ated by two successive treatments with methyl iodide and silver oxide in dimethylformamide.[20,21] The methylated galactomannan was fractionated from chloroform solution by gradual addition of hexane (b.p. 64–65°). The bulk of the material precipitated between hexane concentrations of 84 to 86%; $[\alpha]^{25}_{D}$ +58° (*c*, 1.0 in chloroform); methoxyl content 44.1%.

Hydrolysis and Isolation of Methylated Sugars.—Two grams of methylated galactomannan were methanolized 10 hr. in methanol containing 5% hydrogen chloride to a constant optical rotation of $[\alpha]^{25}_{D}$ +66.2°. The mixture was concentrated under reduced pressure to a sirup and after addition of water and boiling for 7 hr., again concentrated. The solution was neutralized with silver carbonate and deionized with Amberlite IR 120 H. The solution, free of silver and chloride ions, was concentrated to a sirup (2.0 g.). Chromatographed on paper with ethyl acetate:pyridine:water, as above, indicated three components with R_f values of 0.82, 0.77 and 0.57, respectively. An aliquot from the above hydrolyzate was quantitatively analyzed by paper chromatography. The paper was irrigated as above and the sugars determined with alkaline hypoiodite.[22] The results correspond to a ratio of tetra-*O*-methyl- to di-*O*-methyl- to tri-*O*-methyl-sugar of 2.1:2:1.

A portion (1.48 g.) of the methylated sugar sirup was separated on a cellulose column with benzene:ethanol:water (167:47:15 v./v.) as an irrigant and using an automatic fraction collector.[13] The first fraction of 0.604 g. with R_f of 0.82 and $[\alpha]^{25}_{D}$ +101° (*c*, 1.0 in water) was 2,3,4,6-tetra-*O*-methyl-D-galactose. Calcd.: OCH_3, 52.5. Found: OCH_3, 52.5. When 25 mg. of the sirup was boiled with 15 mg. of distilled aniline in 10 ml. of absolute ethanol, there was obtained 28 mg. of N-phenyl-D-galactopyranosylamine 2,3,4,6-tetramethyl ether,[23] m.p. 192–193°. Calcd.: N, 4.5. Found: N, 4.6. The second effluent sirup of 0.257 g. with an R_f value of 0.77 had an optical rotation of $[\alpha]^{25}_{D}$ +27.9° (*c*, 1.0 in ethanol) and was 2,3,6-tri-*O*-methyl-D-mannose. Calcd.: OCH_3, 41.8. Found: OCH_3, 42.7. On demethylation of 5 mg. in 1 ml. of 48% hydrobromic acid for 5 minutes at 100°, only mannose was obtained by paper chromatographic examination of the products. When 50 mg. of the methylated sirup was boiled with 0.18 of distilled aniline in 10 ml. of absolute ethanol, N-phenyl-D-mannopyranosylamine 2,3,6-trimethyl ether[24] was obtained; m.p. 128–130° unchanged when mixed with an authentic sample. When 0.1 g. of the methylated sirup was oxidized with 10 ml. of bromine water and the solution concentrated, 2,3,6-tri-*O*-methyl-D-mannonolactone was obtained as a sirup. This on boiling with phenylhydrazine in ethanol gave 2,3,6-tri-*O*-methyl-D-mannonic acid phenylhydrazide[25] (60 mg.), m.p. 130° unchanged on admixture with an authentic sample. Calcd.: N, 8.5. Found: N, 8.4.

The third effluent sirup of 0.453 g. with an R_f value of 0.57 had an optical rotation of $[\alpha]^{25}_{D}$ +9.4° (*c*, 2.0 in ethanol) and was 2,3-di-*O*-methyl-D-mannose. Calcd.: OCH_3, 29.8. Found: OCH_3, 29.9. Oxidation with bromine water gave 2,3-di-*O*-methyl-D-mannonolactone,[26] m.p. 110–111°. Calcd.: OCH_3, 30.1. Found: OCH_3, 28.6. When the lactone was boiled with phenylhydrazine in ethanol, there was produced 2,3-di-*O*-methyl-D-mannonic acid phenylhydrazide,[26] m.p. 168–170°, and $[\alpha]^{25}_{D}$ −22° (*c*, 0.5 in water). Calcd.: N, 8.9. Found: N, 9.0.

