of 2.7 g, was recrystallized from 150 ml of water to give 12.5 g of colorless platelets of **25** with unchanged melting point. The 4′-position of the sulfonate group was confirmed by the nmr spectrum. Unlike the 3′ isomer, **25** is quite insoluble in cold water.

2-Ethyl-5-phenylisoxazolium 3′-Sulfonate (1).—A suspension of 78.2 g of **24** in a solution consisting of 400 ml of ethanol, 100 ml of water, and 100 ml of hydrochloric acid (*d* 1.19) was stirred at 25° for 16 hr. The resulting clear solution was concentrated to 200 ml in a 35° bath, and 1800 ml of ethanol was added. The crude, colorless crystals which separated on cooling were recrystallized from dilute ethanol to give 43 g (78% yield) of fine crystals.

2-Methyl-5-phenylisoxazolium 3′- and 4′-Sulfonates (26 and 27).—A solution of 5.0 g of the 2:1 mixture of 5-(3- and 4-chlorosulfonylphenyl)isoxazole and 5 ml of dimethyl sulfate in 10 ml of acetonitrile was held at 40° for 70 hr, and the solvent was evaporated. The residual oil was washed with ether and hydrolyzed in 6.5 ml of water and 10 ml of ethanol during 18 hr at 25°. By fractional crystallization from water and dilute ethanol were isolated 1.35 g of the less soluble 3′ isomer **26** from water and 0.55 g of the more soluble 4′ isomer (**27**) from dilute ethanol. The positions of the anionic sulfonate substituent were determined by comparison of the infrared and nmr spectra with those of the known 2-ethyl homologs. It is interesting to note that the solubilities of the 3′ and 4′ isomers in the two sets (methyl and ethyl) are reversed.

5-(3-Chlorosulfonyl-*p*-tolyl)isoxazole. A.—A solution of 16 g (0.1 mole) of 5-*p*-tolylisoxazole and 59 g (0.5 mole) of distilled chlorosulfonic acid was held at 20–25° for 24 hr, protected from the atmosphere by a tube of Drierite. Essentially no reaction occurred at this temperature; therefore, the temperature of the solution was raised, with stirring, to 58–60° (HCl evolution) and held there for 18 hr. The solution was cooled and poured into ice, and the yellow solid which separated was filtered, washed with cold water, and dissolved in chloroform. The chloroform solution, after drying over magnesium sulfate, followed by a charcoal treatment, yielded 19 g (74%) of crude product on evaporation. Recrystallization from 300 ml of carbon tetrachloride produced 16.8 g (65%) yield) of pure, cream-colored plates, mp 140–142°. An analytical sample melted at 141–142.5°.

Anal. Calcd for $C_{10}H_8ClNO_3S$: C, 46.6; H, 3.1; Cl, 13.8. Found: C, 46.6; H, 3.2; Cl, 14.0.

B.—In a similar, earlier run in which the temperature was held at 25° for 2 hr, followed by 73–75° for 24 hr, only a 10% yield of the sulfonyl chloride was obtained from chloroform extracts of the drowned reaction mixture. A second fraction (*ca.* 7% yield) was isolated from the carbon tetrachloride recrystallization filtrates. This, after several recrystallizations (methylcyclohexane), melted at 93–98° and was indicated by its infrared spectrum and elemental analysis to be largely a di(chlorosulfonyl) derivative of 5-*p*-tolylisoxazole contaminated with the monosubstituted compound.

The aqueous solution from the chloroform extraction was treated with an aqueous solution containing 364 g of barium acetate. After removal of the precipitated barium sulfate from the hot aqueous solution, 59 g of a crystalline, white solid separated on cooling. Another 29.5 g was obtained on further treatment of the filtrate with 50 g of barium acetate. Recrystallization from water gave 66 g of what was judged by the nmr spectrum to be the pure barium salt of 5-*p*-tolylisoxazole-3′,4-disulfonic acid.

Anal. Calcd for $C_{10}H_7BaNO_7S_2$: C, 26.4; H, 1.5; Ba, 30.1; N, 3.1; S, 14.1. Found: C, 26.4; H, 1.7; Ba, 30.1; N, 2.8; S, 13.8.

2-Methyl-5-*p*-tolylisoxazolium 3′-Sulfonate (28).—By a procedure similar to that employed for **26** and **27**, a 63% yield of this product was obtained with recrystallization from dilute ethanol. The over-all yield from 5-*p*-tolylisoxazole was 41%. The 3′-position of the sulfonate substituent was indicated by the nmr spectrum.

