Comparative Capabilities of 1-Phenylpropane-*1*-^{13}C and 1-Phenylbutane-*1*-^{13}C toward the Alkylbenzene Automerization[1]

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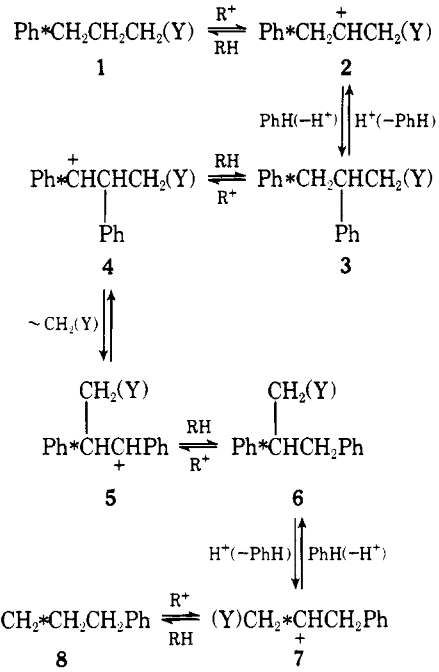
1-Phenylbutane-*1*-^{13}C failed to undergo rearrangement of the isotopic label from C-1 to C-2 of the side chain (automerization) when heated with $AlCl_3$ or $AlBr_3$ under conditions which produce complete equilibration of isotopic carbon between C-1 and C-2 in labeled 1-phenylpropane (*n*-propylbenzene). When equimolar mixtures of 1-phenylbutane-*1*-^{13}C and 1-phenylpropane-*1*-^{13}C were treated with $AlCl_3$ and $AlBr_3$, neither hydrocarbon underwent automerization when the usual concentration of catalysts was used; with a much higher concentration of $AlBr_3$, 1-phenylpropane-*1*-^{13}C showed isotopic automerization but 1-phenylbutane-*1*-^{13}C could not be recovered. Various compounds, known to be produced from 1-phenylbutane under the conditions of the reaction, were tested as potential inhibitors of the isotopic automerization. Di- and tri-*n*-butylbenzenes appeared to be the most likely candidates. The failure of 1-phenylbutane-*1*-^{13}C to undergo isotopic automerization may be ascribed partly to alternative reactions which it undergoes but which are not available to 1-phenylpropane-*1*-^{13}C. These alternative reactions are cyclialkylations to indan and indene derivatives via the secondary carbocation produced by hydride abstraction at the 3 position in the side chain of 1-phenylbutane. In accord with this explanation, significant amounts of indans and indenes have been identified among the products from 1-phenylbutane. A second factor in the failure of 1-phenylbutane-*1*-^{13}C to undergo automerization is the lesser tendency of a 1,2-ethyl shift in an intermediate carbocation compared with a 1,2-methyl shift. This was demonstrated in the reaction of 1,2-diphenylbutane-*2*-^{13}C with aluminum chloride, which gave only 8–10% isotopic rearrangement in recovered 1,2-diphenylbutane and the 1-phenylbutane produced from it.

In 1957 a surprising isotopic rearrangement (automerization) was observed in *n*-propylbenzene (1-phenylpropane-*1*-^{14}C), induced by heating the hydrocarbon with aluminum chloride.[2] The isotope became equilibrated between C-1 and C-2 of the 1-phenylpropane, but none was introduced into C-3. Subsequently other structural, nonisotopic rearrangements of several alkylbenzenes were discovered and correlated with the isotopic *n*-propylbenzene automerization. These included *sec*-butylbenzene, isobutylbenzene, and some pentylbenzenes.[3] A mechanism proposed independently by Streitwieser and Reif[4] and by us[3c] for the isotopic automerization of 1-phenylpropane has been given additional support from results of experiments with ^{13}C-labeled molecules.[5] An isotopic automerization of 1-phenylbutane-*1*-^{14}C might be expected to follow an analogous mechanism in which the only differences would be the intermediacy of 1,2-diphenylbutane instead of 1,2-diphenylpropane, and the 1,2 shift of an ethyl group instead of a methyl group (Scheme I).

Early tests on ^{14}C-labeled *n*-butylbenzene showed an unexpectedly small amount of automerization, compared to that of the lower homologue.[6] However, these experiments were carried out before the optimum conditions for automerization of *n*-propylbenzene were worked out. It was found later that the extent of automerization was highly dependent on the nature of the catalyst (e.g., $AlCl_3$ or $AlBr_3$), the concentration of the catalyst, the presence of a cocatalyst (H_2O, HCl or HBr, etc.), and the choice of solvent, if any.[3c,7] Because of the subtlety of the influence of these factors, we felt that a reexamination of the possible isotopic automerization of *n*-butylbenzene under a variety of experimental conditions was justified, especially since the use of ^{13}C instead of ^{14}C would simplify the gathering of experimental data.

Scheme I



a, Y = H
b, Y = CH_3

Results and Discussion

Samples of 1-phenylbutane-*1*-^{13}C were treated with water-activated aluminum chloride or bromide, usually in the presence of benzene, at 85–95 °C. The recovered 1-phenylbutane was investigated by mass spectrometry and in some cases by ^{1}H NMR spectroscopy in order to determine the position and percentage of the isotopic carbon label within the molecules.

In order to determine the percentage of monolabeled molecules and the position of the label in samples of 1-phenylbutane-*1*-^{13}C before and after treatment with aluminum chloride, mass spectra of (1) unlabeled 1-phenylbutane, (2) 1-phenylbutane-*1*-^{13}C, and (3) 1-phenylbutane-*1*-^{13}C recovered after treatment with aluminum halide were obtained. The mass spectrometric analysis of ^{13}C-labeled 1-phenylbutane samples was performed by the same process as that described for labeled 1-phenylpropane[5] except that the P (parent) and P + 1 peaks for the labeled 1-phenylbutane are found at *m/e* 134 and 135, respectively. The method of Biemann[8] was used to calculate the mole percentage of ^{13}C-singly labeled molecules (*m/e* 135) and unlabeled molecules (*m/e* 134), and the mole percentage of molecules labeled in C-1 of the side chain (*m/e* 92) and those not labeled in C-1 (*m/e* 91),[9] as in the case of labeled 1-phenylpropane.[5]