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[20] R. Kuhn, H. Trischmann and I. Löw, *Angew. Chem.*, **67**, 32 (1955).

[21] J. Saarnio, Ph.D. Thesis, University of Helsinki, Finland, 1956.

[22] S. K. Chanda, E. L. Hirst, J. K. N. Jones and E. G. V. Percival, *J. Chem. Soc.*, 1289 (1950).

[23] J. C. Irvine and D. McNicoll, *ibid.*, **97**, 1449 (1910).

[24] W. N. Haworth, E. L. Hirst and H. R. L. Streight, *ibid.*, 1349 (1931).

[25] F. Klages, *Ann.*, **509**, 159 (1934); *ibid.*, **512**, 185 (1935).

[26] E. H. Goodyear and W. N. Haworth, *J. Chem. Soc.*, 3136 (1927); F. Smith, THIS JOURNAL, **70**, 3249 (1948).

LAFAYETTE, IND.

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF WAYNE STATE UNIVERSITY]

Nitrogen Analogs of Ketenes. III. Formation of Hydroperoxides and Vinylamines by Reaction with Lithium Aluminum Hydride and Organometallic Reagents[1,2]

BY CALVIN L. STEVENS AND ROBERT J. GASSER[3]

RECEIVED MARCH 20, 1957

Reduction of diphenylketene-*p*-tolylimine (I) with lithium aluminum hydride gave the amino alcohol II by reaction *via* a hydroperoxide. The ketenimine I reacted with phenylmagnesium bromide to give a stable hydroperoxide III which could be reduced catalytically to the ketone imine IV or with lithium aluminum hydride to the amino alcohol V. Mesitylmagnesium bromide also yielded a stable hydroperoxide VI when allowed to react with I. Hydroperoxide III was cleaved by acid to give benzophenone (VII) and the toluide of benzoic acid (VIII). Mesitylphenylketene-*p*-tolylimine (IX) was reduced by lithium aluminum hydride to give the stable vinylamine X and reacted with mesityllithium to give the vinylamine XI.

Early in the investigation of the reactions of the nitrogen analogs of ketenes an attempt was made to characterize diphenylketene-*p*-tolylimine (I) by reduction with lithium aluminum hydride. The fact that the product was an amino alcohol prompted the present investigation on the course of this type of reaction and resulted in the isolation and characterization of the hydroperoxides III and VI and the stable vinylamines X and XI.

The reduction of the ketenimine I with lithium aluminum hydride in ether solution gave a 60% yield of crude amino alcohol II, which was characterized by analysis and an acetate derivative. The structure was established by independent synthesis from α-hydroxydiphenylacetic acid *p*-toluide by reduction with lithium aluminum hydride.

The introduction of an oxygen atom into the product suggested a probable reaction course involving reduction of the ketenimine linkage with one equivalent of hydride, followed by oxidation of the resulting metal salt of the vinylamine with molecular oxygen to form the hydroperoxide salt and then further reduction of the hydroperoxide linkage to the alcohol and of the ketone imine linkage to the amine.

The oxidation of an enolate salt formed from a ketone and a Grignard reagent to give a hydroperoxide has been studied by Kohler and Mydans.[4] Also, the alkoxide-catalyzed autoxidative cleavage

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[1] Presented before the Organic Division at the 127th Meeting of the American Chemical Society, Cincinnati, Ohio, April, 1955, p. 13N.

[2] The preceding paper in this series was submitted by C. L. Stevens and J. C. French, THIS JOURNAL, **76**, 4398 (1954).

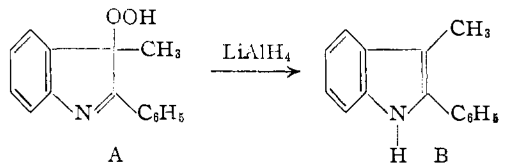
[3] Public Health Service Research Fellow of the National Heart Institute, 1955–1956.