Acknowledgments.—The assistance of Miss Thelma J. Davis with infrared spectra and that of Mr. C. M. Combs and Dr. J. K. O'Loane with the nmr spectra is gratefully appreciated. Tests of the thermal and shock sensitivity of the perchlorates were run by Dr. R. D. Coffey.

An Unusual Stevens Rearrangement of a Tetrahydropyridinium Salt

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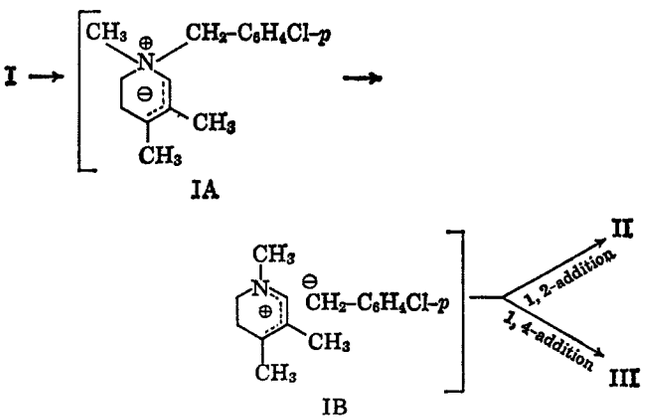
In the presence of ethereal phenyllithium, 1,3,4-trimethyl-1-*p*-chlorobenzyl-1,2,5,6-tetrahydropyridinium chloride (I) undergoes rearrangement to the expected product, 1,3,4-trimethyl-2-*p*-chlorobenzyl-1,2,5,6-tetrahydropyridine (II) in about 15% yield, and to two other products, 1,3,4-trimethyl-4-*p*-chlorobenzyl-1,4,5,6-tetrahydropyridine (III), and 1,3,3-trimethyl-2-*p*-chlorophenyl-4-methylenepiperidine (IV). Their structures have been proven by infrared, pmr, and mass spectral data. Possible routes for these rearrangements are discussed.

1,3,4-Trimethyl-1-*p*-chlorobenzyl-1,2,5,6-tetrahydropyridinium chloride (I) was prepared because it was expected to yield 1,3,4-trimethyl-2-*p*-chlorobenzyl-1,2,5,6-tetrahydropyridine (II) under Stevens rearrangement conditions.[1] Compound II was desired as a precursor for the benzomorphan structure V, which was considered interesting for testing as an analgesic.[2]

The pyridinium salt I was subjected to Stevens rearrangement conditions with phenyllithium, and the biphasic mixture was worked up in the usual way. A glpc of the product showed that it was a mixture of three main components, in the ratio 2:1:2. The product was distilled through a spinning-band column, and the three fractions which were collected were further purified by repeated recrystallization of their picrates. Microanalysis showed that the three compounds were isomers, with the formula $C_{15}H_{20}ClN$ (free base). One of these isomers, the intermediate fraction obtained from the distillation, was the expected



(1) E. M. Fry and E. L. May, *J. Org. Chem.*, **26**, 2592 (1961).
(2) A. E. Jacobson and E. L. May, *J. Med. Chem.*, **8**, 563 (1965).

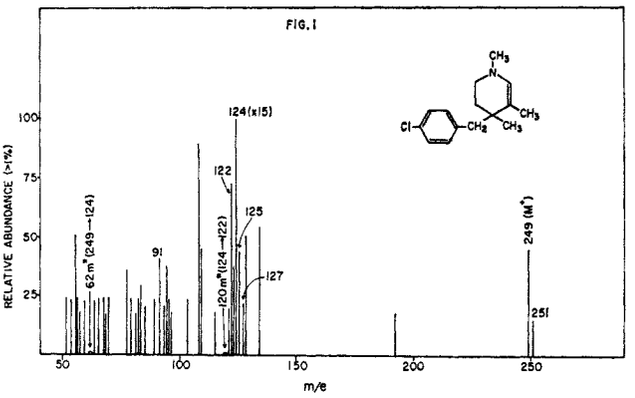
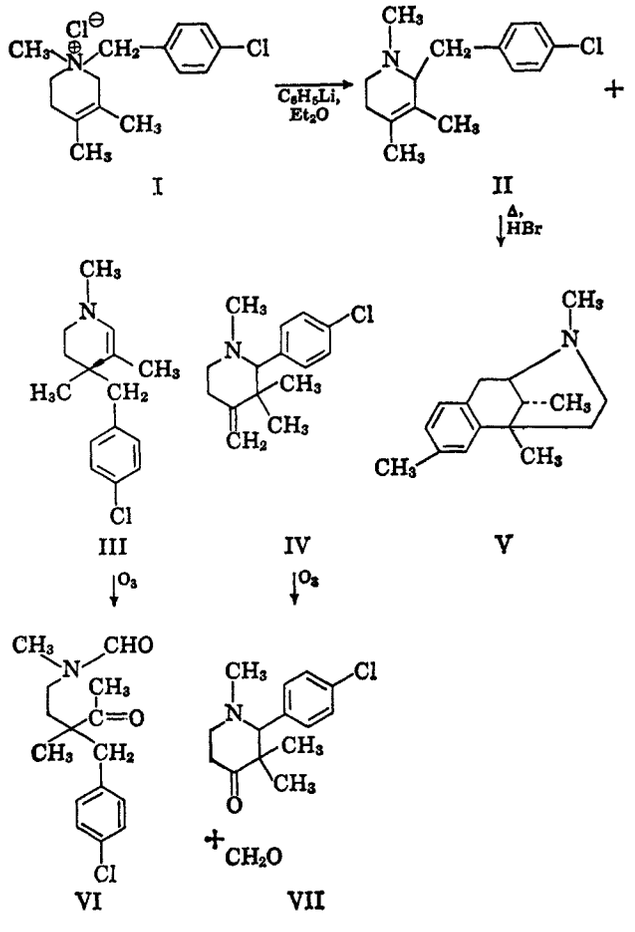


