A Fragmentation–Recombination Mechanism for the Beckmann Rearrangement in Strong Acid

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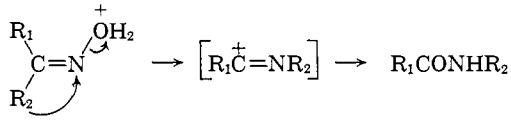
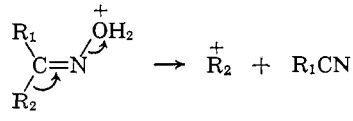
The intermediacy of a two-step, fragmentation–recombination mechanism for the Beckmann rearrangement of α-trisubstituted oximes in strong acid media has been demonstrated by crossover experiments and a stereochemical study. In the crossover experiments, a mixture of the oximes of pinacolone and 2-methyl-2-phenylpropiophenone rearranged in polyphosphoric acid to form a mixture of four secondary amides: the two normal products, III and V, as well as the crossed products, VI and VII. Although the oxime of 9-acetyl-cis-decalin rearranges normally with toluenesulfonyl chloride in pyridine, in sulfuric or polyphosphoric acids it rearranges to the trans amide (XI). These results demonstrate a new mechanism for certain Beckmann rearrangements, in which the oxime first cleaves to a nitrile and carbonium ion, which then recombine by a Ritter reaction.

The Beckmann rearrangement[4,5] is one of the classic examples of rearrangement to an electron-deficient nitrogen atom. Nearly all of the standard methods of studying the mechanism of rearrangements: kinetic studies, variation of rates with structural changes, demonstration of retention of configuration of the migrating group, etc., attest to its description as a concerted rearrangement in which the migration of an alkyl or aryl substituent is synchronous with the breaking of the N–O bond in the protonated or esterified oxime.

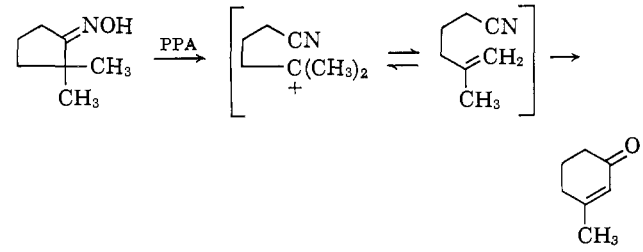


It was recognized early that certain oximes behave in an abnormal manner when subjected to Beckmann rearrangement conditions, and a wide variety of oximes are now known which undergo "fragmentation" into a nitrile and a carbonium ion.[6]

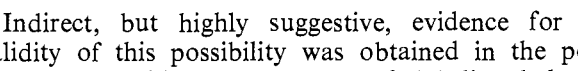


In general, this "Beckmann fission" is displayed by oximes of structural types which furnish carbonium ions R_2^+ possessing considerable stability.[7]

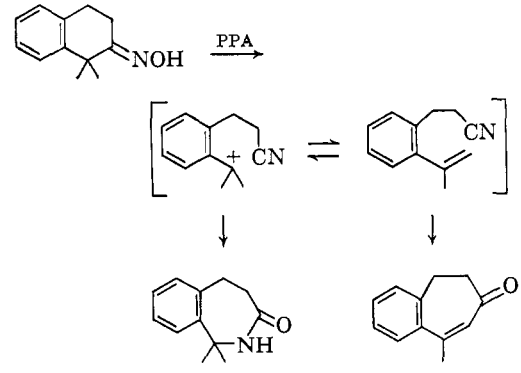
For several years we have been investigating the effects of changes in catalyst and oxime structure on the course of these fragmentation reactions.[7,8] One of the most interesting results to come from this work has been the formation of α,β-unsaturated ketones from α-trisubstituted oximes in polyphosphoric acid, arising from initial fragmentation followed by intramolecular acylation; a typical example[8d] is the rearrangement of 2,2-dimethylcyclopentanone oxime to 3-methylcyclohex-2-enone.



Once it had been demonstrated that the functional groups created by fragmentation were capable of interacting with each other in acid solution, an intriguing question arose. Might it be possible that the carbonium ion and nitrile produced by oxime fission could recombine in still another fashion, by a Ritter[9] reaction? Such an addition could produce an amide identical with the product of normal rearrangement, and would offer the novel possibility of forming a "normal" product by an "abnormal" mechanism.



Indirect, but highly suggestive, evidence for the validity of this possibility was obtained in the polyphosphoric acid rearrangement of 1,1-dimethyltetralone-2 oxime,[8e] which affords products of both types of olefin–nitrile reactions.



