TABLE VI
$AlR_3 \cdot Do$ COMPOUNDS PREPARED

$AlR_3 \cdot Do$	Bp, °C (0.5 mm)	Calcd Al, %	Calcd Mol wt	Calcd R_3Al/Do	Found Al, %	Found Mol wt	Found R_3Al/Do^b	Nmr[a] δ_{CH_3C}	Nmr[a] δ_{CH_2Al}	Nmr[a] $\Delta\delta_{CH_2CH_3}$	ΔH_f,[c] kcal/mol
$Et_3Al \cdot OEt_2$	63–64	14.33	188.3	1.00	14.32	180.5	1.00	1.41	0.17	−1.24	11.2[d]
$Et_3Al \cdot THF$	62–63	14.49	186.3	1.00	14.35	183.2	0.97	1.44	0.20	−1.24	14.0[d]
$Et_3Al \cdot NEt_3$	77–78	12.53	215.4	1.00	12.58	214.8	0.99	1.53	0.25	−1.28	
$Et_3Al \cdot Py$	92–93	13.96	193.3	1.00	13.89	191.1	0.91	1.46	0.37	−1.09	19.4[d]
$Me_3Al \cdot OEt_2$	22.5–23	18.45	146.2	1.00	17.45	146.6	1.00		−0.45[f]		20.2[e]
$Me_3Al \cdot THF$	31–32	18.71	144.2	1.00	17.56	148.0	1.00		−0.50[f]		22.9[e]
$Me_3Al \cdot NEt_3$	Mp 66	15.57	173.3	1.00	14.59	163.8	0.98		−0.41[f]		26.5[e]
$Me_3Al \cdot Py$	64–66	17.85	151.2	1.00	17.41	148.2	1.00		−0.29[f]		17.5[e]

[a] Chemical shift in benzene solution at 60 MHz. Values are internally standardized from benzene proton assumed as 7.37 ppm. [b] Determined from nmr spectra. [c] Heats of formation of complexes $AlR_3 \cdot Do$. [d] Reference 19. [e] Reference 20. [f] δ_{CH_3Al}.

Reaction of Acetaldehyde with R_2AlZM.—For Et_2AlOLi four runs were carried out with 3 molar equiv of acetaldehyde for 24 hr (at −78°, −20, and 0°) and with 100 molar equiv of acetaldehyde for 20 hr at 0°. Acetaldehyde was recovered almost unchanged. No detectable peaks were observed other than the solvent and the starting aldehyde. For Me_2AlOLi, three runs were made with 3 molar equiv of acetaldehyde for 20 hr at −78, −20, and 0°. The results were identical with the case of Et_2AlOLi. For $Et_2AlNPhLi$, two runs were made of reactions with 3 molar equiv of acetaldehyde for 20 hr at −78 and at −20°. The results were also identical with the case of Et_2AlOLi. For Et_2AlSNa, with 3 molar equiv of acetaldehyde, the reaction for 24 hr at −78° was identical with the case of Et_2AlOLi. At −20°, 0.14 molar equiv of ethyl acetate was observed as a sole reaction product. With 100 molar equiv of the aldehyde, 1.08 molar equiv of ethyl acetate accompanied by trace amounts of ethanol, methyl ethyl ketone, and *sec*-butyl acetate was detected after 24 hr at −20°.

Registry No.—Acetaldehyde, 75-07-0.

Acknowledgment.—We are grateful to Messrs. N. Oguni and M. Mikumo for preparation of some organoaluminum complexes.