Figure 1.—Mass spectrum of 1,3,4-trimethyl-4-*p*-chlorobenzyl-1,4,5,6-tetrahydropyridine (III) hydrochloride.

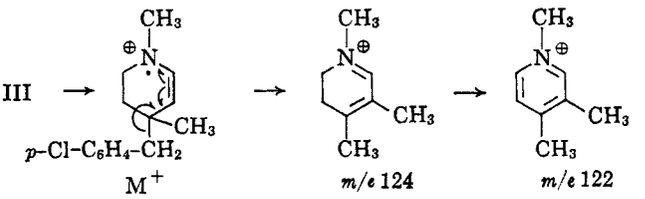
product of the rearrangement, 1,3,4-trimethyl-2-*p*-chlorobenzyl-1,2,5,6-tetrahydropyridine (II) (Chart I). This was established by the pmr spectrum, identity with II obtained by unequivocal synthesis,[2] and conversion to α-2′-chloro-2,5,9-trimethyl-6,7-benzomorphan (V). The formation of II can be explained by an ion pair mechanism.[3]

CHART I

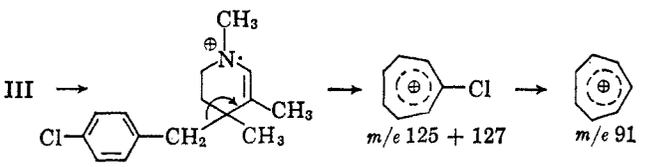


The third fraction obtained from the distillation contained isomer III, whose formation can be rationalized by a 1,4-addition to Ib.[4] The pmr spectrum of III[5] had signals indicative of a methyl group on a quaternary carbon, and a second methyl group on an unsaturated carbon atom 1,3-coupled to an hydrogen atom. A 2.48-ppm singlet was ascribed to N–CH_3 on the basis of its shift to 3.6 ppm in the picrate salt. These data are accommodated by structure III, 1,3,4-trimethyl-4-*p*-chlorobenzyl-1,4,5,6-tetrahydropyridine.

The infrared spectrum[5] showed bands consistent with a trisubstituted double bond and the absorption for a *para*-substituted aromatic ring. The mass spectrum of the hydrochloride salt supported the structure having peaks for the parent and for rationalizable fragmentation products (Figure 1). The largest peak, by far, was *m/e* 124, assigned to $C_8H_{14}N$, which could be expected to be the major fragmentation product *via* the route



The *p*-chlorobenzyl or tropylium ion is also observed in the spectrum. This could arise *via*



Since this was believed to occur in the one-step fragmentation, it should yield the calculated metastable ion at *m/e* 61.8. A small amount of metastable ion was detected at *m/e* 62. Other fragmentation products arise through aromatization of the dihydropyridinium ion, and loss of chloride from the *p*-chlorobenzyl ion. The aromatization can also be considered a one-step fragmentation process, the metastable ion *m/e* 120 being observed (*m/e* 124 → 122).

Additional evidence was obtained from the perchlorate derivative of III. A 2,3-double bond in a tetrahydropyridine is known[6] to rearrange to the 1,2-position in the presence of strong acid. The infrared spectrum of the perchlorate indicated that the double bond had migrated by the shift of the 1650 (C=C) to 1690 (C=N^+) cm^{-1} band.