The results of experiments in which samples of 1-phenylbutane-*1*-^{13}C were treated with aluminum chloride or aluminum bromide are given in Table I. Comparison of the mole percentage of labeled molecules before and after reaction (columns 2 and 3) showed no loss of ^{13}C from the phenylbutane molecules, and comparison of the mole percentage of molecules labeled in C-1 before and after reaction (columns 3 and 4) indicated no change within experimental error in the distribution of the ^{13}C label in any sample of 1-phenylbutane-*1*-^{13}C. This complete lack of rearrangement in 1-phenylbutane-*1*-^{13}C was confirmed by ^{1}H NMR analysis. The integrals of the triplet at δ 2.61 ppm and its ^{13}C-satellite triplet at δ 3.66 ppm showed the same ratio before and after reaction in all of the experiments of Table I except expt 2 and 6, in which no NMR analysis was applied. It should be noted that the reaction conditions of catalyst concentration, temperature, solvent, and reaction time employed in the experiments of Table I were those which produced complete automerization of isotopic carbon between C-1 and C-2 of the *n*-propylbenzene side chain.[3c,5]

Although these new experiments with 1-phenylbutane-*1*-^{13}C confirmed and extended the earlier evidence that *n*-butylbenzene was much less susceptible to isotopic automerization than *n*-propylbenzene, it occurred to us that the best opportunity for a direct comparison of the behavior of the two homologous alkylbenzenes would be afforded by heating a mixture of 1-phenylpropane-*1*-^{13}C and 1-phenylbutane-*1*-^{13}C with aluminum halide, recovering and separating the alkylbenzenes by gas chromatography, and determining the distribution of the ^{13}C in each of them. The results of such experiments are shown in Table II, as determined by mass spectrometry. Water-activated $AlCl_3$ at 85 °C for 6.5 or 12 h (expt 1 and 2) produced no isotopic automerization in either alkylbenzene. The result of expt 1 was confirmed by NMR analysis. The same lack of automerization was observed when the mixture of alkylbenzenes was heated with water-activated $AlBr_3$ and benzene in sealed tubes at 95 °C, using a molar ratio of combined alkylbenzenes:$AlBr_3$ = 1:0.5 (expt 3). However, when the molar ratio of catalyst to hydrocarbon was raised to 1:1 (expt 4), partial automerization of ^{13}C occurred in the 1-phenylpropane-*1*-^{13}C: 33.7/47.2 × 100 = 71% ^{13}C remained in C-1 after heating. Not enough 1-phenylbutane for analysis could be recovered from this reaction mixture. Experiment 5, in which the same reactant ratio was used, but a longer heating period, gave complete equilibration of the ^{13}C label in the 1-phenylpropane (23.6/47.2 × 100 = 50.1% ^{13}C remained in C-1), but the recovered material with the same GLC retention time as 1-phenylbutane was chiefly (ca. 80%) a side-reaction product with a molecular ion of *m/e* 132, presumably 1-methylindan. It has previously been demonstrated that heating 1-phenylbutane with aluminum chloride in benzene produces some 1,3-diphenylbutane, and the latter is converted to 1-methylindan.[3c,10]

The experiments on ^{13}C-labeled 1-phenylpropane and 1-phenylbutane separately and in mixtures clearly demonstrated three facts: (1) 1-phenylbutane is much less susceptible to isotopic automerization than is 1-phenylpropane; (2) 1-phenylbutane is much less resistant to structural modification by aluminum chloride than is 1-phenylpropane; (3) the presence of 1-phenylbutane has an inhibitory effect on the isotopic automerization of 1-phenylpropane. We shall now describe further studies designed to explain the basis of each of these facts and their possible interrelationships.

The first approach had as its aim discovery of the cause of the inhibitory effect of 1-phenylbutane on the automerization of 1-phenylpropane-*1*-^{13}C. Mixtures of 1-phenylpropane-*1*-^{13}C and unlabeled 1-phenylbutane in various proportions were treated with aluminum chloride in the presence of benzene and water cocatalyst. The recovered 1-phenylpropane samples were examined by mass spectrometry to determine the effect of the concentration of 1-phenylbutane in the reaction mixture on the extent of the rearrangement of ^{13}C label from C-1 to C-2. The crude reaction mixtures were also analyzed by GLC to observe changes in the composition of the mixture of starting materials during the reaction.

Table I. Mass Spectrometric Analysis of 1-Phenylbutane-*1*-^{13}C before and after Reaction with Aluminum Halides in Benzene Solution[a]

		Mol % ^{13}C-labeled Molecules[b]		Mol % ^{13}C label in C-1[c]	
Expt[d]	Catalyst	Before reaction	After reaction	Before reaction	After reaction
1	$AlCl_3$	26.3	26.1	24.4	25.3
2	$AlCl_3$	26.3	26.2	24.4	25.1
3	$AlCl_3$	26.3	26.6	24.4	25.0
4	$AlCl_3$	40.9	40.8	37.6	37.9
5	$AlCl_3$	40.9	41.2	37.6	35.9
6	$AlCl_3$	40.9	41.9	37.6	39.4
7	$AlCl_3$	40.9	39.7	37.6	37.0
8	$AlBr_3$	40.2	39.5	37.3	36.2

[a] For molar ratios of reactants and reaction times see Experimental Section. [b] Mole % ^{13}C-labeled molecules was determined from *m/e* 135 ($C_9{}^{13}CH_{14}{}^+$) compared to *m/e* 134 ($C_{10}H_{14}{}^+$). [c] Mole % ^{13}C label in C-1 of 1-phenylbutane was determined from *m/e* 92 ($C_6{}^{13}CH_7{}^+$) compared to *m/e* 91 ($C_7H_7{}^+$). [d] Expt 1–3, CEC 21-110 mass spectrometer, ±2% uncertainty; expt 4–8, CEC 21-491 mass spectrometer, ±5% uncertainty.

As seen in Table III, there was complete or nearly complete scrambling of the label in 1-phenylpropane-*1*-^{13}C between C-1 and C-2 when the starting proportion of 1-phenylbutane in the reaction mixture was less than 0.8 mol of 1-phenylbutane per mol of 1-phenylpropane, and in these reaction mixtures only a small part of the added 1-phenylbutane remained after the treatment with aluminum chloride. The missing 1-phenylbutane was converted into 2-phenylbutane, 1-methylindan (major product), di-*n*-butylbenzenes, and diphenylbutanes, the same products observed when 1-phenylbutane was treated with aluminum chloride and benzene in the absence of 1-phenylpropane.