A Mechanistic Study of the Reaction of Lithium Aluminum Hydride with *N*-Methylbenzanilides

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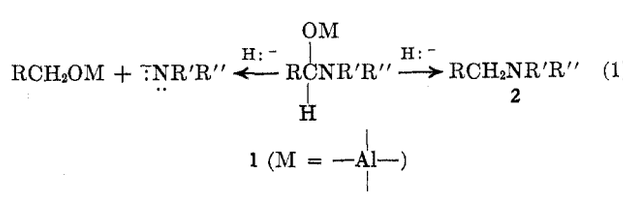
The relative rates of reduction *vs.* cleavage for various *N*-methylbenzanilides under the influence of lithium aluminum hydride are strongly dependent on the nature of substituents in the *N*-phenyl group. The effect of substituents in the *C*-phenyl moiety is small. The mechanistic implications of these observations are discussed. Investigations directed towards using *N*-methyl-*p*-chloranilides for the preparation of aldehydes and the use of $LiAlH_4$–$AlCl_3$ for the reduction of *N*-methylbenzanilide are also described.

The reduction of tertiary carboxamides with lithium aluminum hydride normally results in the formation of the corresponding amine.[1] In a significant number of cases, however, reductive cleavage (hereafter referred to simply as cleavage) of the peptide bond occurs to yield an aldehyde and/or an alcohol, as well as the amine derived from the cleavage process.[1-7] In spite of the great utility of both types of reactions in the synthesis of amines and aldehydes, no systematic study of electronic factors and their influence on the relative importance of reduction *vs.* cleavage has been conducted. Accordingly, we have conducted such a study in hopes of increasing the mechanistic understanding and synthetic utility of these reactions.

Both the reduction and cleavage of tertiary carboxamides are commonly believed to result from partitioning of an initially formed tetrahedral adduct (**1**).[1-4] Aldehyde has been proposed to result from hydrolysis of **1**, while the other products arise from nucleophilic attack by hydride on **1** (eq 1).[2] An alternate proposal[8] suggests that expulsion of amide ion from **1** yields aldehyde,[9] while formation and subsequent reduction of **3** is responsible for the "normal" reduction process to yield **2** (eq 2).



(1) N. G. Gaylord, "Reduction with Complex Metal Hydrides," Interscience, New York, N. Y., 1956, Chapter 10.
(2) H. C. Brown and A. Tsukamoto, *J. Amer. Chem. Soc.*, **83**, 4549 (1961).
(3) W. Weygand, E. Eberhardt, H. Linden, F. Schofer, and I. Eigen, *Angew. Chem.*, **65**, 525 (1953).
(4) V. M. Micovic and M. L. Mihailovic, *J. Org. Chem.*, **18**, 1190 (1953). These authors suggest different intermediates for reduction and cleavage. They subsequently propose a single intermediate for both processes; see V. M. Micovic and M. L. Mihailovic, "Lithium Aluminum Hydride in Organic Synthesis," Izdavacko Preduzece, Belgrade, Yugoslavia, 1955, pp 58–60.
(5) F. Weygand and R. Mitgau, *Chem. Ber.*, **88**, 301 (1955).
(6) H. C. Brown and A. Tsukamoto, *J. Amer. Chem. Soc.*, **81**, 502 (1959).
(7) T. Axenrod, L. Loew, and P. S. Pregosin, *J. Org. Chem.*, **33**, 1274 (1968).
(8) Reference 1, p 545.
(9) Further reduction by $LiAlH_4$ would, of course, produce the corresponding alcohol.

The above mechanisms are based on experiments directed towards optimizing aldehyde yields. Accordingly, the main thrust of previous studies has been to delineate those structural features which enhance the rate of formation of **1** relative to subsequent steps.[10] In contrast, our experiments were designed to study the partitioning of **1** between the available reaction routes.

Experimental Design.—The *N*-methylbenzanilide system was selected for these studies since *N*-methylanilides had previously been shown to undergo cleavage,[3] substituents of varying electronic properties could be introduced while maintaining a constant steric environment about the reaction center, and finally certain desirable substituents were expected to be inert to $LiAlH_4$ under our reaction conditions.[11]

A 100% excess of standardized[12] $LiAlH_4$ solution (ether) was injected into a stirred amide solution contained in a bath thermostated at 25°. In spite of rigorous drying of reagents and equipment, small amounts of precipitate commonly separated at this stage. To minimize the significance of possible surface effects and for other reasons which are stated below, equimolar amounts of *N*-methylbenzanilide and the substituted *N*-methylbenzanilide were combined and simultaneously treated with $LiAlH_4$ in the same reaction vessel. After hydrolysis, analyses were conducted by quantitative glpc.

