon temperature and acid/substrate ratio provided that a sufficient amount of superacid is present initially. The low concentration of 2,*X*′-species is remarkable.

Deuterium−Hydrogen Exchange. We described recently a fast H−D exchange (at NMR time scale) between toluene-d_8 and HOTf.[15] The speculation was that a protonated analogue of Wheland complex could facilitate the formation on Pd−C bond through a transmetalation reaction with consecutive elimination of H^+:



The same type of carbocations could be responsible for isomerization of dmbp. The tentative isomerization scheme could be as follows:



Main products of the isomerization

The rate-determining step may be an isomerization of carbocationic species because all other transformations (proton exchanges) are fast.

Reaction Kinetics. The acid-catalyzed isomerization of 3,3′-dmbp was examined to determine the reaction kinetics at the following temperatures: 5, 20 and 35 °C. The data were collected at low conversion so that the reverse reaction was not a factor when the data were extrapolated to zero conversion. The raw data for isomerization of 3,3′-dmbp at 35 °C are shown in Figure 4. The concentration of the initial product (3,4′-dmbp) was plotted as a function of time for five, different, initial concentrations of 3,3′-dmbp (0.05−0.2 M) denoted here as tests 1 → 5. The conversion of the reactant was kept low (0.005−0.06) so that the data could be treated by the “differential reactor” technique.

Thus, the slope of the concentration versus time data extrapolated to zero time gave the initial reaction rate at the corresponding initial concentration of reactant. A curve-fit of the data, Figure 4, showed the slopes and intercepts for all five tests at 35 °C. We now cross-plot the slopes of these five tests versus the initial concentration of each test to develop Figure 5 that gives the initial, reaction rate versus initial concentration for $T = 5$, 20, and 35 °C.

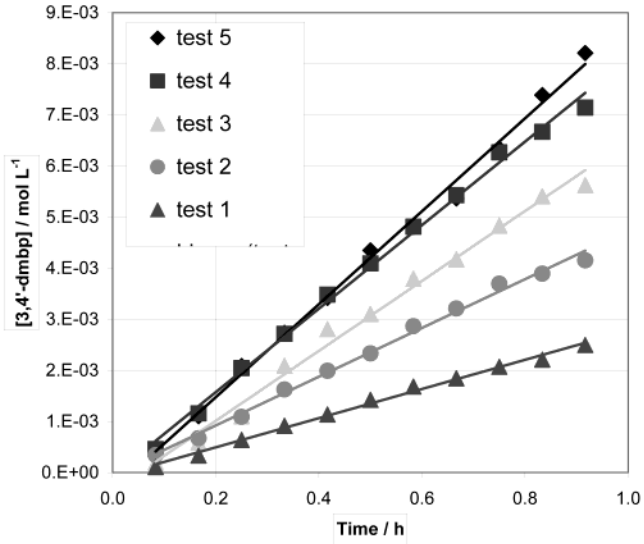


Figure 4. Data of 3,4′-dmbp isomer versus time at 35 °C.

The data of Figure 5 suggest shifting-order kinetics. These rate data were fit to a reciprocal rate plot to confirm the shifting-order kinetics (Figure 6), to determine the order of the reaction, and to extract the coefficients of the curve-fits. The appropriate fitting function was as follows:

$$R = \alpha[\text{dmbp}]/[\gamma + \beta[\text{dmbp}]]$$

Where R was the reaction rate, M/min; α, β, and γ were fitting coefficients. The solid curves in Figure 5 were produced using this fitting equation and the coefficients. These coefficients may be related to kinetic constants governing the reaction, provided that a mechanism can be established to explain all of the data. This mechanism is discussed in a following section.