(1) Frick Chemical Laboratory, Princeton University.
(2) Alfred P. Sloan Research Fellow.
(3) Part of this work was supported by Grant NB-03628 from the National Institute of Neurological Disease and Blindness.
(4) L. G. Donaruma and W. Z. Heldt, *Org. Reactions*, **11**, 1 (1960).
(5) P. A. S. Smith in "Molecular Rearrangements," Vol. I, P. de Mayo, Ed., John Wiley and Sons, Inc., New York, N. Y., 1963, pp. 483–507.
(6) See ref. 5, pp. 501–504.
(7) R. K. Hill, *J. Org. Chem.*, **27**, 29 (1962).
(8) (a) R. K. Hill and R. T. Conley, *J. Am. Chem. Soc.*, **82**, 645 (1960); (b) R. T. Conley and M. C. Annis, *J. Org. Chem.*, **27**, 1961 (1962); (c) R. T. Conley and B. E. Nowak, *ibid.*, **27**, 1965 (1962); (d) R. T. Conley and B. E. Nowak, *ibid.*, **27**, 3196 (1962); (e) R. T. Conley and R. J. Lange, *ibid.*, **28**, 210 (1963).
(9) J. J. Ritter and P. P. Minieri, *J. Am. Chem. Soc.*, 70, 4045 (1948).

We set about, in two completely independent investigations, to obtain conclusive evidence for this two-stage mechanism, and have reported in two preliminary communications[10,11] proof that it indeed is possible. This joint paper presents the details of two independent methods of investigation, a crossover study and a stereochemical study, which demonstrate the existence of a fragmentation–recombination mechanism for Beckmann rearrangements in strong acid.[12]

Crossover Study

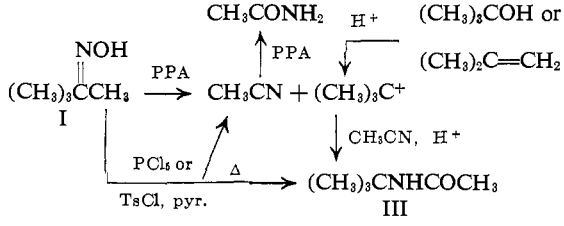
The two-stage mechanism, in which the molecule first completely dissociates into two fragments, which then recombine, should be detectable by the familiar crossover technique, of the sort used to reveal, for example, the intermolecular nature of the Fries rearrangement.[13] Two oximes of similar structure, each with a fully substituted α carbon, were chosen for the study: pinacolone oxime (I) and 2-methyl-2-phenylpropiophenone oxime (II). The separate rearrangement of each was first examined.

Pinacolone Oxime. In polyphosphoric acid (PPA) at 120°, pinacolone oxime (I) rearranged almost quantitatively to N-*t*-butylacetamide (III). When the rearrangement was carried out at a lower temperature (80°), 13% of acetamide was formed as well as III. Heating the pure amide III in PPA at 120° also yielded about 10% of acetamide in addition to recovered III.

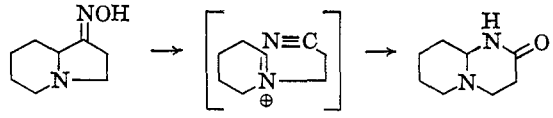
Treated with phosphorus pentachloride, oxime I gave a high yield of III, confirming an earlier report,[14] though if the reaction mixture was heated, acetonitrile was detected. The use of *p*-toluenesulfonyl chloride in pyridine gave similar results.

The formation of the "normal" product III in high yield from the PPA rearrangement, even though most oximes of this type fragment in PPA,[8] and the presence of small amounts of acetamide, are hints that I rearranges by the fragmentation–recombination path in PPA. The validity of the Ritter recombination step is known from the acid-catalyzed formation of III from isobutene and acetonitrile,[9] and was checked using *t*-butyl alcohol as the carbonium ion source. Chart I summarizes these reactions.

Chart I. Beckman Rearrangements of Pinacolone Oxime



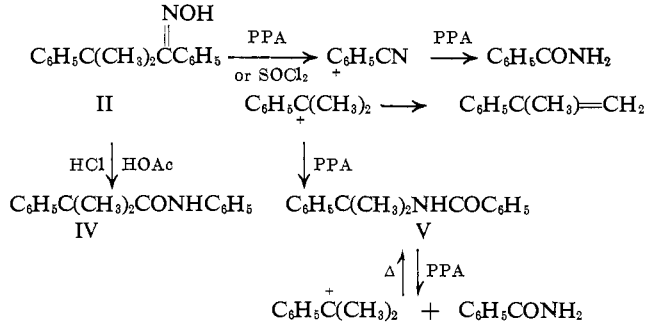
(10) R. K. Hill and O. T. Chortyk, *J. Am. Chem. Soc.*, **84**, 1064 (1962).
(11) R. T. Conley, *J. Org. Chem.*, **28**, 278 (1963).
(12) Another example of the fragmentation–recombination mechanism for Beckmann rearrangement was subsequently shown for an α-amino-oxime.