When the starting amount of 1-phenylbutane was more than 0.8 mol per mol of 1-phenylpropane-*1*-^{13}C, there occurred little or no rearrangement of the isotopic label in 1-phenylpropane-*1*-^{13}C (Table III). These results indicated that either 1-phenylbutane or products formed from it can, in fact, inhibit the isotopic automerization of 1-phenylpropane-*1*-^{13}C catalyzed by aluminum chloride.

Several of the hydrocarbons which are products of the treatment of 1-phenylbutane with aluminum chloride were tested for their effects on the isotopic automerization by adding them singly to reaction mixtures with 1-phenylpropane-*1*-^{13}C as was done with 1-phenylbutane in the preceding experiments. The mass spectrometric data from the recovered samples of 1-phenylpropane-*1*-^{13}C treated in the presence of the various hydrocarbons are presented in Table IV.

In four experiments, the presence of 1,3-diphenylbutane clearly did not inhibit the isotopic automerization of 1-phenylpropane-*1*-^{13}C, as smaller molar quantities of 1-phenylbutane did in the preceding experiments. The 1,3-diphenylbutane added to the reaction mixture actually appeared to *increase* the extent of the isotopic automerization, if it had any effect.

In expt 5 and 6, in which the mole ratio of 1-phenylpropane-*1*-^{13}C:1-methylindan was 1:0.2 and 1:0.8, respectively, complete scrambling of the ^{13}C label between C-1 and C-2 of the side chain in the labeled 1-phenylpropane was observed.

Table II. Treatment of Equimolar Mixtures of 1-Phenylpropane-*1*-^{13}C and 1-Phenylbutane-*1*-^{13}C in Benzene with Aluminum Chloride and Bromide[a]

				1-Phenylpropane ^{13}C label in C-1, mol %		1-Phenylbutane ^{13}C label in C-1, mol %	
Expt	Catalyst	Temp, °C	Time, h	Before reaction	After reaction	Before reaction	After reaction
1[b]	$AlCl_3$[c]	85	6.5	41.2	37.5	37.3	37.4
2	$AlCl_3$[c]	85	12	31.4	32.2	37.3	36.2
3	$AlBr_3$[d]	95	12	46.5	46.7	37.6	35.2
4	$AlBr_3$[e]	85	1.2	47.2	33.7	37.3	None recovered
5	$AlBr_3$[e]	95	2.5	47.2	23.6	37.3	None recovered

[a] Mole % ^{13}C label in C-1 of 1-phenylpropane or 1-phenylbutane was determined from *m/e* 92 ($C_6{}^{13}CH_7{}^+$) compared to *m/e* 91 ($C_7H_7{}^+$). In expt 2, 4, and 5, CEC 21-110 mass spectrometer was used (±2% uncertainty). [b] In these experiments, a CEC 21-491 mass spectrometer was used (±5% uncertainty). [c] Molar ratio alkylbenzenes:$AlCl_3$:benzene:water = 1:0.5:6:0.1. [d] Molar ratio alkylbenzenes:$AlBr_3$:benzene:water = 1:0.5:4:0.1. [e] Molar ratio alkylbenzenes:$AlBr_3$:benzene:water = 1:1:4:0.2.

Table III. Mass Spectrometric Analysis of 1-Phenylpropane-*1*-^{13}C before and after Reaction with Aluminum Chloride in the Presence of 1-Phenylbutane[a]

Expt	1-Phenylpropane-*1*-^{13}C: 1-phenylbutane, mole ratio of starting mixture	Percentage of ^{13}C in C-1 after reaction[b]
1	1:0	6.9
2	1:0	7.5
3	1:0	7.9
4	1:0.1	6.2
5	1:0.2	6.8
6	1:0.4	6.3
7	1:0.4	6.7
8	1:0.4	6.8
9	1:0.6	8.7
10	1:0.6	7.1
11	1:0.8	12.8
12	1:0.8	12.4
13	1:1.0	9.5
14	1:1.0	15.6
15	1:1.2	11.4
16	1:1.2	10.8
17	1:1.5	12.3
18	1:1.5	11.6

[a] % ^{13}C in C-1 obtained by comparing *m/e* 92 ($C_6{}^{13}CH_7{}^+$) with *m/e* 91 ($C_7H_7{}^+$) using the CEC 21-491, ±5% uncertainty. No change in the percentage of ^{13}C-labeled molecules ($C_9{}^{13}CH_{14}{}^+$) was observed. [b] The percentage of ^{13}C in C-1 in the starting material was 13.4 in all experiments.

The reaction mixture in expt 6 clearly contained more 1-methylindan than the amount formed in the preceding series of experiments with mixtures of 1-phenylpropane-*1*-^{13}C and 1-phenylbutane in which the isotopic rearrangement was completely blocked. This observation means that 1-methylindan is unlikely to be the cause of the inhibition of ^{13}C rearrangement in the presence of 1-phenylbutane. In expt 7, a massive amount of 1-methylindan (1.5 mol per mol of 1-phenylpropane-*1*-^{13}C) only caused partial inhibition of the isotopic automerization. A much smaller amount of 1-phenylbutane (1.0 mol per mol of 1-phenylpropane-*1*-^{13}C) was sufficient to completely block the ^{13}C rearrangement in the preceding experiments.

In a series of six experiments, a mixture of di- and tri-*n*-butylbenzenes (also containing 1-phenylbutane) was added to 1-phenylpropane-*1*-^{13}C and the mixture was treated with aluminum chloride as in the preceding experiments. By comparison of the total number of moles of the mono-, di-, and tributylbenzenes used in these experiments with the moles of 1-phenylbutane (without the others) used in the earlier series of experiments, it was found that the di- and tri-*n*-butylbenzenes inhibit the isotopic automerization in 1-phenylpropane-*1*-^{13}C more than an equal molar quantity of 1-phenylbutane does.[11]

An experiment similar to the preceding ones was performed except that the hydrocarbons added to 1-phenylpropane-*1*-^{13}C were a mixture containing unlabeled 1-phenylpropane, di-*n*-propylbenzenes, and tri-*n*-propylbenzenes. Comparison of the calculated value for the mole percent of monolabeled 1-phenylpropane-^{13}C molecules with the mole percent of molecules labeled in C-1 of the side chain indicated that complete automerization took place.