Results: Calculated Equilibrium Compositions

The observation of shifting-order kinetics does not necessarily contradict the hypothesis that the rate-determining step of the isomerization of dmbp is the transformation of a protonated dmbp. To elaborate this consideration, we calculated the differences in free energy of formation with the most stable carbocations and consequently the composition of the reaction mixture at the equilibrium using the AM1 method (Table 1). The data of the neutrals were that obtained for coupling of toluene with $Pd(OAc)_2$ in pentanedione at long reaction times.[13] We showed that the isomer distribution did not change significantly in absence of a strong acid.[15] These predictions suggest that the 3,3′- and 3,4′-dmbp isomers are major products in superacid media, whereas a distribution of all six isomers is predicted for reactions in weak acids. This approach was extended to predict the equilibrium distribution of isomers among others substituted arenes in the presence of strong acids. These predictions matched well the reported experimental data of these same equilibria for xylenes, trimethylbenzenes, tetramethylbenzenes and the observations in our laboratories for dimethylbiphenyl. The most stable isomer predicted for the neutral species was not the most stable isomer predicted for the corresponding carbocation. The final distribution of isomers was achieved by quenching the reaction with water and thus preserving the distribution established in the carbocationic equilibria.

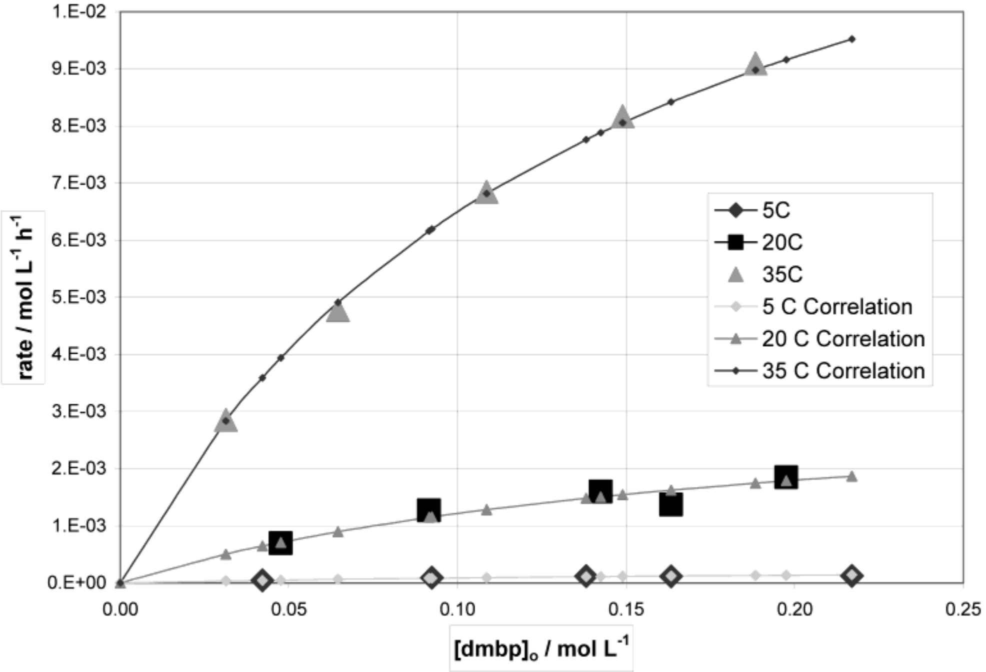


Figure 5. Initial rates plot.

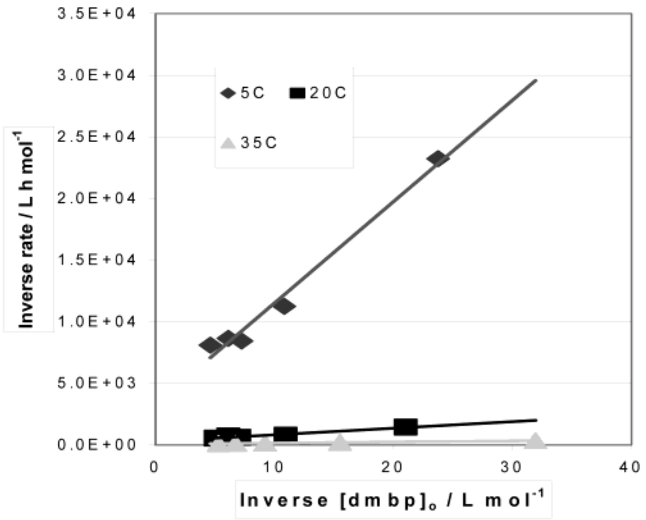


Figure 6. Shifting order kinetics plot.