C. A. Grob, H. P. Fischer, H. Link, and E. Renk, *Helv. Chim. Acta*, **46**, 1190 (1963).
(13) K. W. Rosenmund and W. Schnurr, *Ann.*, **460**, 56 (1927).
(14) R. Scholl, *ibid.*, **338**, 16 (1905).

2-Methyl-2-phenylpropiophenone Oxime. The Beckmann rearrangement of 2-methyl-2-phenylpropiophenone oxime (II) was studied some years ago by Lyle and Lyle,[15] who showed that it rearranged normally in Beckmann's mixture (hydrogen chloride in acetic acid) to the anilide (IV) of 2-phenylisobutyric acid, but underwent fission with thionyl chloride to α-methylstyrene and benzonitrile. It has been found in the present study that in PPA at 80°, II rearranges to N-benzoyl-α,α-dimethylbenzylamine (V), along with a small quantity of benzamide. At 120°, the yield of benzamide rose to 62% at the expense of V, which was isolated in 25% yield. The suspicion that V is cleaved by hot PPA was verified by heating V in PPA at 120° for 10 min., whereupon a 50% yield of benzamide was obtained. This fission is, at least to a certain extent, reversible,[16] since a 20% yield of V can be obtained by reacting benzamide with α-methylstyrene at 120° in PPA. The greater ease of eliminating benzamide from V, as compared with the elimination of acetamide from III, must reflect the greater stability of the cumyl carbonium ion. These results, summarized in Chart II, support the two-step mechanism for the rearrangement of II in PPA.

Chart II. Beckmann Rearrangement of 2-Methyl-2-phenylpropiophenone Oxime



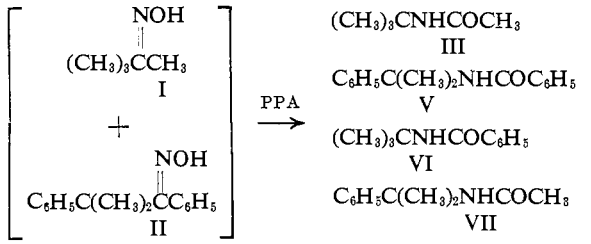
Rearrangement of Mixture of I and II. An equimolar mixture of oximes I and II was heated in PPA at 120° for 10 min., and the products were separated by preparative v.p.c. (see Chart III). In addition to the expected amides III (41%), V (21%), and benzamide (35%), two "crossed" products, N-*t*-butylbenzamide (VI) and N-acetyl-α,α-dimethylbenzylamine (VII) were isolated in yields of 11 and 39%, respectively. Similar results were obtained from a run at 80°, which led to III (37%), V (42%), VI (22%), VII (30%), benzamide (13%), and acetamide (9%).

It was essential to show that the crossed products VI and VII were not being produced by decomposition and recombination of the normal products III and V. Heating a mixture of III and V in PPA at 120° led to a 94% recovery of III, while V had partly undergone elimination, as expected, to form benzamide (40% isolated). A completely clearcut result was obtained when the experiment was repeated at 80°; however, both III and V were recovered unchanged, in yields over 90%, when their mixture was heated in PPA at this temperature, conditions which effect the oxime rear-

(15) R. E. Lyle and G. G. Lyle, *J. Org. Chem.*, **18**, 1058 (1953).
(16) (a) R. K. Hill, *ibid.*, **22**, 830 (1957); (b) R. T. Conley, R. Evans, and B. E. Nowak, Abstracts of Papers, 139th National Meeting of the American Chemical Society, St. Louis, Mo., March 1961, p. 9-O; (c) R. T. Conley and W. N. Knopka, Abstracts of Papers, 146th National Meeting of the American Chemical Society, Denver, Colo., Jan. 1964, p. 57C.

rangement. No trace of either of the crossed products could be detected by v.p.c.

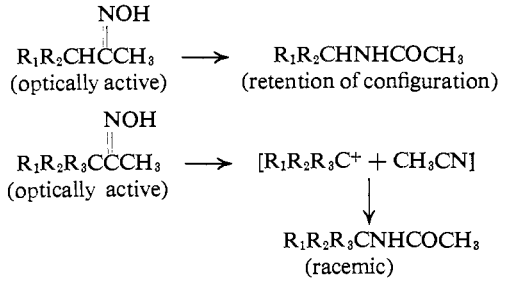
Chart III. Rearrangement of a Mixture of I and II



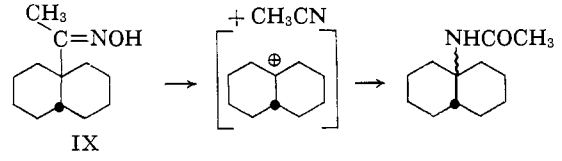
These results provide unambiguous evidence that the rearrangement of α-trisubstituted oximes in strong acid is not, like the normal Beckmann rearrangement, an intramolecular process, but rather a two-step, intermolecular, fragmentation–recombination reaction.