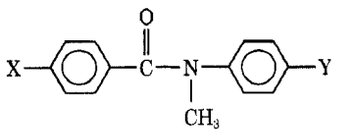
Each run thus produced benzyl alcohol, *N*-methylaniline, and *N*-methyl-*N*-benzylaniline. By comparing the yield of substituted benzyl alcohol or *N*-methylaniline with that of the unsubstituted material, a direct study of substituent effects on cleavage could be made under identical reaction conditions. Similarly, the effect of the substituents on reduction could be evaluated by comparing yields of the two tertiary amines. Any change in the nature of the reducing agent caused by traces of impurities such as water or by the interaction of reaction products with $LiAlH_4$, which could conceivably result in anomalous reduction *vs.* cleavage rates for the substituted compound, should be reflected in the reaction of *N*-methylbenzanilide as well.[13] The latter reaction thus served as a standard reaction for each run, and only the difference in reactivity between the standard and the substituted amide (Δ values given in Table I) need be considered for our purposes.

Results

The results of our studies are summarized in Table I. No products other than those expected from reduction and cleavage were observed in any of the reactions. Except where noted, each entry is the average of results for at least two different reactions. In at least one of the reactions for each entry the material balance exceeded 90%, and the percentages given are percentages of the reaction mixture. Product distributions for reactions yielding poorer material balances (generally >80%) did not vary significantly from reactions with good material balances. The per cent cleavage of *N*-methylbenzanilide (the standard reaction) for the 15 reactions yielding the data in Table I was 80 ± 5%.

TABLE I

SIMULTANEOUS REDUCTION OF *N*-METHYLBENZANILIDE AND SUBSTITUTED *N*-METHYLBENZANILIDE



Entry	Registry no.	Unsubstituted % cleavage	Substituted X	Substituted Y	Substituted % cleavage	Δ[d]
1[a]	1934-92-5	83				
2[b]	33672-81-0	84	OMe	H	72	12
3[b]	37950-87-1	80	F	H	86	−6
4[a]	1517-46-0	80	Cl	H	73	7
5[a]	33675-68-2	80	H	OMe	35	45
6[c]	2054-12-8	88	H	F	83	5
7[a]	10278-51-0	70	H	Cl	86	−16

[a] Average of two runs. [b] Average of three runs. [c] Single run; ratio of tertiary amines determined by nmr; see Table VI. [d] Δ = % cleavage for unsubstituted minus % cleavage for substituted.

Discussion

Reasonably constant values for the per cent cleavage of *N*-methylbenzanilide were obtained for all reactions except for those yielding data for entry 7 of Table I. Those values were reproducible (69%, 71%), and their large deviation from the mean (81 ± 3% excluding these data) may indicate some alteration in the nature of the reducing agent during the reaction progress.

Assuming that **1** is a common intermediate in the foregoing reactions, our data must be considered in terms of the effect of substituents on the competitive processes of reduction to tertiary amine and cleavage to a benzyl alcohol and an *N*-methylaniline. Hence, we discuss substituents in terms of their effect on the *relative* rates of reduction *vs.* cleavage for each amide.

Examination of Δ values in Table I for entries 5, 6, and 7 reveals that substituents in the *N*-phenyl group promote cleavage relative to reduction in the order *p*-Cl > *p*-H > *p*-F > *p*-OCH_3. This ordering conforms to the order of increasing σ^+ constants[14] and provides experimental support for the previously proposed mechanisms for cleavage (eq 1 and 2) both of which require enhancement in the rate of cleavage relative to reduction as the basicity of the departing nitrogen is decreased.[15]

The effects of substituents in the *C*-phenyl moiety on the relative rates of reduction and cleavage, as can be seen from entries 2, 3, and 4, were quite small. Moreover, decreased cleavage was observed for both *p*-methoxy (σ −0.27)[16] and *p*-chloro (σ 0.27).[16] We can provide two plausible explanations for this behavior.