Ozonolysis of III in chloroform, followed by treatment with zinc and acetic acid, gave a product presumed to be VI, judging by the infrared and pmr data. The infrared spectrum showed bands at 1673 cm^{-1} (s) for an N–CHO group, and at 1699 cm^{-1} (m) with a broad overtone at about 3450 cm^{-1} (w) for the ketone. The pmr spectrum corroborated the interpretation of the infrared, having chemical shifts at 1.1 ppm (singlet) for the CH_3 group on a quaternary carbon atom, 2.0 ppm (singlet) for the CH_3 group next to the carbonyl,

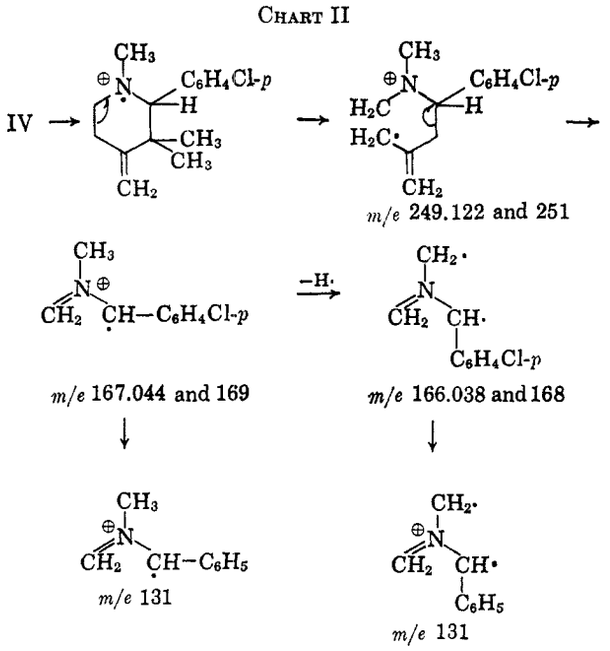
(3) D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press Inc., New York, N. Y., 1965, p 226.

(4) It might, *a priori*, be postulated that I → II which then undergoes an allylic rearrangement to III. However, when II was treated with phenyllithium in ether, none of compound III was produced, II remaining unchanged under these conditions.

(5) See Experimental Section.

(6) N. J. Leonard and F. P. Hauck, Jr., *J. Am. Chem. Soc.*, **79**, 5279 (1957).

CHART II



N–CH_3 centered about 2.8 ppm, and the formyl proton at about 8 ppm.[7a]

The remaining isomer, which had the lowest boiling point of the three, was isolated in lower yield than either II or III, although the glpc of the crude material indicated that its yield was equal to III and twice that of II. The pmr spectrum of IV had chemical shifts indicating a *gem*-dimethyl group on a quaternary carbon atom, and an N–CH_3 group. There were also four aromatic protons and one proton (2.98 ppm, singlet) near a deshielding group [compound III clearly showed a methylene group adjacent to an aromatic ring (2.68 ppm, two-proton singlet); no such absorption was present in IV]. The spectrum lastly showed a two-proton singlet at 4.71 ppm, a terminal methylene group, analogous to methylenecyclohexane (4.55 ppm, singlet).[7b]

Conversion of IV to the hydrochloride salt produced a marked change in the configuration of the molecule due to the introduced rigidity. The *gem*-dimethyl group no longer appeared as a singlet. One of the C-methyl groups was deshielded and the second methyl group exhibited a diamagnetic shift. Practically every other proton in the molecule was paramagnetically shifted including, of course, the N–CH_3 group which now appeared as a doublet at 2.9 ppm. Evidently it was fortuitous that a singlet was exhibited for the *gem*-dimethyl group in the free base. Thus, one must have a structure in which each of the C–CH_3 groups can appear in different environments in the hydrochloride salt, and which revert to indistinguishable environments in the free base.

The pmr spectra obviously impose severe restrictions on the structures which can be written for IV. The infrared spectrum was consistent with the evidence obtained by pmr. There is only one structure which can be written for this isomer which would satisfy the data, and that is IV, 1,3,3-trimethyl-2-*p*-chlorophenyl-4-methylenepiperidine. Molecular models[8] indicate that, in the hydrochloride salt, the methyl groups do appear in different environments.