In an experiment similar to the preceding, except that 2-phenylbutane was the added hydrocarbon, complete rearrangement of the label in the recovered 1-phenylpropane-^{13}C within experimental error occurred.

The results of the experiments involving the treatment of mixtures of 1-phenylpropane-*1*-^{13}C and various hydrocarbons with aluminum chloride clearly indicated that the isotopic automerization was inhibited by the presence of 1-phenylbutane. The inhibition of this reaction required a 1-phenylbutane concentration of ≥0.8 mol per mol of 1-phenylpropane-*1*-^{13}C. The 1-phenylbutane was converted to 1-methylindan and other products. Among these products only the di- and tri-*n*-butylbenzenes were found to have a strong inhibiting effect on the isotopic automerization. In fact, adding di- and tri-*n*-butylbenzenes to the reaction mixture caused greater inhibition than adding the same molar quantity of 1-phenylbutane. Thus, the di- and tri-*n*-butylbenzenes, which are always formed from 1-phenylbutane in the presence of aluminum chloride, may be the major cause of the observed inhibition. An obvious explanation is the known ability of di- and trialkylbenzenes to form relatively unreactive complexes with aluminum halide catalysts. Why the di- and tri-*n-propyl*benzenes do not have a comparable inhibitory effect is not clear.

Although no completely satisfactory explanation of the inhibitory effect of 1-phenylbutane on the isotopic automerization of 1-phenylpropane was deduced, further consideration of the failure of 1-phenylbutane itself to undergo appreciable isotopic automerization was more successful. Referring to Scheme I again, in terms of this mechanism, one difference between an isotopic automerization of 1-phenylbutane and 1-phenylpropane would be the 1,2 shift of an *ethyl* group in the 1,2-diphenylalkane carbocations (**4b, 5b**) produced from the former instead of a 1,2-methyl shift in the analogous intermediates (**4a, 5a**) from the latter alkylbenzene. One could hardly expect the difference in the migratory aptitudes of methyl and ethyl groups to be great enough to be responsible for the wide discrepancy in the behavior of the homologous alkylbenzenes in reaction with aluminum halides.[13] However, an approach to ascertaining the magnitude of this difference for this particular system would be to pre-

Table IV. Rearrangement of 1-Phenylpropane-*1*-^{13}C after Treatment with Aluminum Chloride in the Presence of Various Hydrocarbons

Expt	1-Phenylpropane:HC, mole ratio of starting mixture	Hydrocarbon added	^{13}C label in C-1, mol %[a]	
			Before reaction	After reaction
1	1:0.4	1,3-Diphenylbutane	13.4	6.7
2	1:0.6		13.4	8.1
3	1:1.0		13.4	6.1
4	1:1.2		13.4	6.4
5	1:0.2	1-Methylindan	13.4	6.3
6	1:0.8		13.4	6.4
7	1:1.5		13.4	9.2
8	1:0.2	Mixture of mono-, di-, and tri-*n*-butylbenzenes	19.8	11.2
9	1:0.2		19.8	10.1
10	1:0.5		19.8	18.3
11	1:0.5		19.8	22.7
12	1:0.5		19.8	20.9
13	1:0.8		19.8	18.8
14	1:1.2		19.8	22.0
15	1:1.0	Mixture of mono-, di-, and tri-*n*-propylbenzenes		4.4/10.3[b]
16	1:0.8	2-Phenylbutane	19.8	10.8

[a] Mass spectrometric analysis with CEC 21-491, ±2–5% uncertainty. [b] Mol % ^{13}C in C-1/mol % labeled molecules measured after reaction.

pare an isotopically labeled 1,2-diphenylbutane and compare its behavior with that of labeled 1,2-diphenylpropane. 1,2-Diphenylpropane-2-^{14}C has previously been shown to undergo equilibration of the isotope between C-1 and C-2 when treated with aluminum chloride even at room temperature (27 °C), and the 1-phenylpropane produced in the reaction also had the isotope evenly distributed between C-1 and C-2.[14]

1,2-Diphenylbutane-2-^{13}C was synthesized by conventional methods and the percentage of ^{13}C was determined to be 58% by the method of Biemann.[8] Treatment of the labeled diphenylbutane with aluminum chloride in benzene (molar ratio 1:0.5:6, respectively) at reflux for 1 h gave a mixture from which the starting material (mainly) and 1-phenylbutane were isolated by preparative gas chromatography. ^{13}C magnetic resonance analysis of the recovered 1,2-diphenylbutane indicated about 8% ^{13}C was at C-1 and 92% remained at C-2. Mass spectrometric analysis of the 1-phenylbutane produced showed 59% total ^{13}C, with only 10% of the isotope at C-1.[15] A second sample of 1,2-diphenylbutane-2-^{13}C was heated with aluminum chloride in benzene (in the same molar proportions as before) for 7 h. The 1-phenylbutane produced was separated and analyzed by mass spectrometry as before and found to have 8% of the ^{13}C at C-1.

These results showed that only 8–10% rearrangement of ^{13}C occurred in 1,2-diphenylbutane and in the 1-phenylbutane produced from it, whereas under much milder treatment 1,2-diphenylpropane-2-^{14}C gave complete equilibration of the isotopic label between C-1 and C-2 of the diphenylpropane and in the 1-phenylpropane produced from it.[14]

There is another significant factor to be considered in comparing the reaction of 1-phenylpropane and 1-phenylbutane with aluminum halides. In the first step of Scheme I, hydride abstraction from the β carbon opens the way for production of a 1,2-diphenylalkane intermediate, which is essential for allowing the 1,2 shift of a methyl or ethyl group without producing a primary carbocation. In the case of 1-phenylbutane, hydride abstraction may take place at either the 2 carbon or the 3 carbon, producing a secondary carbocation in either event (**10** and **11** in Scheme II). The capability of forming the carbocation **11** by attack at the 3 position with subsequent production of a 1,3-diphenylalkane as well as indan and indene derivatives, as outlined in Scheme II, is of course not possible for 1-phenylpropane *except via a primary carbocation.* We proposed that this difference in the structure of 1-phenylpropane and 1-phenylbutane was mainly responsible for the lesser resistance of the higher homologue to structural modification by aluminum chloride, and indeed that the additional reaction capability of 1-phenylbutane might well be an important factor in its failure to show isotopic automerization comparable to that of 1-phenylpropane. Thus