(10) In the presence of a stoichiometric quantity of $LiAlH_4$, the maximum yield of aldehyde would be obtained if all the hydride were consumed in the formation of **1**. Aldehyde yields decrease to the extent that **1** or its reaction products react with hydride. Rapid formation of **1** is favored by decreased p–π interaction in the peptide bond and low steric requirements for groups bonded to nitrogen.

(11) G. J. Karabatsos and R. L. Shone, *J. Org. Chem.*, **33**, 619 (1968).

(12) H. Felkin, *Bull. Soc. Chim. Fr.*, **18**, 347 (1951).

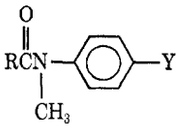
(13) Lithium alkoxyaluminum hydrides, for example, are known to be weaker reducing agents than $LiAlH_4$: H. C. Brown, *J. Chem. Educ.*, **38**, 173 (1961).

(14) J. Hine, "Physical Organic Chemistry," McGraw-Hill, New York, N. Y., 1962, p 90.

(15) (a) E. S. Gould, "Mechanism and Structure in Organic Chemistry," Holt, Rinehart and Winston, New York, N. Y., 1959, p 261; (b) reference 14, p 182.

(16) G. B. Barlin and D. D. Perrin, *Quart. Rev., Chem. Soc.*, **20**, 75 (1966).

TABLE II
COMPARISON OF ALDEHYDE YIELDS FROM SUBSTITUTED N-METHYLBENZANILIDES



R	Y	Yield,[a] %	Lit. yield, %
C_6H_5	H	70	68[b]
C_6H_5	Cl	72	
p-$CH_3OC_6H_4$	H		51[c]
p-$CH_3OC_6H_4$	Cl	51	
o-$CH_3OC_6H_4$	H		30[b]
o-$CH_3OC_6H_4$	Cl	25	

[a] Yields were determined by the weight of unpurified 2,4-DNP derivatives, all of which had narrow melting ranges and agreed with literature values. [b] Reference 3. [c] Reference 5.

Assuming that the Brown mechanism (eq 1) is correct, the observed substituent effects are similar to those generally found for bimolecular nucleophilic substitution on benzyl halides.[17] Only if bond breakage in the transition state were equivalent for both C–N and C–O cleavage should no substituent effect be observed. The effect should be qualitatively the same for both processes, and hence one might anticipate only small substituent effects.

Alternatively the observed substituent effects may indicate a change in mechanism caused by the variation of substituents. If, for example, **1** were being partitioned simultaneously between the four processes outlined in eq 1 and 2, one would not necessarily anticipate a simple relationship between σ constants and the relative rates of reduction and cleavage. Substituents could clearly influence the rates of all four processes and thereby determine the predominant mechanism.

Studies with a "Mixed" Hydride Reagent.—Modifications in the reaction technique which would enhance reduction relative to cleavage would be of some synthetic utility. It has been reported[18] that use of $LiAlH_4$–$AlCl_3$ in place of $LiAlH_4$ alone significantly decreases the extent of cleavage of *N*-acetylpyrrole.

We accordingly investigated the use of $LiAlH_4/AlCl_3$ ratios of 1:1 and 1:2 in the reduction of *N*-methylbenzanilide. The product distributions observed for these reactions were virtually unchanged from that observed in previous reactions using $LiAlH_4$ alone.

Use of *N*-Methyl-*p*-chloroanilides for Aldehyde Preparation.—Successful aldehyde synthesis *via* partial reduction of tertiary carboxamides with $LiAlH_4$ should require rapid formation of **1** and relatively slower loss of amide ion. Since both of these processes should be enhanced by electron-withdrawing substituents in the *N*-phenyl group, the net result of such a substituent on the obtainable yield of aldehyde is uncertain. Accordingly, we conducted a series of experiments with the *N*-*p*-chlorophenyl group to evaluate its effect on aldehyde yield. The results summarized in Table II suggest that this group increases the rate of formation of **1** to about the same extent as subsequent steps and indicate a lack of synthetic advantage in using the *N*-*p*-chlorophenyl group in such reactions.