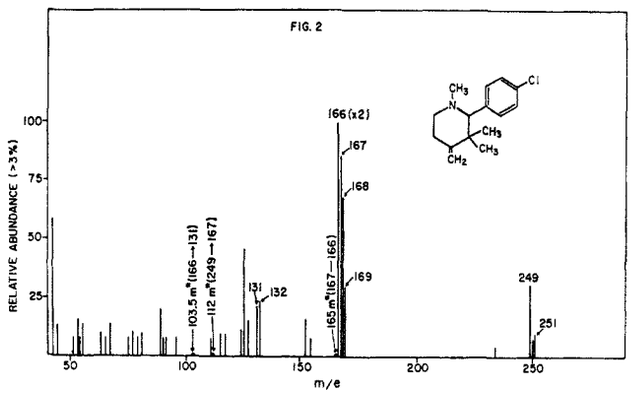


Figure 2.—Mass spectrum of 1,3,3-trimethyl-2-*p*-chlorophenyl-4-methylenepiperidine hydrochloride (IV).

The mass spectrum of the hydrochloride salt of IV (Figure 2) supported the structural assignment. There are peaks for the parent and for rationalizable fragments. The major fragment had *m/e* 166.038, and it contained chlorine (the ion with *m/e* 168 was about one-third as abundant as the ion with *m/e* 166). This was assigned to the C_9H_9ClN fragment of Chart II.

The one-step process from *m/e* 249 to *m/e* 167[9] gives rise to the observed metastable ion at *m/e* 112. The other metastable ions arise from two further one-step processes (167 → 166 → 131).

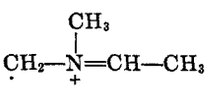
It is possible to rationalize this rearrangement in several different ways. One of the more likely possibilities[10] requires the removal of the benzylic proton and ring opening to form an allylic carbanion (IVA). Proton transfers (IVA and C) and rotations about single bonds (IVB and D) can lead to a different allylic carbanion (IVE), which can close to form the product (Chart III). Further work is contemplated to elucidate this mechanism. It should be noted that this structure (IV) has a hydrogen atom in an axial position on C-2 which should appear in the pmr spectrum as a singlet in a somewhat deshielded position.[7c]

Compound IV was ozonized, the formaldehyde which was produced in the reaction being trapped as the dimedone derivative, giving a ketone, VII, which had a 1700-cm^{-1} band in the infrared with an overtone at 3450 cm^{-1}. The pmr spectrum indicated a four-proton aromatic singlet, an N–CH_3 at 2.18 ppm (singlet), one methyl at 1.38 ppm (singlet), the second methyl at 1.6 ppm (singlet), and a one-proton singlet at 3 ppm for the axial hydrogen atom at C-2. Presumably, both C-methyls are affected by the deshielding influence of

(7) "NMR Spectra Catalogs," Varian Associates, Palo Alto Calif., 1962 and 1963: (a) Spectrum 39. The N–CH_3 signal in N,N-dimethylformamide appears at about 2.9 ppm, with the formyl proton occurring at 8.02 ppm. (b) Spectrum 180. (c) Spectra 240 and 478. Axial hydrogen atoms next to nitrogen in heterocyclic rings are usually more shielded than equatorial hydrogen atoms. The major deshielding effect in IV, however, is apparently due to the aromatic ring (*e.g.*, the axial hydrogen atoms next to nitrogen in 3-methylenepiperidine exhibit chemical shifts at 1.55 and 2.21 ppm, while the single proton in cumene, on the α carbon, appears at 2.9 ppm).

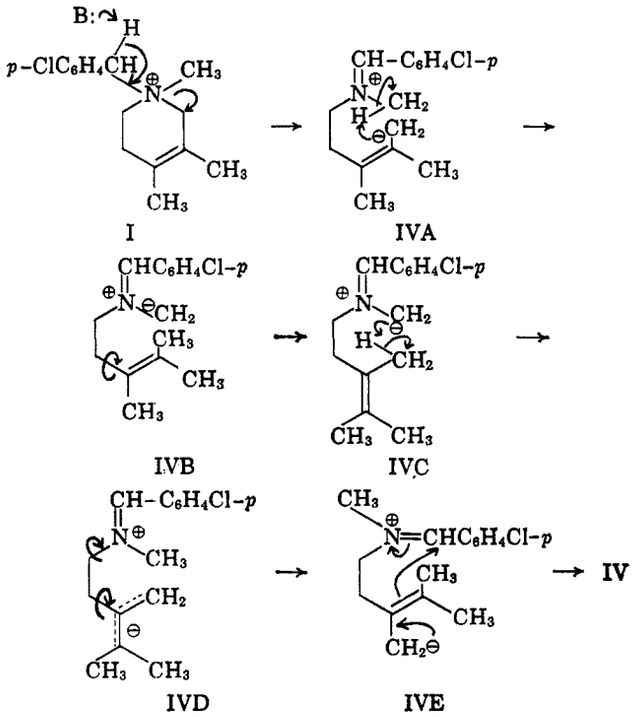
(8) Catalin molecular models, Catalin Ltd., Waltham Abbey, Essex, U. K.