Scheme II

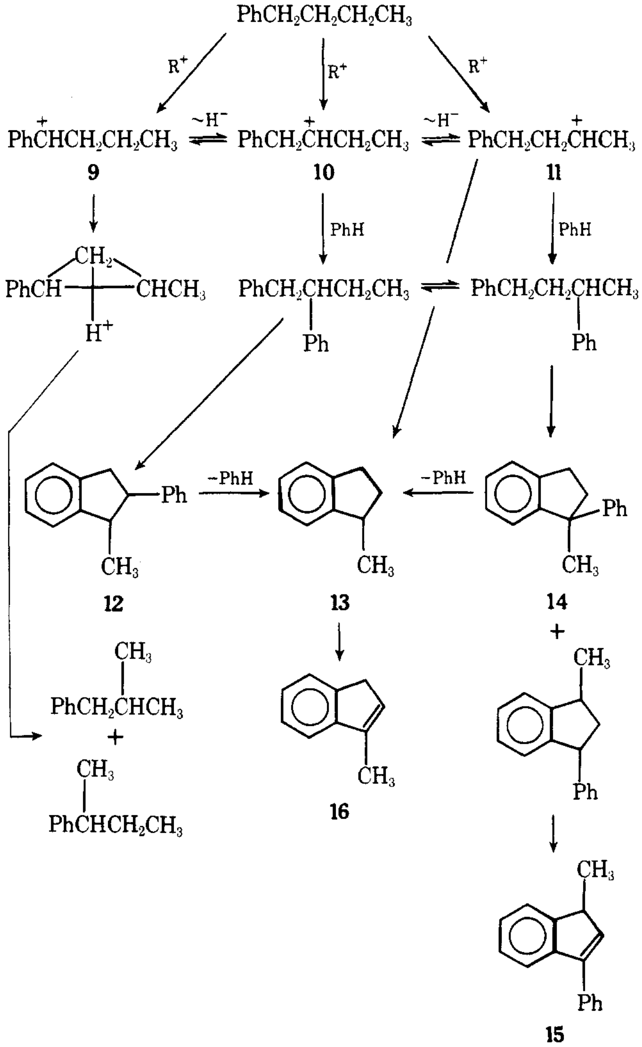


Table V. Products from the Reaction of 1-Phenylbutane in Benzene with Water-Activated Aluminum Chloride[a]

Temp, °C	24			52			81		
Time, h	1	6	13	1	2	4	0.5	1	2
Products	Relative distributions, wt %[b]								
1-Phenylbutane	84	54	50	84	65	60	43	51	50
2-Phenylbutane		Tr	0.5		1.5[c]	3[c]	8[c]	14[c]	14[c]
1-Methylindan							3	5	2
3-Methylindene		0.2	1		1	1	3	9	16
Dibutylbenzenes	16	45.5	48	16	31.5	33.5	39	15	6
Phenylcyclohexane									3
3-Methyl-6-butylindene							0.5	2	6
1,2-Diphenylbutane									0.5
1,3-Diphenylbutane		0.3	0.5	Tr	1	2	2	2	1
1-Methyl-3-phenylindene					Tr	0.5	1.5	2	1.5

[a] Molar ratios, 1-phenylbutane:benzene:aluminum chloride:water = 1:6:1:0.2. [b] Higher molecular weight compounds such as tributylbenzenes were not included in these distributions. [c] Assumed to contain isobutylbenzene, which is not separated by the GLC column.

Table VI. Treatment of 1,3-Diphenylbutane and 1,2-Diphenylbutane in Benzene

	Starting material	
Products, %	1,3-DPB	1,2-DPB
1-Phenylbutane	17	13
1-Methylindan	35	5
3-Methylindene	7	3
1,2-Diphenylpropane		3
1,2-Diphenylbutane	7	73
1,3-Diphenylbutane	34	3

a careful examination was made of the products formed from 1-phenylbutane and aluminum chloride.

Treatment of 1-phenylbutane with aluminum chloride in benzene at reflux temerature (ca. 82 °C) produced a variety of products that may be classified as (1) transalkylation products (di- and tributylbenzene); (2) rearrangement products (2-phenylbutane and isobutylbenzene); (3) cyclialkylation products (1-methylindan, 3-methylindene, 3-methyl-6-butylindene, 1-methyl-3-phenylindene); and (4) alkylation products (1,2- and 1,3-diphenylbutane). The progress of the reaction was monitored by withdrawing aliquots after various time intervals from reactions run at reflux and at lower temperatures, and analyzing the product aliquots by GLC and mass spectrometry. The results from samples taken after three reaction times at three different temperatures are shown in Table V.

Considering first the reaction at 24 °C, the initial products were dibutylbenzenes, formed by transalkylation (disproportionation).[15] After 13 h these were still the major products, with only traces of rearrangement, cyclialkylation, and alkylation products having appeared. The results of the reaction at 55 °C were similar, but the minor products appeared sooner, as might be expected. At 82 °C the rearrangement and cyclialkylation reactions became much more significant. 1,2-Diphenylbutane was detected for the first time after a 2-h reaction time and 1,3-diphenylbutane was present in slightly larger amount. No 1,1- or 1,4-diphenylbutane was detected.

All of the cyclialkylation products (indans and indenes) in the reaction mixture from the 2-h treatment at 82 °C can be rationalized as derived from the carbocation **11** produced from 1-phenylbutane by hydride abstraction at C-3. For example, 1-methylindan (**13**) and 3-methylindene (**16**) may be produced by the direct cyclization of **11**, or by its alkylation to 1,3-diphenylbutane followed by cyclization to 1-methyl-1-phenylindan (**14**) and dephenylation. 1,3-Diphenylbutane may also be formed from 1,2-diphenylbutane by a 1,2-phenyl shift. The facility of this latter route could be tested. If the two diphenylbutanes are readily interconverted, they should give the same product mixtures when treated separately and identically with aluminum chloride. In Table VI it may be seen that they were not readily interconverted and that they gave quite different mixtures of products when heated with aluminum chloride in benzene at 55 °C. Calculated on the basis of the diphenylbutane converted, 1,2-diphenylbutane gave 48% dealkylation to 1-phenylbutane and 30% cyclization (to 1-methylindan and 3-methylindene), whereas 1,3-diphenylbutane gave 26% dealkylation and 64% cyclization. Although these results did not rule out interconversion of the two diphenylbutanes, it showed that they do not reach an equilibrium composition before secondary reactions set in.