Stereochemical Study

A second method of showing the intermolecularity of the reaction in question would be a study of the course of the reaction on an optically active oxime. Kenyon[17] has proved that the normal Beckmann rearrangement proceeds with retention of configuration of the migrating group. If the asymmetric carbon were trisubstituted, however, fission of the oxime to nitrile and carbonium ion would lead to a symmetric intermediate and racemic product.



Difficulties in the preparation of the required optically active oximes led us to choose a variant of this approach in which a change in *relative* configuration could be observed. The compound selected for this purpose was the oxime (IX) of 9-acetyl-*cis*-decalin. Fragmentation of IX would yield the symmetrical 9-decalyl carbonium ion, and the resulting amide product could be a mixture of both geometrical isomers, probably predominantly *trans*.[18]



Accordingly, *cis*-9-decalincarboxylic acid[19] was converted to the methyl ketone by treatment of the acid chloride with dimethylcadmium. The oxime was prepared by the usual procedure in pyridine–ethanol, though 3 days of refluxing was necessary to obtain a good yield. Rearrangement of the oxime was carried out under a variety of conditions.

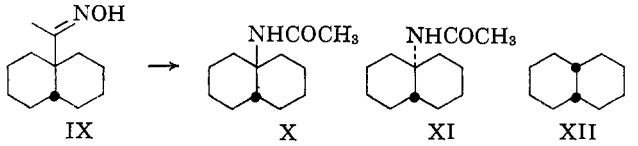
(a) With *p*-toluenesulfonyl chloride in pyridine, the oxime rearranged normally to afford a 92% yield of N-(*cis*-9-decalyl)acetamide (X), m.p. 126°, identified by comparison with an authentic sample of proved stereochemistry.[20] This result incidentally strengthens the belief that the arylsulfonyl chloride–base method is one of the mildest available for effecting Beckmann rearrangements, especially for bringing about normal rearrangements of oximes which are susceptible to fragmentation.[8a,21]

(b) Treating IX with phosphorus pentachloride in chloroform liberated acetonitrile, identified by its infrared spectrum and v.p.c. retention time.

(c) Heating IX in PPA at 125° for 10 min. gave a mixture of products, separated by column chromatography. First eluted was *cis*-decalin (55%), identified by its infrared and n.m.r. spectra. It was followed by an amide, which proved to be the known[20] N-(*trans*-9-decalyl)acetamide (XI), m.p. 182°. Carrying out the PPA rearrangement at room temperature eliminated the formation of decalin, and gave XI as the sole product.

(d) Rearrangement in sulfuric acid paralleled the PPA runs. In 85–90% sulfuric acid, rearrangement was incomplete, giving about 60% of recovered oxime in addition to 40% of XI. In 98% sulfuric acid, the product was a mixture of XI (47%) and *cis*-decalin (34%).

Chart IV. Rearrangement of 9-Acetyl-*cis*-decalin Oxime



Reagent	Products
$C_7H_7SO_2Cl$, pyridine	X (92%)
PPA, 25°	XI (61%)
PPA, 125°	XI (12%) + XII (55%)
H_2SO_4, 85–90%	XI (40%)
H_2SO_4, 98%	XI (47%) + XII (34%)
PCl_5	Acetonitrile

The formation of the stereoisomerized *trans* amide (XI) from rearrangements in strong acid provides compelling evidence for the fragmentation–recombination mechanism. The possibility that the *cis* amide X might have been initially formed in all rearrangements and subsequently isomerized to XI by the acid medium was ruled out by showing that nearly 90% of X could be recovered unchanged from either PPA or sulfuric acid, with no detectable amount of XI formed.

Evidence for the feasibility of the recombination step of the two-step mechanism was obtained by subjecting *cis*-β-decalol to the Ritter reaction with acetonitrile in sulfuric acid; *cis*-β-decalol has been observed[18] to be a source of the 9-decalyl carbonium ion by hydride shifts from the initial 2-decalyl cation. The sole product isolated was the *trans* amide XI. The factors responsible for the formation of only the *trans* isomer in this addition are probably similar to those operating in the carbonylation of the 9-decalyl carbonium ion, where *trans*-decalin-9-carboxylic acid is the kinetically

(17) J. Kenyon and D. P. Young, *J. Chem. Soc.*, 253 (1941); A. Campbell and J. Kenyon, *ibid.*, 25 (1946).

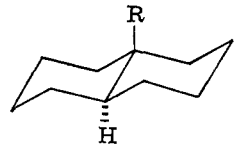
(18) H. Christol, R. Jacquier, and M. Mousseron, *Bull. soc. chim. France*, 1027 (1957), reported that the Ritter reaction of β-decalol and potassium cyanide gave N-(*trans*-9-decalyl)formamide.