(9) H. Budzikiewicz, *Tetrahedron*, **20**, 2267 (1964). An analogous fragmentation occurs in the steroidal alkaloid conanine, giving rise to the fragment



(10) The author thanks Dr. D. J. Cram (personal communication) and both referees for their aid in postulating this mechanism.

CHART III



the adjacent carbonyl, but one considerably more than the other. The chemical shift of the C-2 proton is unchanged, reflecting the unchanged environment about C-2.

Attempts made to cleave compounds III and IV under Hofmann degradation conditions were fruitless. Molecular models indicated that IV would exhibit considerable steric hindrance to a reaction with methyl iodide and, indeed, the methiodide could not be obtained in acetone solution. The methiodide of III was prepared, but it gave only the free base, III, after it was subjected to Hofmann degradation under any of the attempted reaction conditions. There are two β-hydrogens available for the Hofmann degradation in III methiodide. Neither of them appears to be particularly acidic, and apparently the preferred reaction is the loss of methanol to give starting material.

Lastly, it should be noted that the more complex of the three rearrangements is not limited to this particular pyridinium salt. A product whose pmr spectrum was very similar to that of IV was isolated from the reaction of 1,3,4-trimethyl-1-benzyl-1,2,5,6-tetrahydropyridinium chloride with phenyllithium.[11]

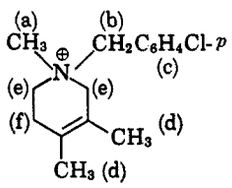
Experimental Section

Melting points were taken in a capillary (Hershberg apparatus, total immersion thermometers). Microanalyses were by the Analytical Services Section of these Institutes. Mass spectra were determined on an Associated Electronics Industries, MS-9, double-focusing mass spectrometer, introducing the compound directly into the inlet. Accurate mass measurements were made relative to perfluorokerosene internal standard where C = 12.00000, and were within 0.006 mass unit of the theoretical values. The pmr spectra were determined by Mrs. J. Goodwin on a Varian A-60 spectrometer. All of the spectra were obtained in $CDCl_3$ with tetramethylsilane as the internal standard except where indicated. Chemical shifts are listed as δ values (ppm); single values for multiplets represent the approximate center. Assignment was made on the basis of the integrated values obtained for the number of protons.

Infrared spectra (liquid film) were obtained on a Perkin-Elmer 237-B grating spectrophotometer. The glpc were run isothermally at 170° on a Warner-Chilcott 1600 series chromatograph. A 1.83-m glass column, 6.3 mm in diameter, was used, silanized, and packed with 5% SE 30 on 80–100 mesh Chromosorb G. It was equipped with a flame ionization detector.

1,3,4-Trimethyl-1-*p*-chlorobenzyl-1,2,5,6-tetrahydropyridinium Chloride (I).—1,3,4-Trimethyl-1,2,5,6-tetrahydropyridine[1] was treated with *p*,α-dichlorotoluene in acetone to give a white solid, I, mp 220–221° dec, after recrystallization from acetone–ether (Chart IV).

CHART IV[a]



[a] Pmr (δ) of I: a = 3.3 (singlet); b = 5.34 (singlet); c = 7.46 and 7.89 (two apparent doublets, with further splitting apparent); d = 1.72 (broad singlet); e = 3.9–4.2 (multiplet); f = 2.4 (multiplet).

Anal. Calcd for $C_{15}H_{21}Cl_2N$: C, 62.94; H, 7.40. Found: C, 62.90; H, 7.51.

Stevens Rearrangement of 1,3,4-Trimethyl-1-*p*-chlorobenzyl-1,2,5,6-tetrahydropyridinium Chloride (I).—The salt (I, 69 g, 0.24 mole) was suspended in ether (*ca.* 200 ml) and a phenyllithium solution[12] (150 ml, 2.25 *M*, diluted with an additional 150 ml of ether, 0.33 mole) was added rapidly with vigorous stirring. The stirring was continued for 5 hr at 25° after the initial heat evolution. The mixture was poured into cold water, and the aqueous phase was extracted with ether. The combined ethereal solution was extracted with dilute hydrochloric acid. The acidic solution was cooled in ice and made basic with concentrated ammonium hydroxide. Three extractions with chloroform and one with ether, followed by drying over magnesium sulfate and removal of solvent, gave a brown oil (41 g). The glpc of the product showed it to be a mixture of at least three components, in the ratio 2:1:2. The oil was distilled at 0.1 mm through a spinning-band column[13] and three fractions were collected. The first fraction, 5.8 g, collected at 82–98°, was found by glpc to be IV, 1,3,3-trimethyl-2-*p*-chlorophenyl-4-methylenepiperidine, contaminated only slightly (10%) with compound II. The second fraction, collected at 100–107°, 16.8 g, was found to be a mixture of all three components but mainly II (~60%), 1,3,4-trimethyl-2-*p*-chlorobenzyl-1,2,5,6-tetrahydropyridine. The third fraction, collected at 107–109°, 9.6 g, was found to be III, 1,3,4-trimethyl-4-*p*-chlorobenzyl-1,4,5,6-tetrahydropyridine, with perhaps 10% of a contaminant (II).