1-Methylindan (**13**) and 3-methylindene (**16**) might also be derived from carbocation **10** via 1,2-diphenylbutane and 1-methyl-2-phenylindan (**12**). However, the small extent of cyclialkylation of 1,2-diphenylbutane to **13** and **16** made this route appear less important than the route from **11** via 1,3-diphenylbutane and 1-methyl-1-phenylindan (**14**).

Conclusions

The difference in the degree of isotopic automerization which 1-phenylpropane-*1*-^{13}C and 1-phenylbutane-*1*-^{13}C undergo in reaction with aluminum chloride can reasonably be ascribed to two main factors. One is the ability of 1-phenylbutane to give a secondary carbocation at the 3 position of the side chain leading to 1,3-diphenylbutane and several indan and indene derivatives by cyclialkylation. Reaction of 1-phenylpropane with aluminum chloride gives 1,2-diphenylpropane, rather than 1,3-diphenylpropane, and subsequent methyl shifts in carbocations derived from the 1,2-diphenylpropane may lead to automerization of isotopic carbon between the 1 and 2 positions of 1-phenylpropane. The second factor is that even though some 1,2-diphenylbutane may be produced from 1-phenylbutane, the ethyl shifts which would lead to automerization do not take place readily, as has been demonstrated by the lack of automerization of 1,2-diphenylbutane-*2*-^{13}C.

Experimental Section

Synthesis of 1-Phenylbutane-*1*-^{13}C. 1-Phenylbutane-*1*-^{13}C was prepared by the method used to prepare 1-phenylpropane-*1*-^{14}C.[16] The reaction of the carbon dioxide produced from barium carbonate-^{13}C (6.4 g, 32 mmol, Monsanto Chemical Co., Mound Lab, A. E. C., 92.9 mol % ^{13}C) with *n*-propylmagnesium bromide gave sodium butanoate-*1*-^{13}C. Acylation of benzene with the sodium butanoate-*1*-^{13}C in the presence of aluminum chloride produced butyrophenone-*1*-^{13}C, which was catalytically (Pd/C) hydrogenated to 1-phenylbutane-*1*-^{13}C. When very vigorous conditions [hydrogen pressure 72 psig, 2.4 g of butyrophenone-*1*-^{13}C, 1.2 g of Pd/C (5%) in 80 mL of glacial acetic acid and 2 mL of perchloric acid (72%) reacting for 24 h] were used, a mixture containing about 75% 1-cyclohexylbutane and 25% 1-phenylbutane-*1*-^{13}C was produced. Better results were obtained with more moderate conditions; no 1-cyclohexylbutane was formed using hydrogen pressure 72 psig, 2.5 g of butyrophenone-*1*-^{13}C, 0.80 g of Pd/C (5%) in 80 mL of glacial acetic acid, and 9 drops of perchloric acid (72%) shaken for 2 h (Parr hydrogenator). Preparative GLC (30% SE-30 on Chromosorb P) afforded the product in 30% yield based on ^{13}C.

Di- and Tri-*n*-propylbenzenes. A sample of 1-phenylpropane (4.0 g, 33 mmol) was treated with aluminum chloride (2.7 g, 20 mmol) at room temperature with stirring for 20 h. The reaction mixture was quenched with water, and the organic product mixture was distilled (boiling range 40–84 °C, 0.1 mm). Analysis of the product mixture (3.1 g) by GLC, using a Varian 600-D instrument with a 10 ft × 0.125 in. (5%) SE-30 column operating at 182 °C, indicated that the product mixture contained 39% (by weight) 1-phenylpropane, 33% di-*n*-propylbenzenes, and 28% tri-*n*-propylbenzenes.

Di- and Tri-*n*-butylbenzenes. A sample of 1-phenylbutane (4.2 g, 31 mmol) was treated with aluminum chloride (2.7 g, 20 mmol) at room temperature with stirring for 12 h. The reaction mixture was quenched with water, and the organic product mixture was distilled (boiling range 45–98 °C, 0.1 mm). Analysis of the product mixture (3.8 g) by GLC under the same conditions as described above indicated that the mixture contained 60% (by weight) 1-phenylbutane, 20% di-*n*-butylbenzenes, and 20% tri-*n*-butylbenzenes.

1,3-Diphenylbutane. A pure sample of 1,3-diphenylbutane prepared by Dr. Ali A. Khalaf[10] was used as the source of this compound.

1-Methylindan. 1-Methylindan was prepared by the method of Khalaf and Roberts.[17]

Treatment of 1-Phenylbutane-*1*-^{13}C with Aluminum Halides. Three samples of 1-phenylbutane-*1*-^{13}C (160 mg, 1.20 mmol, 26.3 mol % monolabeled) were treated with aluminum chloride in the presence of benzene and water in a 1.0:0.5:6.0:0.1 mole ratio, respectively, at reflux (heated by oil bath at 85 °C) for 7 h. The reaction conditions and workup were the same as those used for the 1-phenylpropane-*1*-^{13}C rearrangement.[5] The treated 1-phenylbutane-*1*-^{13}C was recovered by preparative GLC with a Varian Autoprep A-700 instrument on a 12 ft × 0.375 in. SE-52 column at 95 °C giving 78.2 mg (49%), 73.9 mg (46%), and 81.7 mg (51%) in expt 1, 2, and 3, respectively (Table I).