(17) A. Streitwieser, *Chem. Rev.*, **56**, 571 (1956); see also ref 14, p 172.
(18) R. F. Nystrom and C. Rainer Berger, *J. Amer. Chem. Soc.*, **80**, 2896 (1958).

Experimental Section

Lithium Aluminum Hydride Stock Solution.—Lithium aluminum hydride (15.20 g, 0.40 mol) was extracted with 350 ml of anhydrous ether using a Soxhlet extractor. The resultant solution was standardized[12] before each use and was found to be 1.2–1.5 *M*.

Substituted Benzyl Chlorides.—To a refluxing solution of 8.00 g (0.063 mol) of 4-fluorobenzyl alcohol and 5 ml of pyridine in 50 ml of benzene was added dropwise with stirring 7.54 g (0.063 mol) of thionyl chloride. After refluxing for 4 hr, the reaction was cooled to room temperature and the pyridine hydrochloride removed by filtration. The filtrate was washed successively with 1 *M* hydrochloric acid, water, 5% sodium hydroxide, and water, and then dried over magnesium sulfate. Upon distillation 7.65 g (83%) of 4-fluorobenzyl chloride was obtained, bp 89° (35 mm), $n^{26}D$ 1.5095. The ir spectrum was identical with Sadtler spectrum no. 16978. Other substituted benzyl halides were synthesized in similar fashion and produced infrared spectra which were identical with those published by Sadtler.

Substituted *N*-methylanilines were prepared by lithium aluminum hydride reduction of the corresponding formanilides[19,20] (Table III).

Substituted *N*-methylbenzanilides were prepared from the appropriate acid chlorides and *N*-methylanilines (Table IV).

Substituted *N*-Methyl-*N*-benzylanilines.—To the appropriate *N*-methylaniline was added dropwise with stirring at 90° in a helium atmosphere an equimolar quantity of the appropriate benzyl chloride. After 2 hr, heating was ceased and the reaction allowed to stand overnight at room temperature. The residue was stirred for 1 hr with an equal volume of 25% sodium hydroxide, and the resultant solution was extracted twice with ether. After drying over anhydrous magnesium sulfate, the ethereal solution was concentrated and then vacuum distilled. The purity of the distillate was ascertained by glpc and, when necessary, residual secondary amine was removed by benzoylation. The foregoing method gave acceptable yields (30–73%) for all of the required compounds (Table V) with the exception of *N*-methyl-*N*-(4-methoxybenzyl)aniline.

Substituted Benzyl Alcohols.—All of the required benzyl alcohols were commercially available with the exception of *p*-fluorobenzyl alcohol, which was prepared by lithium aluminum hydride reduction of the acid chloride in ether.

Reduction, General Procedure.—All glassware was predried at 110° for 24 hr before use. All reductions were conducted in a 100-ml three-neck flask equipped with a condenser, drying tube, precision ground stirrer, and an adapter of our own design which was sealed with a rubber septum. A solution containing *N*-methylbenzanilide (2.4 mmol) and the substituted *N*-methylbenzanilide (2.4 mmol) in 25 ml of anhydrous ether was stirred in the foregoing apparatus for 15 min at 25° (water bath). Stock $LiAlH_4$ solution (5 mmol) was injected using a syringe, and stirring continued for 24 hr. The reaction was hydrolyzed with 2.0 ml of H_2O, and the precipitated aluminum salts were removed by filtration. The precipitate was washed with 5 ml of ether, refluxed briefly with an additional 10 ml of ether, and then discarded. The original filtrate and washings were combined for analysis.