(19) H. Koch and W. Haaf, *Ann.*, **618**, 251 (1958).

(20) W. G. Dauben, R. C. Tweit, and R. L. MacLean, *J. Am. Chem. Soc.*, 77, 48 (1955). The samples of *cis*- and *trans*-N-(9-decalyl)-acetamides were generously furnished by Professor W. G. Dauben, University of California, to whom we express our thanks.

(21) M. Gates and S. P. Malchick, *J. Am. Chem. Soc.*, **79**, 5546 (1957); S. Kaufmann, *ibid.*, **73**, 1779 (1951).

favored product.[22] In both cases a small, linear group adds in the axial orientation to the decalyl cation, giving an intermediate (XIII) which has the decalin framework in the presumably more stable *trans* geometry.



XIII, R = $-\overset{\oplus}{N}\equiv C-CH_3$ or $-C\equiv O^{\oplus}$

The formation of *cis*-decalin from runs in concentrated sulfuric or hot polyphosphoric acids requires some further comment. Though no further investigation was made as to its mode of origin it seems very likely that it originates by the disproportionation of the decalyl carbonium ion in the manner so elegantly demonstrated by Deno and Pittman.[23] We have previously observed the formation of unexpected saturated products from other Beckmann rearrangements in polyphosphoric acid,[8a] and had also attributed these to hydride-transfer reactions. A particularly interesting aspect of the disproportionation is that the product is the apparently stereochemically homogeneous *cis* isomer. Deno and Pittman[23] found that the 1,3-dimethylcyclohexane formed by disproportionation of the 1,3-dimethylcyclohexyl cation was also exclusively the *cis* isomer, though the reasons for the stereospecificity are not yet apparent.

Conclusions. Both the crossover experiments and the stereochemical results demonstrate the existence of an alternate mechanism, a fragmentation–recombination pathway, for Beckmann rearrangement of α-trisubstituted oximes in strong acid. This two-step mechanism seems likely to intrude whenever structural features present in the oxime favor its fission to a stable carbonium ion, and caution must be exercised in interpreting the results of apparently normal rearrangements of this sort.[24] Experiments are now in progress with optically active α-trisubstituted oximes to further test this mechanism and that of related rearrangements.

Experimental Section

V.p.c. analyses were performed on a Perkin-Elmer Model 154 gas chromatograph, using a silicone SE-30 column at 250° and helium flow rate of 60 ml./min.

Crossover Studies. The following general procedure was used for rearrangements in PPA. A mixture of 0.01 mole of the oxime and 25 g. of PPA was stirred and heated slowly to the temperature used. After 10 min. at 120° (or 25 min. at 80°), the reaction mixture was hydrolyzed over crushed ice and extracted with five 100-ml. portions of chloroform (in several cases continuous extraction with chloroform for several days was necessary). The extracts were dried over magnesium sulfate and concentrated under reduced pressure.

Pinacolone Oxime. A. Rearrangement of pinacolone oxime (1.15 g.) in PPA at 120° gave 1.09 g. (96%) of N-*t*-butylacetamide, m.p. 97–98°, not depressed by mixing with an authentic sample.

B. Rearrangement in PPA at 80° gave a mixture of products. V.p.c. analysis showed 68.3% of N-*t*-butylacetamide and 12.7% acetamide, with retention times of 4.3 and 17.5 min., respectively.

C. A solution of pinacolone oxime in benzene was treated with 1 equiv. of phosphorus pentachloride in portions in the cold and allowed to stand overnight at room temperature. Work-up gave the amide III in 86% yield. If the reaction mixture was instead directly distilled, a fraction (b.p. 82°) was obtained, identified by its infrared spectrum as acetonitrile.

D. A solution of 15 g. of pinacolone oxime in 150 ml. of pyridine was treated with a solution of 15 g. of *p*-toluenesulfonyl chloride in 75 ml. of pyridine, and the mixture was stored for 24 hr. Distillation gave a fraction (1.9 g.), boiling at 82–85°, identified by its infrared spectrum as acetonitrile. The remaining mixture was poured onto ice and water, neutralized with hydrochloric acid, and extracted with chloroform. Evaporation of the chloroform and recrystallization of the solid residue from hexane gave 6.9 g. (46%) of N-*t*-butylacetamide, m.p. 96–98°.

If the reaction mixture was worked up in this way, omitting the distillation, v.p.c. analysis showed the presence of III in 84% yield.

Reaction of III with PPA. A 0.01-mole sample of N-*t*-butylacetamide was heated in PPA at 120° for 10 min. as described for pinacolone oxime. V.p.c. analysis of the mixture after work-up showed the presence of 89% of recovered III and 11% of acetamide.