[4] E. P. Kohler and W. E. Mydans, THIS JOURNAL, **54**, 4667 (1932).

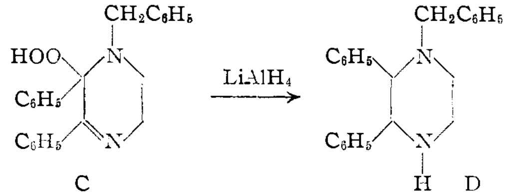
of ketones has been formulated as oxidation of the ketone enolate with molecular oxygen followed by base-catalyzed cleavage.[5] The vinylamine salt in the present work is the nitrogen analog of the enolate salt in the work of these authors.

In addition to these salts, organic compounds containing the triad $R_2C{=}X{-}Y$ ($X = CR$, $Y = NHR, OH$; $X = N$, $Y = NHR$) are known to react with molecular oxygen to form hydroperoxides. Fuson[6] and his students have studied the reaction of stable vinyl alcohols with oxygen and the reaction of a stable vinylamine, tetrahydrocarbazole, with molecular oxygen to give a stable hydroperoxide was reported by Beer, McGrath and Robertson.[7] Criegee[8] recently has reinvestigated the formation of hydroperoxides from the reaction of hydrazones with oxygen and certain Schiff bases[9] have been found to react in a like manner. Witkop and co-workers[10] have recognized that molecular oxygen may participate in the metal hydride reduction of compounds containing carbon–nitrogen double bonds.

Lithium aluminum hydride reduction of the hydroperoxide of α-phenylskatole (A) gave only the parent skatole[11] (B) while the hydroperoxide of 1-benzyl-2,3-diphenyl-2,3-dehydropiperazine (C) gave 1-benzyl-2,3-diphenylpiperazine (D) under essentially the same conditions.[12]



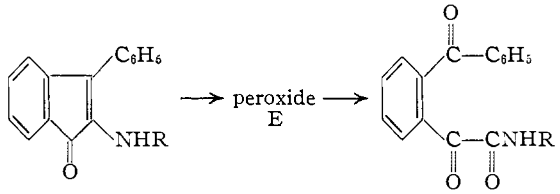
A B



C D

That a hydroperoxide of the type proposed as an intermediate is reduced by hydride to an amino alcohol was demonstrated by the isolation, characterization and reduction of the hydroperoxide III. Phenylmagnesium bromide and diphenylketene-p-tolylimine were allowed to react in refluxing ether for 24 hr., after which the relatively stable hydroperoxide III could be isolated in 68% yield. Evidence for the structure of III, which liberated iodine from acidified potassium iodide solution, was the catalytic reduction of the hydroperoxide linkage with platinum in acetic acid to give the α-hydroxy Schiff base IV in 92% yield. IV was hydrolyzed to the known α-hydroxy-α,α-diphenylacetophenone and p-toluidine, isolated in 91 and 77% yield, respectively.

Acid decomposition of the hydroperoxide III provided further evidence for the structure. From an acetone solution of III containing hydrochloric acid, benzophenone (VII) was isolated in 85% yield as the dinitrophenylhydrazone and benzoic acid p-toluide (VIII) was isolated in 77% yield. This cleavage is exactly analogous to the rearrangement of the vinylamine hydroperoxide (E) reported by Pfeiffer and deWaal[13] in 1935 and recognized by Schönberg and Michaelis[14] in 1937. More recently, Witkop[15] has investigated this type of reaction in some detail, and Lutz[12] has reported an example in the piperazine series.



Reduction of the hydroperoxide III by lithium aluminum hydride gave the amino alcohol V in 78% yield. The same compound resulted from the catalytic reduction of the α-hydroxy Schiff base IV using platinum and acetic acid solvent. The structure of this amino alcohol was confirmed by independent synthesis from N-p-tolyldesylamine and phenylmagnesium bromide.