Table 1. Isomerization of Dimethylbiphenyls at 25 °C

	predicted and observed equilibrium composition, mol %		
		cation	
isomer	neutrals[a]	predicted[b]	observed
2, 2′-dmbp	2.0	0.0	0.0
2, 3′-dmbp	13.0	0.1	0.0
2, 4′-dmbp	10.0	0.0	0.0
3, 3′-dmbp	27.0	21.6	26.3
3, 4′-dmbp	35.0	77.5	73.7
4, 4′-dmbp	13.0	0.8	0.0

[a] Data of ref 13. [b] Determined from AM1 calculations.

Calculations: Substituted Benzenes

AM1 calculations of the free energies of formation were used to predict the distribution of isomeric xylenes carbocations. These results are shown (Table 2) for a reaction temperature of 80 °C along with the literature results.[16] The results of our calculations appear to predict well the distribution of protonated xylenes at equilibrium as rationalized by McCaulay and Lien.[16] For comparison, we repeated these calculations for the isomerization of trimethyl- and tetramethylbenzene. We used this same approach to model the results of Olah for the isomerization of diisopropylbenzene in superacids at room temperature.[19]

Table 2. Isomerization of Alkylbenzenes[a]

	equilibrium composition, mol %		
		cation	
isomer	neutrals[14]	obsd[16]	predictions
1,2-dimethylbenzene	18	0	0.2
1,3-dimethylbenzene	58	100	99.5
1,4-dimethylbenzene	24	0	0.3
1, 2, 3-trimethylbenzene	9	0	0.0
1, 2, 4-trimethylbezene	60	0	0.3
1, 3, 5-trimethylbenzene	31	100	99.7
1, 2, 3, 4-tetramethylbenzene	0	0	0.5
1, 2, 4, 5-tetramethylbezene	70	0	2.4
1, 2, 3, 5-tetramethylbezene	30	100	97.1
1,2-diisopropylbenzene	0	0	0.0
1,3-diisopropylbenzene	66	99	99.2
1,4-diisopropylbenzene	34	1	0.8

[a] Note: calculations and data for dimethylbenzenes were for a temperature of 80 °C and for tri- and tetramethylbenzenes of 100 °C.

The semiempirical method apparently showed a remarkable agreement with the experimental results for isomerization of the substrates by superacids to produce a mixture that is rich in the meta isomer. In each case, this observed equilibrium composition is much different from what could be expected considering the free energy of formation for the neutral species.

Discussion

The data for isomerization of either 3,3′- or 4,4′-dimethylbiphenyl showed that only three (3,3′-/3,4′-/4,4′- = ~40/~55/~5%) out of the six dmbp isomers were produced when the catalyst was triflic acid. No 2,*X*′-dmbp isomers ($X = 2$, 3, or 4) were observed even after very long reaction times. Changing the reaction temperature and or the ratio of acid/substrate altered the rate of approach to this equilibrium mixture. The same equilibrium distribution was observed with a single reactant, such as 3,3′- or 4,4′-dmbp or a mixture of all six dmbp's. Thus, we conclude that the composition observed at long reaction times was the equilibrium composition. This distribution of isomers was different from that observed from the catalytic coupling of toluene in weak acids over a Pd^{2+} catalyst. However, recent results[15] for the coupling of toluene in strong acids over the same Pd^{2+} catalyst show distributions of isomers that are rich in the 3,4′- and 4,4′-dmbp isomers. Apparently, the strong acid influenced the distribution of isomers either during and/or after the coupling reaction.

Different solvents also influenced the rate of isomerization. The more basic methylated aromatic solvents slowed the isomerization rate, whereas nonaromatic or weakly basic solvents did not. In the extreme case of mesitylene, the solvent was protonated preferentially to the substrate and the isomerization ceased.