Experiments 4–7 were carried out similarly with samples of 1-phenylbutane-*1*-^{13}C which were 40.9 mol % labeled, and the mole ratios of $C_{10}H_{14}$:$AlCl_3$:C_6H_6:H_2O were varied as follows: expt 4, 1:0.5:6:0.1; expt 5, 1:0.75:6:0.15; expt 6, 1:0.5:6:0; expt 7, 1:0.5:6:0.2. The reaction time was 8 h in expt 5 and 6.5 h in the others. Experiment 8 was carried out in a sealed NMR tube with a 180-mg (1.3 mmol) sample of 1-phenylbutane-*1*-^{13}C, 40.9 mol % monolabeled, which was heated at 95 °C for 9 h with $AlBr_3$, benzene, and water in the mole ratio 1:0.5:4:0.1. The recovery of 1-phenylbutane in expt 4–7 ranged from 22 to 42%. The results of mass spectrometric analysis of expt 1–8 are given in Table I.

The 1-phenylbutane samples recovered from expt 1, 3, 4, 5, and 7 were examined in a Perkin-Elmer R-12 NMR spectrometer. The integrals of the ^{1}H triplet centered at δ 2.66 ppm and its ^{13}C satellite centered at δ 3.66 ppm showed the same ratio in samples before and after heating with aluminum chloride. The sample heated with aluminum bromide was monitored by NMR after 2.2, 6, and 9 h and showed no change.

Treatment of Mixtures of 1-Phenylpropane-*1*-^{13}C and 1-Phenylbutane-*1*-^{13}C with Aluminum Halides. These experiments were conducted as indicated in Table II.

Treatment of 1-Phenylpropane-*1*-^{13}C with Aluminum Chloride in the Presence of Various Hydrocarbons. These experiments were conducted as described in the text and in Tables III and IV.

Synthesis of 1,2-Diphenylbutane-*2*-^{13}C. Sodium propionate-*1*-^{13}C was prepared by carbonating ethylmagnesium bromide (70 mmol) with $^{13}CO_2$ produced from 5.92 g (30 mmol) of barium carbonate (92 mol % ^{13}C, Monsanto Chemical Co., Mound Lab, A. E. C.) and 20 mL of 85% phosphoric acid according to conventional procedures. The usual workup yielded 2.15 g (75%) of sodium propionate-*1*-^{13}C.

Propiophenone-*1*-^{13}C was synthesized by the reaction of the sodium propionate-*1*-^{13}C (2.15 g, 22 mmol) with benzene (50 mL) in the presence of anhydrous aluminum chloride (12 g, 90 mmol), heating under reflux with stirring for 10 h. The reaction mixture was cooled and decomposed with cold dilute hydrochloric acid and extracted with ether; the ether solution was washed with water and dried over $MgSO_4$. One gram of ordinary propiophenone was added to the ether solution, the ether was distilled at atmospheric pressure, and the residue was distilled to give 3.0 g of propiophenone-*1*-^{13}C, bp 64–65 °C (1 mm). Assuming the distilled product to contain all of the added ordinary propiophenone, the yield of labeled material was 68%.

Propiophenone-*1*-^{13}C (2.8 g, 21 mmol) was allowed to react with 40 mmol of benzylmagnesium chloride. Reduction of the resulting alcohol using hydrogen with Pd/C catalyst in 100 mL of glacial acetic acid and 0.5 mL of perchloric acid at a pressure of 60 psi gave 4.3 g (94%) of 1,2-diphenylbutane-*2*-^{13}C, bp 91–94 °C (0.2 mm). The product was further purified by preparative gas chromatography.

The pure 1,2-diphenylbutane-*2*-^{13}C was analyzed by mass spectrometry and ^{13}C NMR. By comparing the parent peak (P) at *m/e* 210 and the P + 1 peak at *m/e* 211 of the unlabeled compound with the same peaks in the mass spectrum of the labeled compound, and making calculations according to the method of Biemann,[8] the degree of ^{13}C labeling was found to be 58%. The ^{13}C NMR spectrum (Varian HA-100) of unlabeled 1,2-diphenylbutane in dioxane showed four equal peaks at 1.88 (C-2), 2.66 (C-1), 3.28 (C-3), and 6.14 ppm (C-4) relative to dioxane. The labeled product showed only one peak at 1.88 ppm (C-2).

Reaction of 1,2-Diphenylbutane-*2*-^{13}C with Aluminum Chloride. Treatment of the labeled hydrocarbon with anhydrous aluminum chloride in benzene (molar ratio 1:0.5:6, respectively) for 1 h at reflux temperature gave a mixture that consisted mainly of the starting material and 1-phenylbutane. These were separated by preparative GLC.

Recovered 1,2-diphenylbutane showed two peaks in the ^{13}C NMR spectrum with relative intensities corresponding to 92% at C-2 and 8% at C-1.

By comparing the P and P + 1 peaks in the mass spectrum of the 1-phenylbutane isolated from the reaction with the same peaks in the spectrum of ordinary (unlabeled) 1-phenylbutane, it was possible to determine that the total ^{13}C mol % was 59, and by comparing the *m/e* 91 and 92 peaks[9] it was shown that 5.7 mol % of ^{13}C was at C-1, corresponding to 9.7% rearrangement.

The experiment was repeated using the same proportion of 1,2-diphenylbutane-2-^{13}C, benzene, and aluminum chloride, but heating for 7 h under reflux. Using the same technique and calculations as before, the 1-phenylbutane produced was found to contain 4.5 mol % ^{13}C at C-1, corresponding to 7.6% rearrangement.

Reaction of 1-Phenylbutane with $AlCl_3$–H_2O in Benzene. 1-Phenylbutane (13.4 g, 0.10 mol), benzene (47 g, 0.60 mol), $AlCl_3$ (13.3 g, 0.10 mol), and water (0.36 mL, 0.020 mo) were heated and stirred under reflux for 8 h. The cooled reaction mixture was quenched with cold dilute hydrochloric acid and extracted with ether. The ether extract was dried over K_2CO_3 and distilled to remove the ether. The residue was distilled through a 2-cm Vigreux column. Three fractions were collected: (1) 0.7 g, bp 80–160 °C; (2) 6.2 g, bp 169–180 °C; (3) 0.5 g, bp 130–170 °C (0.2 mm); residue, 2.4 g. The distillate fractions were separated further by preparative GLC using a 6 ft × 0.25 in. 10% SE-30 silicone column and the components, identified by NMR and mass spectrometry, with approximate yields, were as follows: 1-phenylpropane (4%), 2-phenylbutane (9%), 1-phenylbutane (59%), 1-methylindan (8%), 3-methylindene (4%), phenylcyclohexane (4%), 1,2-diphenylbutane (1.5%), 1,3-diphenylbutane (3%), and 1-methyl-3-phenylindene (1.5%).