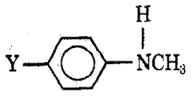
Analysis of Simultaneous Reductions.—Analyses were conducted by glpc under the conditions summarized in Table VI. Peak areas were determined using a planimeter or a Disc integrator. Each analysis consisted of determinations of a substituted and unsubstituted tertiary amine and of a substituted and unsubstituted cleavage product (either a benzyl alcohol or an *N*-methylaniline). Reactions which failed to produce >90% material balances for substituted and unsubstituted products alike were repeated until they did so.

Reductions with Mixed Hydride Reagents.—To a stirred mixture of 1.33 g (10 mmol) of aluminum chloride and 0.19 g (5 mmol) of lithium aluminum hydride in 10 ml of ether was added dropwise at 0° 1.05 g (5 mmol) of *N*-methylbenzanilide in 10 ml

(19) F. Benington, R. D. Moris, and L. C. Clark, *J. Org. Chem.*, **23**, 19 (1958).
(20) E. C. Horning, Ed., "Organic Syntheses," Collect. Vol. III, Wiley, New York, N. Y., 1955, p 590.

TABLE III

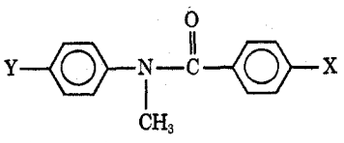
PROPERTIES OF SUBSTITUTED *N*-METHYLANILIDES



Y	Registry no.	Bp, °C (mm)	$n^{25}D$	Anal., % Calcd C	Calcd H	Calcd N	Found C	Found H	Found N
F	459-59-6	136 (120)	1.5314	67.18	6.44	11.19	66.93	6.43	11.32
OCH_3	5961-59-1	67 (0.15)	1.5640	70.09	8.03	10.22	69.84	7.81	10.30
Cl[a]		91-92 (4.2)	1.5820						

[a] F. D. Chattaway and K. J. P. Orton, *J. Chem. Soc.*, **79**, 461 (1901).

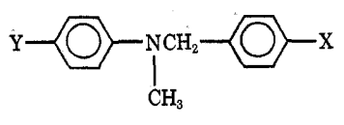
TABLE IV



X	Y	Mp, °C	Anal., % Calcd C	Calcd H	Calcd N	Found C	Found H	Found N
OCH_3	H	74-75 (lit.[a] 74)						
F	H	90.5-91.5	73.33	5.29	6.11	73.10	5.23	6.10
Cl	H	51-52 (lit.[b] 51)						
H	OCH_3	73.5-76.5	74.66	6.27	5.81	74.62	6.22	5.88
H	F	84-88	73.33	5.29	6.11	73.19	5.26	6.03
H	Cl	67.5-70	68.43	4.92	5.70	68.60	5.06	5.57
OCH_3[c]	Cl	108.5-109.6	65.33	5.11	5.07	65.28	5.22	4.99
o-OCH_3[c]	Cl	86-86.5	65.33	5.11	5.07	65.43	5.25	5.02

[a] Reference 5. [b] J. S. Pizey and R. L. Wain, *J. Sci. Food Agr.*, **10**, 577 (1959). [c] These compounds were used only for aldehyde preparation (*vide infra*).

TABLE V

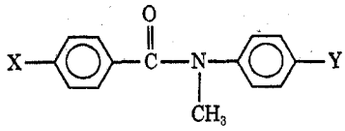


X	Y	Registry no.	Bp, °C (mm)	n_D (°C)	Anal., % Calcd C	Calcd H	Calcd N	Found C	Found H	Found N
OCH_3	H	37931-52-5	122 (0.05)	1.5984 (27)	79.26	7.54	6.16	79.24	7.55	6.13
F	H		103 (0.15)[a]	1.5817 (26)[a]						
Cl	H		120 (0.10)[b]	1.6080 (25)[b]						
H	OCH_3	18606-61-6	115 (0.05)	1.5937 (26)	79.26	7.54	6.16	79.42	7.54	6.11
H	F	37931-54-7	95-96 (0.15)	1.5788 (26)	78.10	6.56	6.51	78.00	6.51	6.69
H	Cl	37931-55-8	110-120 (0.10)	1.6126 (23)	72.56	6.09	6.04	72.42	6.11	5.84