Ritter Reaction of t-Butyl Alcohol and Acetonitrile. A mixture of 24 g. of *t*-butyl alcohol and 9 g. of acetonitrile in 100 ml. of glacial acetic acid containing 20 g. of concentrated sulfuric acid was kept overnight, then poured into water, neutralized with sodium carbonate, and extracted with ether. Concentration of the dried extracts and recrystallization from hexane gave 13.7 g. of N-*t*-butylacetamide, m.p. 97–98°.

Beckmann Rearrangement of 2-Methyl-2-phenylpropiophenone Oxime (II). A mixture of 2.39 g. (0.01 mole) of oxime II[15] and 25.5 g. of PPA was heated at 80° for 25 min. Work-up as described gave N-benzoyl-α,α-dimethylbenzylamine (V),[25] m.p. 161–162° after sublimation (lit.[25] m.p. 159°). V.p.c. analysis showed that V was formed in 77% yield along with 3% of benzamide. An authentic sample of V was prepared for comparison from α,α-dimethylbenzylamine and benzoyl chloride, and melted at 160.5–161.5°.

Anal. Calcd. for $C_{16}H_{17}NO$: C, 80.30; H, 7.17; N, 5.85. Found: C, 80.14; H, 6.96; N, 5.69.

When a run of the same size was carried out at 120° for 10 min., work-up gave 1.35 g. of a brown powdery solid. V.p.c. analysis showed two peaks with retention times of 24.6 and 8.0 min., corresponding to benzamide (62%) and V (25%), respectively.

Cleavage of V in PPA. A mixture of 2.39 g. of V and 24.2 g. of PPA was heated at 120° for 10 min., and afforded 1.56 g. of crude solid after work-up. V.p.c. analysis showed that the mixture consisted of V (50%)

(22) R. E. Pincock, E. Grigat, and P. D. Bartlett, *J. Am. Chem. Soc.*, 81, 6332 (1959).
(23) N. C. Deno and C. U. Pittman, Jr., *ibid.*, 86, 1744 (1964).
(24) See, *e.g.*, H. A. Bruson, F. W. Grant, and E. Bobko, *ibid.*, 80, 3633 (1958).
(25) M. Brander, *Rec. trav. chim.*, 37, 67 (1917).

and benzamide (49%). A similar experiment carried out at 80° for 25 min. gave 93% of recovered V.

Addition of Benzamide to α-Methylstyrene. A mixture of 1.21 g. of benzamide and 1.17 g. of α-methylstyrene was heated in PPA (26.8 g.) at 120° for 25 min. The mixture was worked up as before and analyzed by v.p.c., showing 71% of recovered benzamide and 20% of V.

Rearrangement of a Mixture of Oximes I and II. A. A mixture of 1.15 g. (0.01 mole) of oxime I and 2.39 g. (0.01 mole) of oxime II in 52.7 g. of PPA was heated at 120° for 10 min. and worked up as described, to provide 2.85 g. of crude products. The mixture was taken up in the minimum volume of chloroform and chromatographed on alumina, eluting with ether–petroleum ether (b.p. 60–70°) mixtures increasingly rich in ether.

(1) After eluting first with 500 ml. of 2:1 petroleum ether–ether, a 1:1 solvent mixture eluted 0.285 g. (24.6%) of N-*t*-butylacetamide (III). After sublimation *in vacuo* it melted at 97–98°, alone or admixed with an authentic sample.

(2) Elution with 2:1 ether–petroleum ether yielded 0.163 g. (9%) of N-*t*-butylbenzamide (VI), m.p. 134.5–135° after sublimation *in vacuo* (lit.[25] m.p. 136.5°). The melting point was not depressed by mixing with an authentic sample prepared from *t*-butylamine and benzoyl chloride.

(3) Later fractions of the 2:1 ether–petroleum ether eluates gave 0.111 g. (6%) of N-acetyl-α,α-dimethylbenzylamine (VII),[9] m.p. 90–92° after vacuum sublimation. The melting point was not depressed by mixing with an authentic sample, prepared from α,α-dimethylbenzylamine and acetyl chloride.

Anal. Calcd. for $C_{11}H_{15}NO$: C, 74.54; H, 8.53; N, 7.90. Found: C, 74.43; H, 8.61; N, 7.93.

(4) Elution with ether gave 0.51 g. (21%) of N-benzoyl-α,α-dimethylbenzylamine (V), which melted at 161–162° after vacuum sublimation. The melting point of a mixture with an authentic sample was not depressed.

B. The rearrangement of a mixture of oximes I and II was repeated to give 2.56 g. of crude products. V.p.c. analysis gave the following percentages of products: III (41%), VI (11%), VII (39%), VI (32%), and benzamide (35%).

C. A run of the same size was carried out in PPA at 80° for 25 min. Work-up as before gave 3.26 g., which was analyzed by v.p.c. with the following results: III (37%), VI (22%), VII (30%), V (42%), benzamide (13%), and acetamide (9%).