1,3,3-Trimethyl-2-*p*-chlorophenyl-4-methylenepiperidine (IV).—Fraction one was dissolved in ethanol and a picrate was prepared. It was recrystallized twice from ethanol–acetone, mp 150° (final, dec).

Anal. Calcd for $C_{21}H_{23}ClN_4O_7$: C, 52.67; H, 4.84; N, 11.70. Found: C, 52.85; H, 4.70; N, 11.86.

The free base was liberated and a hydrochloride salt was prepared and recrystallized from acetone–methanol–ether, mp 209–211°.

Anal. Calcd for $C_{15}H_{21}Cl_2N$: C, 62.94; H, 7.40; Cl, 24.78. N, 4.89. Found: C, 62.96; H, 7.25; Cl, 25.10; N, 4.87.

Infrared[14] (free base): 3083 (m), 1636 (m), 1410 (m–s), and 888 (s) cm^{-1} for the terminal methylene; 3027 (w), 1900 (w), 1775 (w), 1720 (w), 1590 (w–m), 1480 (s), and 825 (s) cm^{-1} for the *para*-substituted aromatic ring; 2785 (s), 1080 (s), 1185 (m), and 1120 (m), or 1080 (s), and 1040 (m) cm^{-1} for the N–CH_3; 1170 (sh) on 1185 (m) or 1215 (sh) on 1240 (m) cm^{-1} for the *gem*-dimethyl (Chart V).

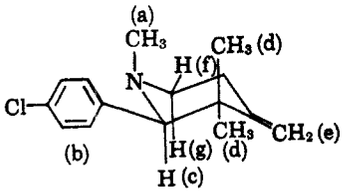
(11) A. E. Jacobson, unpublished data.

(12) Lithium Corp. of America, Inc.

(13) Intermediate laboratory-size spinning-band column, Nester and Faust.

(14) Band assignments are comparable with known absorptions [K. Nakanishi, "Infrared Absorption Spectroscopy," Holden-Day, Inc., San Francisco, Calif., 1962].

CHART V[a]



[a] Pmr (δ) of IV (free base): a = 2.18 (singlet); b = 7.23 (singlet); c = 2.98 (singlet); d = 1.25 (singlet); e = 4.71 (broad singlet); f = 3.26 (mult plet); g = 2.44 (multiplet).

IV·hydrochloride: a = 2.9 (doublet, J = 5 cps); b = 7.52 (multiplet); d = 1.16 (singlet) and 1.48 (singlet); e = 5.17 (doublet, J = 5 cps, one line of which appeared to be further split into a doublet, J = 1 cps).

1,3,4-Trimethyl-2-*p*-chlorobenzyl-1,2,5,6-tetrahydropyridine (II).—A picrate was prepared from the second fraction of the distillation, and it was recrystallized several times from acetone–ethanol. This was converted to the free base by a lithium hydroxide solution. A hydrochloride was prepared and washed with acetone, which removed the more soluble IV hydrochloride. The free base was liberated once again and distilled. A picrate was prepared from this oil, mp 158–159° (lit.[2] mp 157–158°). The free base which was liberated from this picrate was converted to a hydrochloride salt and recrystallized from acetone–methanol–ether; mp 180–181°; pmr (δ) (free base): 1.58 (singlet) for the methyls on the double bond, 2.3 (singlet) for N–CH_3, 7.12 (singlet) for aromatic protons.

Anal. Calcd for $C_{15}H_{21}Cl_2N$: C, 62.94; H, 7.40; Cl, 24.77. Found: C, 63.20; H, 7.21; Cl, 24.52.