From the reaction of mesitylmagnesium bromide with the ketenimine I, the hydroperoxide VI was isolated in only 35% yield; the products of rearrangement, benzophenone and mesitoic acid p-toluide, were found in the mother liquors. VI was characterized by acid-catalyzed decomposition, which proceeded in excellent yield.

Hydroperoxide formation was inhibited when mesitylphenylketene-p-tolylimine (IX) was substituted for I. The reduction of IX with lithium aluminum hydride under essentially the same conditions as those with I yielded a crystalline product which was isolated from the reaction in 50% yield; it contained no oxygen and was assigned the structure of the stable vinylamine X. Catalytic hydrogenation of X proceeded with the absorption of one equivalent of hydrogen to give N-p-tolyl-2-mesityl-2-phenylethylamine (XII) in 88% yield. XII was synthesized independently in 89% yield from mesitylphenylacetic acid p-toluide by reduction with lithium aluminum hydride. The choice between the vinylamine structure X and the alternate tautomeric Schiff base structure was made on the basis of a comparison of the infrared and ultraviolet spectra with the spectra of an authentic vinylamine XIII which could not tautomerize. X clearly showed an N–H band at 3.0 μ and an ultraviolet maximum at 334 mμ, ϵ 27,500. The model XIII had $\lambda_{\max}$ 337 mμ, ϵ 21,400.

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(5) W. von E. Doering and R. M. Haines, THIS JOURNAL, **76**, 482 (1954).

(6) *Cf.* R. C. Fuson and H. L. Jackson, *ibid.*, **72**, 1637 (1950).

(7) R. J. S. Beer, L. McGrath and A. Robertson, *J. Chem. Soc.*, 2118, 3283 (1950).

(8) R. Criegee and G. Lohaus, *Ber.*, **84**, 219 (1951).

(9) B. Witkop, THIS JOURNAL, **78**, 2873 (1956).

(10) B. Witkop and J. B. Patrick, *ibid.*, **75**, 4476 (1953); B. Witkop and H. M. Kissman, *ibid.*, **75**, 1975 (1953).