PPA Treatment of a Mixture of Amides III and V. A. A mixture of 0.01 mole each of N-*t*-butylacetamide (III) and N-benzoyl-α,α-dimethylbenzylamine (V) was heated in PPA at 120° for 10 min. and worked up as above. V.p.c. analysis showed recovered III (93.5%), recovered V (48%), and benzamide (40%).

B. A similar experiment at 80° for 25 min. gave 97% of recovered III and 92% of recovered V.

9-Acetyldecalin Series. 9-Acetyl-cis-decalin. A mixture of 49.1 g. of *cis*-decalin-9-carboxylic acid,[19] m.p. 119–120° (lit.[19] m.p. 122°), and 115 g. of thionyl chloride was refluxed for 3 hr. with stirring. The excess thionyl chloride was removed at 45° at aspirator pressure, and the residual oil was distilled, b.p. 79–83° (0.5 mm.), yield 50 g.

The methyl Grignard reagent was prepared in the usual way from 117.1 g. of methyl iodide, 11.95 g. of magnesium turnings, and 480 ml. of anhydrous ether. Freshly fused and powdered cadmium chloride (45.4 g.) was added to the cooled Grignard solution and the mixture was refluxed for 45 min., when a negative Gilman test was obtained. Most of the ether was distilled, then 300 ml. of benzene added and distillation was continued until the head temperature reached 65°. The solution was diluted with 250 ml. of benzene, then cooled in ice while a solution of 49.7 g. of the above acid chloride in 200 ml. of benzene was added slowly. The resulting mixture was refluxed for 30 min., cooled, and poured into 2 l. of ice and dilute sulfuric acid. The organic layer was separated and the aqueous layer was extracted with benzene (two × 200-ml. portions). The benzene extracts were washed with water, 5% sodium carbonate (three 200-ml. portions), and saturated sodium chloride solution. Distillation gave 40.7 g. (91%) of 9-acetyl-*cis*-decalin, b.p. 82–85° (0.8 mm.). It was purified before further use by redistillation, b.p. 84° (1 mm.), $n^{25}D$ 1.4940.

Anal. Calcd. for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 80.13; H, 11.41.

The *2,4-dinitrophenylhydrazone* was prepared in ethanol and aqueous sulfuric acid, and recrystallized from aqueous ethanol, giving orange-red needles, m.p. 140–140.5°.

Anal. Calcd. for $C_{18}H_{24}N_4O_4$: C, 59.98; H, 6.71. Found: C, 60.28; H, 6.91.

The *oxime* (IX) was prepared by refluxing a solution of 13.9 g. of the ketone and 14 g. of hydroxylamine hydrochloride in 100 ml of ethanol and 100 ml. of pyridine for 3 days; shorter reaction times resulted in decreased yields. The reaction mixture was diluted with 100 ml. of water and extracted with ether. The ether extracts were washed with 4 *N* hydrochloric acid, dried, and concentrated. Recrystallization of the solid residue from ethanol gave 11.5 g. of colorless oxime, m.p. 106–108°, raised by another recrystallization to 107.5–108.5°.

Anal. Calcd. for $C_{12}H_{21}NO$: C, 73.80; H, 10.84; N, 7.17. Found: C, 73.72; H, 10.81; N, 7.35.

Rearrangement of 9-Acetyl-cis-decalin Oxime (IX). A. With p-Toluenesulfonyl Chloride and Pyridine. A solution of 0.40 g. of the oxime in 10 ml. each of carbon tetrachloride and pyridine was treated with 0.75 g. of *p*-toluenesulfonyl chloride. The mixture was warmed to 70° for a few minutes, then stirred at 25° for 5 hr. Water (150 ml.) was added and the mixture was extracted with ether. After washing with dilute hydrochloric acid and water, the extracts were dried over magnesium sulfate and concentrated, affording 0.37 g. (92%) of N-(*cis*-9-decalyl)acetamide (X), m.p. 125–126.5°. The amide was identified by comparison of infrared spectra and mixture melting point determination with an authentic sample,[20] m.p. 126–127°.

B. With Phosphorus Pentachloride. A solution of 1.0 g. of the oxime (IX) in 15 ml. of chloroform was treated with 1.6 g. of phosphorus pentachloride and kept for 14 hr. The mixture was washed with 5% sodium bicarbonate and dried, and the chloroform was

distilled, collecting 2-ml. fractions. The last two fractions had infrared absorption at 2250, 2285, and 2400 cm.$^{-1}$ characteristic of acetonitrile. V.p.c. analysis of these fractions showed a peak with the same retention time as acetonitrile.