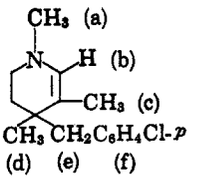
The pmr of the picrate of II was obtained in dimethyl sulfoxide, with tetramethylsilane as the internal standard: 1.48 and 1.68 (singlets) for the methyls on the double bond; 2.8 (singlet) for N^+–CH_3; and 7.44 for the aromatic protons.

1,3,4-Trimethyl-4-*p*-chlorobenzyl-1,4,5,6-tetrahydropyridine (III).—A picrate was prepared from the third fraction of the distillation and it was recrystallized three times from ethanol–acetone, mp 133–135°.

Anal. Calcd for $C_{21}H_{25}ClN_4O_7$: C, 52.67; H, 4.84; N, 11.70. Found: C, 52.95; H, 4.99; N, 11.94.

The free base was liberated from the picrate and distilled, and a hydrochloride salt was made and recrystallized from acetone–methanol–ether. This salt was converted back to a free base and a methiodide was prepared and crystallized in acetone; mp 271–273° dec; infrared[14] (free base): 3040 (w–m), 1650 (s), 860 and 810 cm^{-1} (m–s) for the trisubstituted double bond; 3045 (w–m), 1890, 1770, 1725 (w), 1590 (w), 1480 (s), and 830 (m–s) cm^{-1} for the *para*-substituted aromatic ring; 2810 (s) or 2780 (m), 1200 and 1150 (m) or 1150 (m), and 1090 (s) cm^{-1} for the N–CH_3 (Chart VI).

CHART VI[a]



[a] Pmr (δ) of III: a = 2.48 (s nglet); b = 5.58 (quartet, J = 1 cps); c = 1.6 (doublet, J = 1 cps); d = 1.0 (singlet); e = 2.68 (singlet); f = 7.17 (multiplet).

Anal. Calcd for $C_{16}H_{23}ClIN$: C, 49.06; H, 5.92. Found: C, 48.88; H, 6.09.

1,3,3-Trimethyl-2-*p*-chlorophenylpiperidin-4-one (VII).—The 4-methylenepiperidine compound (IV, 0.1 g) was ozonized in chloroform (15 ml) at room temperature according to the method of Boekelheide and Agnello.[15] A water trap placed between the ozonolysis vessel and a potassium iodide solution collected sufficient formaldehyde to give the formaldehyde–dimedone derivative after long standing and refrigeration (*ca.* 3 mg, mp 186–189°).[16] The ozonized product was treated with zinc (1 g) and acetic acid (25 ml, 50%). Most of the chloroform was distilled from the stirred mixture, which was then filtered and made basic with concentrated ammonium hydroxide. Extraction with ether gave a yellow oil, VII. The infrared and pmr spectra of the oil are commented upon in the discussion.

A similar procedure was followed in the ozonolysis of 1,3,4-trimethyl-4-*p*-chlorobenzyl-1,4,5,6-tetrahydropyridine (III), to give VI. The infrared and pmr spectra of VI are discussed in the text.

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(16) "The Merck Index," P. G. Stecher, M. J. Finkel, and O. H. Siegmund, Ed., 7th ed, Merck and Co., Inc., Rahway, N. J., 1960, p 371. The formaldehyde–dimedone derivative is listed having mp 189°.

Kinetics and Substituent Effects in Electrophilic Aromatic Substitution. I. Tritylation of Phenol and Its Alkyl Ethers[1]

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The kinetics of the reaction of phenol, anisole, phenetole, and isopropoxybenzene with trityl perchlorate were followed dilatometrically in nitromethane. Substitution was exclusively at the *para* position by the bimolecular mechanism. The order of activation found for the substituents was $OCH_3 < OH < OC_2H_5 < OCH(CH_3)_2$. This is interpreted as the result of a progressive enhancement of the inductive effect of the alkoxy groups along the series, whereas the higher reactivity of phenol compared with that of anisole is attributed to the ability of the former to establish hydrogen bonds with the solvent. Attempts to carry out the reaction with *t*-butoxybenzene yielded 4-hydroxytetraphenylmethane, that is the substitution product of phenol. The possibility of the process taking place through the rearrangement of an oxygen-tritylated intermediate is deemed improbable.

During the past few years we have been interested in the problem of activation and orientation in the benzene ring toward electrophilic substitution when two groups are present in the ring.[2,3] These studies were carried out qualitatively, or semiquantitatively, by yield determination and product analysis. For a more basic approach to the problem it was decided to follow the

(1) Presented in part at the Third Caribbean Chemical Symposium, Caracas, Jan 1965, and abstracted in N. Barroeta, H. Díaz, G. Chuchani, and J. Zabicky, *Acta Cient. Venezolana*, **15**, 248 (1964).

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