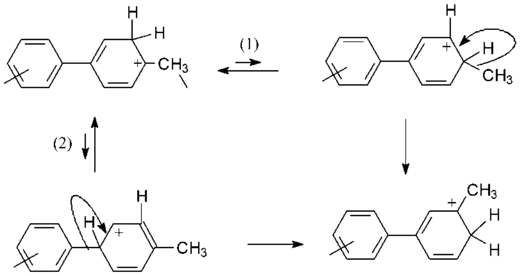
Earlier researchers[16] speculated that methyl-substituted arenes were protonated by HF/BF_3 to form a cation complex, and the product distribution was determined by the free energies of this carbocation complex. The conventional models of arene, cation-complexes were used to argue that the meta-substituted, arene, carbocation was the most stable species for the cases of xylene and trimethyl- and tetramethylbenzene. We calculated the free energies of formation for neutral and carbo-cation complexes at the reaction conditions described in the literature using a semiempirical molecular orbital calculation (AM1) to determine the enthalpy of formation. From these calculations we predicted the equilibrium isomer distributions for the carbocations that agreed with the literature data and expanded it to the isomerization of di-substituted biphenyls. The agreement was good between the calculated equilibrium compositions with experimental data for these substituted arenes. Thus the success of the AM1 algorithm to predict these equilibrium distributions represents both a refinement and a generalization of the previous rationalization based upon qualitative resonance predictions.

The kinetics of the isomerization were correlated by shifting-order kinetics:

$$R = \alpha[\text{dmbp}]/[\gamma + \beta[\text{dmbp}]] \qquad (1)$$

That this shifting-order equation can be used to correlate the data suggests that an equilibrium step is in sequence with a slow, kinetic step. The following discussion elaborates this suggestion in more detail.

Scheme 1



^{1}H NMR and mass spectra data[15] clearly demonstrated that toluene was protonated by triflic acid on the ring to form an equilibrium mixture at room temperature. It is logical to suppose that triflic acid also protonates dimethylbiphenyl in a similar manner. These data together with the data of McCaulay and Lien[16] and the data of Olah[19] for isomerization of substituted benzenes in superacid add credibility to the reaction mechanism that we postulate here. The AM1 calculations show that the distribution of dmbp isomers can be predicted well if it is assumed that carbocations are formed with energies that depend on location of the proton vis-à-vis the methyl groups. The kinetic data are consistent with the following reaction mechanism:

$$\text{isomer}_1 + \text{H}^+\text{A}^- \leftrightarrow [\text{isomer}_1\text{-H}]^+\text{A}^-, \text{ reversible} \qquad (2)$$

$$[\text{isomer}_1\text{-H}]^+\text{A}^- \rightarrow [\text{isomer}_2\text{-H}]^+\text{A}^-, \text{ slow} \qquad (3)$$

$$[\text{isomer}_2\text{-H}]^+\text{A}^- + \text{H}_2\text{O} \rightarrow \text{isomer}_2 + [\text{H}_3\text{O}]^+\text{A}^-, \text{ fast} \qquad (4)$$

Step 1 is the reversible protonation of the arene isomer, by triflic acid, and step 2, the "methyl shift", is the slow, rate-determining step of this process. The methyl shift can take place by one of two processes. The first is ipso protonation to the methyl group, followed by methyl migration. The second is ipso protonation to the phenyl group, followed by phenyl migration (see Scheme 1). Although our studies do not allow us to distinguish kinetically between the two pathways, we note that the protonation ipso to phenyl produces an intermediate having ca. 5.4 kcal/mol higher energy than the first. Thus, we conclude that the first process predominates.

After the reaction was completed, then water was added to quench the reaction, step 3. The reaction of water with the products was very fast and produces a weaker acid than triflic acid. We showed how small amounts of water compromised the reactivity of another reaction catalyzed by triflic acid.[20] Therefore, we believe that the addition of water (1) releases isomer$_2$ from the acid and (2) prevents the back-isomerization of isomer$_2$ into isomer$_1$. This kinetic trapping is the key to synthesis of the thermodynamically unfavored neutral isomer. With this mechanism we may write a rate law assuming that the amount of triflic acid initially is related to the amount of unbound acid and bound acid:

$$[\text{H}^+]^o = [\text{isomer}_{\text{total}} - \text{H}]^+ + [\text{H}^+] \qquad (5)$$

$$[\text{isomer}_{\text{total}} - \text{H}]^+ = [\text{isomer}_1 - \text{H}]^+ + \Sigma_{i=2,6}[\text{isomer}_\text{i} - \text{H}]^+ \qquad (6)$$

$$\text{d}[\text{isomer}_1 - \text{H}]^+/\text{d}t = k_1[\text{isomer}_1][\text{H}^+] - k_{-1}[\text{isomer}_1 - \text{H}]^+ - k_2[\text{isomer}_1 - \text{H}]^+ = 0 \qquad (7)$$

Equations similar to eq 7 may be written for all six protonated isomers, and these equations may be summed to give the following expression for initial rate as a function of initial concentrations.