[a] Lit. bp 132–135° (1.0); $n^{25}D$ 1.5844 [V. Schoellkopf, V. Ludwig, M. Patsch, and W. Franken, *Justus Liebigs Ann. Chem.*, **703**, 77 (1967)]. [b] Lit. bp 144–146° (0.30); $n^{25}D$ 1.6097 (see ref in *a*).

TABLE VI

ANALYSIS OF REACTION PRODUCTS FROM SUBSTITUTED *N*-METHYLBENZANILIDES



X	Y	Column[a]	Temp, °C[b]	Standard[b]
OCH_3	H	A	185 (220)	3-Bromoaniline (*N*-methylbenzanilide)
F	H	B	110 (150)	*N*,*N*-Dimethylaniline (4-methoxybenzyl alcohol)
Cl	H	C	215 (245)	3-Bromoaniline (*N*-methyl-4-fluorobenzanilide)
H	OCH_3	D (E)	205 (250)	2-Methoxyaniline (*o*-ethoxyacetanilide)
H	F[c]	D (A)	195 (195)	2-Methoxyaniline (*o*-ethoxyacetanilide)
H	Cl	C	215 (235)	3-Bromoaniline (*N*-methyl-4-fluorobenzanilide)

[a] Column A, 10 ft × 1/8 in., 10% Carbowax 20M on 70/80 Varaport 30; column B, 10 ft × 1/8 in., 5% XF1150 on 60/80 Chromosorb W; column C, 10 ft × 1/8 in., 10% (4:1) Carbowax 20M–KOH on 100/120 Varaport 30; column D, 10 ft × 1/8 in., 20% (4:1) Carbowax 20M–KOH on 60/80 Chromosorb W; column E, 6 ft × 1/8 in., 20% (4:1) Apiezon L–KOH on 60/80 Chromosorb W. [b] The tertiary amines required higher temperatures and therefore separate standards (in parentheses) for analysis. [c] Only the total weight of the two tertiary amines could be determined by glpc due to poor separation. Their ratio was determined by nmr using the ratio of areas under the two methylene peaks at τ 5.6 and 5.5.

of ether. After the addition was complete, the reaction was allowed to come to room temperature and was stirred for 22 hr. Hydrolysis and product isolation was conducted using the procedure of Micovic and Mihailovic.[4] Reductions in which the molar ratio of $AlCl_3/LiAlH_4$/amide was 1:1:1 were conducted in a similar fashion. Analyses were carried out by glpc on column A (Table VI) at 210°.

Partial Reduction of *N*-Methyl-*p*-chloroanilides.—Into 3 mmol of the anilide in 10 ml of tetrahydrofuran was injected with stirring at 0° 0.83 ml of 1.2 *M* lithium aluminum hydride in tetrahydrofuran. The reaction mixture was stirred at 0° for 10 hr and was then added to 100 ml of a saturated solution of 2,4-dinitrophenylhydrazine in 2 *M* hydrochloric acid. The resultant solution was diluted with 100 ml of 2 *M* hydrochloric acid and allowed to stand for 5 hr; the resultant 2,4-DNP was isolated, dried, and weighed.