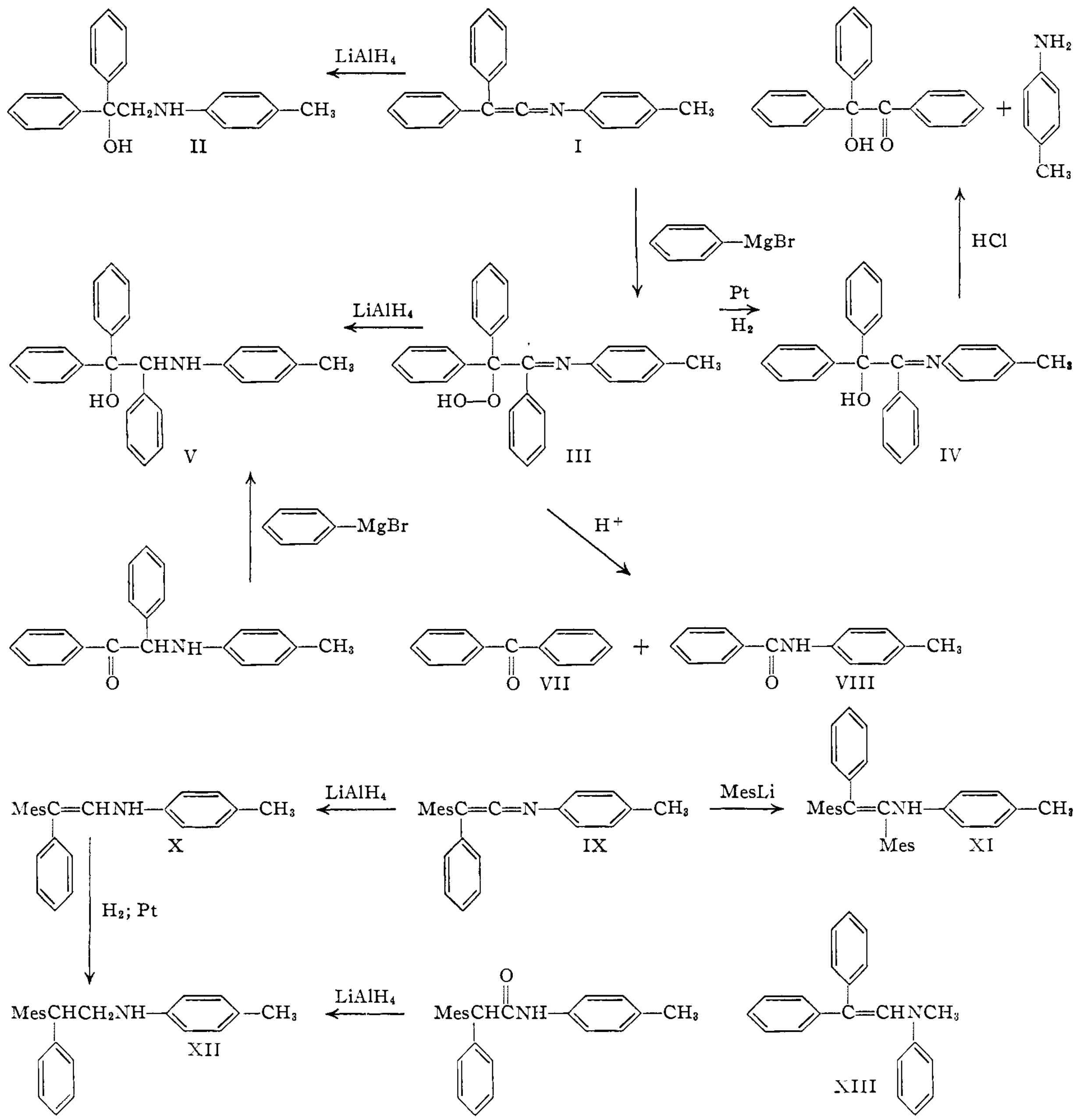
(11) B. Witkop and J. B. Patrick, *ibid.*, **74**, 3855 (1952).

(12) C. D. Lunsford, R. E. Lutz and E. E. Bowden, *J. Org. Chem.*, **20**, 1513 (1955). These authors favor the cyclic peroxide formulation for C.

(13) P. Pfeiffer and H. deWaal, *Ann.*, **520**, 185 (1935).

(14) A. Schönberg and R. Michaelis, *J. Chem. Soc.*, 109 (1937).

(15) B. Witkop and J. B. Patrick, THIS JOURNAL, **73**, 2196 (1951); L. A. Cohen and B. Witkop, *ibid.*, **77**, 6595 (1955); see also references 8 and 10.



The mesitylphenylketenimine IX reacted with mesityllithium to give the stable vinylamine XI as a well-defined crystalline solid in 61% yield. The infrared spectrum contained the N–H band at 3.0 μ, and the ultraviolet curve ($\lambda_{max.}$ 332, ϵ 15,000) was similar to that of the model vinylamine XIII. Vinylamine XI was extremely stable; it was recovered unchanged from basic hydrogen peroxide solution after two days, from acetic anhydride and pyridine after two days and from concentrated hydrochloric acid at the reflux temperature after two days.

Experimental

Diphenylketene-*p*-tolylimine (I).—A mixture of 60.2 g. (0.2 mole) of N-*p*-tolyldiphenylacetamide,[16] 41.71 g. (0.2 mole) of phosphorus pentachloride and 200 ml. of anhydrous thiophene-free benzene was refluxed for 2 hr. The benzene and resulting phosphorus oxychloride were removed by distillation under vacuum from a warm (40°) water-bath. Three additional 100-ml. portions of anhydrous benzene were added and distilled separately to remove the last of the phosphorus oxychloride. The resulting viscous yellow oily iminochloride was not further purified but was used directly in the preparation of the ketenimine.[17]