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(20) Xu, Bo-Qing; Sood, D. S.; Gelbaum, L. T.; White, M. G. *J. Catal.* **1999**, *186*, 345−52.

$$R = (k_1/k_{-1})k_2[I_1]^{o}[\mathrm{H}^+]^{o}/[(1 + k_2/k_{-1}) + (k_1/k_{-1})[\mathrm{I}_1]^{o}] \tag{8}$$

The form of this equation is the same as the equation used to fit the reaction rate data (eq 1) where $\alpha = (k_1/k_{-1})k_2[\mathrm{H}^+]^{o}$, $\beta = (k_1/k_{-1}) = K$, and $\gamma = (1 + k_2/k_{-1})$. Equation 8 may be inverted to find the fitting coefficients using the rate data at 5, 20, and 35 °C (Figure 3).

$$(1/R) = (1 + k_2/k_{-1})/(\mathrm{k}_2K[\mathrm{H}^+]^{o})(1/[\mathrm{I}_1]^{o}) + 1/(k_2[\mathrm{H}^+]^{o}) \tag{9}$$

The slopes (s) and intercepts (i) of the lines in Figure 3 may be related to the rate constant (k_2) and equilibrium constants of protonation (K) through eq 9 as follows:

$$k_2[\mathrm{H}^+]^{o} = 1/i;\ K = (i/s)(1 + k_2/k_{-1}) \tag{10}$$

The kinetic data were reduced by this equation to give Figure 5 assuming that the initial concentrations of protons between each test were nearly the same. Thus, the rate constant is proportional to $1/i$ and the equilibrium constant equals (i/s) assuming that $k_{-1} \gg k_2$.

Therefore, we may relate the fitting coefficients established in Figure 6 with the rate constant of the kinetically slow step, k_2, and the equilibrium constant of the arene protonation, K, for each temperature. These constants as a function of temperature were used to determine the activation energy (22.5 kcal/mol), preexponential factor (1.56×10^{14} h^{-1}), enthalpy (3.2 kcal/mol), and entropy of protonation (−14.2 cal/mol-K). The activation energy is characteristic of a kinetically controlled process as is the preexponential factor.[21] The enthalpy of protonation suggests that the process is endothermic whereas the entropy of protonation reflects a large decrease in the entropy that associates with the protonation. These results are related to the equilibrium of protonation and suggest that the solubility of the hydrocarbon in the acid phase may be responsible for the endothermic enthalpy of protonation, as it was observed that the apparent two-phase system disappears when the reaction temperature is 100 °C. The protonation of the arene is expected to demonstrate a negative entropy change since the proton and substrate become associated and thus the entropy is expected to decrease.[22]

Conclusions

Triflic acid is an efficient catalyst for isomerization of dimethylbiphenyls. The study of this process allowed us to propose the general model of alkyl benzenes isomerization in superacid media. It consists of protonation of aromatic nucleus with consecutive isomerization of the initially-formed Wheland intermediate is the rate-limiting step. The thermodynamically unfavored neutral isomer can be kinetically trapped by quenching the reaction with water. The semiempirical method AM1 provides an extraordinarily accurate tool for prediction of the isomer distribution for substituted arenes based on the free energy of formation for corresponding carbocations.

Abbreviations. α, β, γ, fitting constants for reaction rate equation, eq 1; $[\mathrm{H}^+]$, concentration of hydrogen ion at time t (M); $[\mathrm{H}^+]°$, concentration of hydrogen ion at time t (M); i, intercepts of lines in Figure 2 (time/M); $[\mathrm{I}_n]$, concentration of isomer n at time t (M); $[\mathrm{I}_n]°$, concentration of isomer n at time $t = 0$ (M); k_1, forward rate constant for eq 2 (1/M-time); k_{-1}, reverse rate constants for eq 2 (1/time); k_2, forward rate constant for eq 3 (1/time); K, k_1/k_{-1}; R, reaction rate (M/time); s, slopes of lines in Figure 2 (time); T, temperature (K).

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Supporting Information Available: Tables S1−S6 and data from AM1 calculations. This material is available free of charge via the Internet at http://pubs.acs.org.

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