Experiments were then performed in which 2-mL aliquot samples were withdrawn from the reaction mixtures after stated time intervals and analyzed by GLC on a 6 ft × 0.125 in. 10% SE-30 and a 5 ft × 0.125 in. 10% UCON column. The results of reactions at three different temperatures are presented in Table V.

Registry No.—Barium carbonate-^{13}C, 51956-33-3; sodium butanoate-*1*-^{13}C, 62601-04-1; butyrophenone-*1*-^{13}C, 62601-05-2; sodium propionate-*1*-^{13}C, 62601-06-3; propiophenone-*1*-^{13}C, 62601-07-4; 1,2-diphenylbutane-*2*-^{13}C, 62601-08-5; 1-phenylbutane-*1*-^{13}C, 62601-09-6; 1-phenylpropane-*1*-^{13}C, 62601-10-9; 1-phenylbutane, 104-51-8; 1,3-diphenylbutane, 1520-44-1; 1,2-diphenylbutane, 5223-59-6.

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Nucleophilic Substitution in the Side Chain of Five-Membered Heterocycles. 3. Reactions of Heterocyclic Aldehydes with Aniline and with Benzoylmethylenetriphenylphosphorane

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The rate constants for the reactions of five-membered heteroaromatic aldehydes with aniline in acetonitrile (Schiff reaction) and with benzoylmethylenetriphenylphosphorane in methanol (Wittig reaction) were measured in order to attempt structure–reactivity correlations. The observed reactivity sequence (2-furyl > phenyl > 2-thienyl > 2-pyrrolyl) is the same as previously found in other substitutions at the carbonyl group. The electron-donating character of the heteroatoms in the Schiff reaction is proved by the Hammett treatment of the data. However, extension of this treatment to other reactions at the carbonyl group does not give constant σ_{het} values. Application of the Taft–Pavelich eqation points out a dependence of the rate of reaction on polar and steric effects of heteroaromatic rings. Information from Hammett and Taft–Pavelich equations, however, is not unequivocal owing to inherent features of both free-energy relationships.

In previous articles of this series kinetic data for the reactions of arylmethyl chlorides[1] and arenesulfonyl chlorides[2] with aniline were reported, in order to correlate the reactivity of five-membered heterocycles with that of benzene derivatives and to attempt structure–reactivity correlations. However, no generalization was drawn owing to different behavior of heterocyclic compounds in different kinds of reactions.

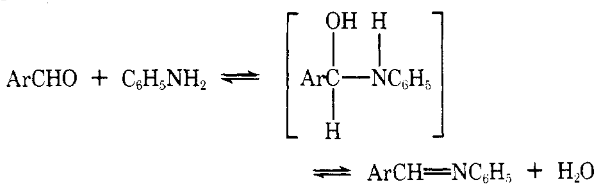
In fact, the reactivity sequence (2-furyl > 2-thienyl > phenyl) observed for the reaction of arylmethyl chlorides with aniline[1] appears to be in agreement with the polarity of heterocycles, given by σ^* values,[3] while the rate sequence for the reaction of arenesulfonyl chlorides with aniline[2] (phenyl > 2-furyl > 2-thienyl) suggests that the conjugative effect, described by σ^+ values, appears to be prevailing.[4,5]

Moreover, a different reactivity sequence (2-furyl > phenyl > 2-thienyl) is observed in some nucleophilic substitutions at the carbonyl group, as in the reaction of arylcarbonyl chlorides with aniline,[6] of aryl chloromethyl ketones with triethyl phosphite,[7] in the alkaline hydrolysis of esters[3] and in the reduction of aryl methyl ketones by sodium borohydride.[8] This fact might formally derive from the balance between the opposite electronic effects in the five-membered heterocycles (−I, +M), even if the role of steric factors in some of these reactions cannot be neglected.[3,9]

To verify the specificity of this sequence for reactions at the carbonyl group, we here report kinetic data relative to the reactions of heterocyclic aldehydes with aniline (Schiff reaction), and with benzoylmethylenetriphenylphosphorane (BMTPP) (Wittig reaction). In this paper we intend also to rationalize the data on nucleophilic substitutions at the carbonyl group in the side chain of five-membered heterocycles, using free-energy relationships.

Results

Reactions of Aldehydes with Anilines. The Schiff base formation from aromatic aldehydes and amines (reaction 1) is a well-known two-step addition–elimination reaction, in which the rate-determining step depends on the aromatic ring structure and on experimental conditions (solvent, pH).[10–12]



$$\mathrm{ArCHO} + \mathrm{C_6H_5NH_2} \rightleftharpoons \left[\mathrm{Ar}\overset{\overset{\displaystyle OH}{|}}{\underset{\underset{\displaystyle H}{|}}{C}}-\overset{\overset{\displaystyle H}{|}}{N}\mathrm{C_6H_5}\right] \rightleftharpoons \mathrm{ArCH{=}NC_6H_5} + \mathrm{H_2O} \qquad (1)$$

Ar = 2-C_4H_3S, 2-C_4H_3NH, *p*-$(CH_3)_2NC_6H_4$, *p*-$CH_3OC_6H_4$, *p*-$CH_3C_6H_4$, *p*-ClC_6H_4, *p*-$O_2NC_6H_4$

Acetonitrile was chosen as a solvent because, being dipolar, it allows an appreciably fast kinetics in the absence of catalyst; moreover, being aprotic, it prevents the hydrolysis of the Schiff bases, a phenomenon that would not give quantitative yields.[13]

The reaction was followed by monitoring the UV absorbance of the Schiff base (see Experimental Section). The kinetics is second order overall, first order with respect to each reactant, as expected for an uncatalyzed reaction, according to the simple rate law

$$\text{rate} = k_2[\text{aldehyde}][\text{nucleophile}] \qquad (2)$$

Rate constants at 25 °C are reported in Table I, showing that the reactivity sequence is the following: phenyl > 2-thienyl > 2-pyrrolyl. The k_2 value for 2-furaldehyde is not re-