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Palladium(II)-Catalyzed Exchange and Isomerization Reactions. VIII. Isomerization of Vinylic Halides in Acetic Acid Catalyzed by Palladium(II) Chloride[1,2]

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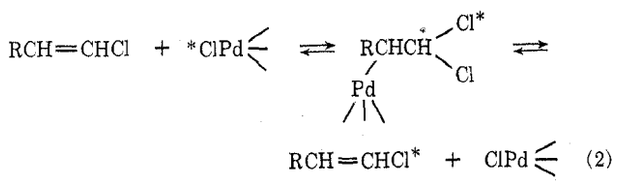
The palladium(II)-catalyzed isomerization of *cis*- and *trans*-1-chloropropene was found to obey the three-term rate expression rate = $(k_1[Li_2Pd_2Cl_6]/[LiCl] + k_2[Li_2Pd_2Cl_6] + k_3[Li_2Pd_2Cl_6]^{1/2})$[1-chloropropene]. 1-Bromopropene isomerization displayed mainly the k_2 and k_3 terms. The k_2 term most likely results from nonstereospecific chloropalladation–dechloropalladation in which the chloride adds to the carbon carrying the methyl and the palladium to the carbon carrying the halide. The k_1 and k_3 terms correspond to formation of monomer and dimeric π complexes, respectively. Isomerization is then accomplished through the π complexes without the intervention of an external reagent. A possible mechanism is rearrangement of the π complex to a Pd(II) σ-bonded carbonium ion which undergoes rotation before reverting to the π complex.

Paper IV[4] of this series describes a study of the radioactive chloride exchange of vinylic chlorides with radioactive lithium chloride. The rate expression for this exchange is given by eq 1.

$$\text{rate} = k[Li_2Pd_2Cl_6][\text{vinylic chloride}] \quad (1)$$

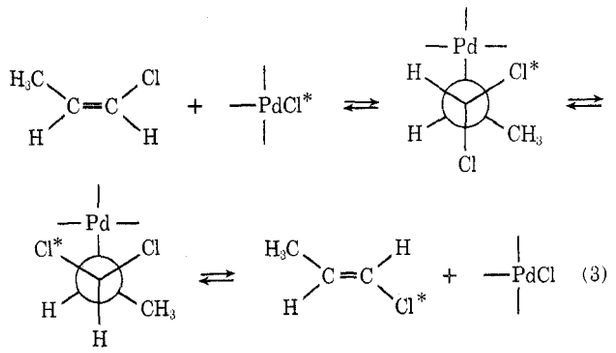
The mechanism which best fits all the experimental facts consists of chloropalladation followed by dechloropalladation to give exchange. Chloropalladation is not completely stereospecific but the main mode is apparently cis chloropalladation from the coordination sphere of Pd(II).



$$RCH{=}CHCl^* + ClPd\lessgtr \quad (2)$$

During the course of this work it was found that *cis*- or *trans*-1-chloropropene isomerized into the other isomer considerably faster than exchange with radioactive chloride. As shown in eq 3, this result would not have been predicted if isomerization occurred by mainly stereospecific cis chloropalladation–dechloropalladation. Thus some other route must be responsible for this isomerization.

This paper will describe a study of this reaction using vinylic chlorides and bromides as reactants.



(3)

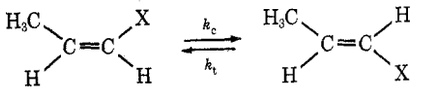
In paper VII of this series the study of a similar isomerization of enol propionates was described.[1] The rate expression for the isomerization is given by eq 4.

$$\text{rate} = \frac{k[Li_2Pd_2Cl_6][\text{enol propionate}]}{[LiCl]} \quad (4)$$

Effects of structure on rate as well as other mechanistic work showed that π-allylic or palladium hydride routes for this isomerization were very unlikely.[1,2]

Results

All runs were made at 25° in acetic acid solvent. The values of k_{obsd} for a given run are the sum of the pseudo-first-order rate constants, k_t and k_c for the reaction given by eq 5 (X = Cl or Br). The values of



(5)

k_c and k_t can readily be calculated from the composition of the equilibrium mixture, which was 74% cis when X is Cl and 70% cis when X is Br. For most

(1) Paper VII: P. M. Henry, *J. Amer. Chem. Soc.*, **94**, 7316 (1972).
(2) For a preliminary account of this work, see P. M. Henry, *ibid.*, **93**, 3547 (1971).
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(4) P. M. Henry, *J. Org. Chem.*, **37**, 2443 (1972).