C. In Concentrated Sulfuric Acid. The powdered oxime (1.5 g.) was stirred into 15 g. of concentrated sulfuric acid and allowed to stand overnight. The reaction mixture was diluted with 150 ml. of ice–water and extracted with ether. Concentration of the dried extracts left a residue which was chromatographed on alumina. Elution with carbon tetrachloride gave 0.36 g. of a hydrocarbon, identified by its infrared and n.m.r. spectra as *cis*-decalin. Further elution with ether gave 0.70 g. of solid, m.p. 181.5–182.5° after recrystallization from ether. It was identified by mixture melting point determination and comparison of infrared spectra with an authentic sample[20] as N-(*trans*-9-decalyl)-acetamide (XI), m.p. 182–183°.

Treating 0.50 g. of the oxime IX with 10 g. of 85% sulfuric acid under the same conditions yielded 0.15 g. of the *trans* amide (XI) and 0.22 g. of recovered starting material.

D. In Polyphosphoric Acid. A mixture of the oxime (1.5 g.) and polyphosphoric acid (30 g.) was stirred for 10 hr. at 25°. The reaction mixture was stirred into 250 ml. of ice–water and extracted with ether. After drying and treatment with charcoal, concentration of the ether extracts left 0.92 g. of N-(*trans*-9-decalyl)-acetamide (XI), m.p. 181.5–182.5°.

Another run was carried out at a higher temperature; the oxime (2.0 g.) was heated with stirring in 80 g. of PPA at 125–130° for 10 min. and worked up as before. Chromatography of the products over alumina gave first *cis*-decalin (0.78 g.), eluted with carbon tetrachloride and identified by its infrared and n.m.r. spectra, followed by N-(*trans*-9-decalyl)acetamide (0.24 g.), m.p. 181–182°, eluted with ether.

Stability of Amide X in Acid. A. N-(*cis*-9-decalyl)-acetamide (0.14 g.) was dissolved in 1.4 g. of 85% sulfuric acid and allowed to stand overnight. On working up as described above, 0.12 g. of starting material, m.p. 125–126°, was recovered.

B. The *cis* amide (0.11 g.) was stirred with 3 g. of PPA at room temperature for 9 hr. Working up as described above led to 0.10 g. of recovered starting amide.

Preparation of XI by Ritter Reaction. To a solution of 3.4 g. of acetonitrile and 5 g. of *cis*-β-decalol (m.p. 105°) in 25 ml. of di-*n*-butyl ether was added 10 ml. of concentrated sulfuric acid dropwise, with stirring. The mixture was stirred for 1 hr., kept overnight, poured onto ice, and made alkaline with ammonium hydroxide. After cooling, the precipitate was collected, washed with water, and dried. Recrystallization from carbon tetrachloride gave colorless crystals, m.p. 179–181°, with an infrared spectrum indistinguishable from that of authentic XI. No amide product could be isolated from runs in which acetic acid was used as solvent.

Intermediates in the Nitrous Acid Deamination of 2-[*p*-(2′-Hydroxyethoxy)phenyl]ethylamine[1]

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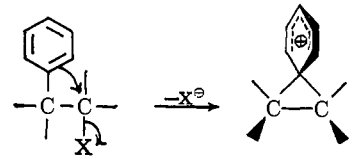
Nitrous acid deamination in water and in acetic acid of the para-substituted 2-phenylethylamine, p-$HOCH_2CH_2OC_6H_4CH_2CH_2NH_2$, and the corresponding deuterated amine p-$HOCD_2CH_2OC_6H_4CH_2CD_2NH_2$, resulted in 39–40% isotope-position migration in the ethyl group as determined from the nuclear magnetic resonance spectra of the products obtained from the deuterated amine. Aryl migration between the oxygens of the hydroxyethoxy group was considered possible but was not observed.

Introduction

The role of phenyl-bridged (phenonium) ions in the ionization reactions of 2-phenylethyl and 3-phenyl-2-butyl derivatives is a topic that has provoked considerable discussion. On the one hand,[3a] it is argued that phenonium ions are discrete intermediates which may be formed by participation of a neighboring phenyl group in ionization reactions of compounds of the type $C_6H_5-\overset{|}{\underset{|}{C}}-\overset{|}{\underset{|}{C}}-X$. The other view is that phenonium



ions are at most merely the transition states for the migration of phenyl groups in between isomeric "open" carbonium ions.

In ionization reactions of 2-phenylethyl derivatives, kinetic and isotopic labeling experiments[4] have revealed that the extent of phenyl migration depends on the mode of carbonium ion formation (solvolysis or

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(2) Participant in the Undergraduate Research Program of the National Science Foundation.

(3) For leading references see (a) D. J. Cram, *J. Am. Chem. Soc.*, **86**, 3767 (1964); (b) H. C. Brown, K. J. Morgan, and F. J. Chloupek, *ibid.*, **87**, 2137 (1965).

(4) S. Winstein, C. R. Lindegren, H. Marshall, and L. L. Ingraham, *ibid.*, **75**, 147 (1953).