The crude imino chloride was dissolved in 100 ml. of anhydrous ether and 200 ml. of anhydrous petroleum ether (30–60°). To the resulting pale yellow solution was added 100 ml. of redistilled anhydrous triethylamine. An immediate precipitation of triethylamine hydrochloride occurred, after which the suspension was refluxed for 12 hr. The resulting reddish-brown suspension was removed by filtration and washed with anhydrous petroleum ether and the solvent evaporated. A dark brown solid, 1.83 g., probably the ketenimine dimer, was insoluble in petroleum ether. The remaining solution was treated with carbon and allowed to crystallize in the refrigerator. The total yield of successive crops of crude ketenimine was 40.14 g.; this was recrystallized

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[16] C. L. Stevens and J. C. French, THIS JOURNAL, 75, 657 (1953).

[17] C. L. Stevens and J. C. French, *ibid.*, 76, 4398 (1954).

from anhydrous petroleum ether to yield 37 g. (65%) of bright yellow ketenimine crystals[18] melting at 82–85.5°.

In another experiment, the crude ketenimine–ether solution resulting from the filtration of triethylamine hydrochloride was evaporated to dryness under vacuum, dissolved in about 2 l. of dry petroleum ether and placed on a neutral alumina column containing 600 g. of alumina.[19] The first 500 ml. of eluate contained pure ketenimine, m.p. 83–84°, yield 60%. Continuing the elution with about 1 l. of 10% ether–petroleum ether yielded a small amount of the pure bright yellow ketenimine dimer. Finally, elution of the column with acetone gave unreacted starting amide.

The ketenimine was characterized by the addition of ethyl alcohol to give the imino ester, ethyl diphenyl-N-(*p*-tolyl)-iminoacetate, m.p. 101–102°.

Anal. Calcd. for $C_{23}H_{23}NO$: C, 83.85; H, 7.04. Found: C, 84.44; H, 7.10.

Compound II by Lithium Aluminum Hydride Reduction of Diphenylketene-*p*-tolylimine.[20]—A solution of 0.74 g. of the ketenimine I in 40 ml. of dry ether was stirred for seven days with 1.08 g. of lithium aluminum hydride. After decomposition of the excess lithium aluminum hydride, the ether layer was extracted with cold 6 *N* hydrochloric acid. Neutralization of the acid extract with ammonium hydroxide gave an oil which crystallized within two days. The crude solid, 0.45 g., was recrystallized from petroleum ether to yield 0.22 g. of α-(N-*p*-tolylaminomethyl)-benzhydrol (II), white needles, m.p. 84–85°.

Anal. Calcd. for $C_{21}H_{21}NO$: C, 83.13; H, 6.98. Found: C, 83.37; H, 7.29.

Upon evaporation, the ether layer from the hydrochloric acid extractions gave 0.16 g. of an oil. Since the infrared spectrum showed the presence of a carbonyl compound, a 2,4-dinitrophenylhydrazone was prepared and found to melt at 224–229°. The mixture melting point with benzophenone 2,4-dinitrophenylhydrazone (m.p. 234–236°) was 229–233°.

Independent Synthesis of α-(N-*p*-Tolylaminomethyl)-benzhydrol.[20]—A solution of 0.11 g. of α-hydroxydiphenylacetic acid *p*-toluide in 15 ml. of dry ether was stirred for 44 hr. with 0.25 g. of lithium aluminum hydride. In addition to 0.05 g. of starting amide, a considerable amount of basic material was isolated which, when crystallized once from petroleum ether, yielded 0.02 g. of needles, m.p. 83–85°. Mixture melting point with the above material was undepressed.

An acetate derivative was prepared from a 1:1 acetic anhydride–pyridine mixture, m.p. 151–152°.

Anal. Calcd. for $C_{23}H_{23}NO_2$: C, 79.97; H, 6.71. Found: C, 80.30; H, 6.69.

Preparation of α,α-Diphenyl-α-hydroperoxyacetophenone *p*-Tolylimine (III).—The Grignard reagent was prepared under nitrogen from 7.3 g. (0.3 g. atom) of magnesium ribbon and 47 g. (0.3 mole) of bromobenzene in 70 ml. of anhydrous ether, the reaction being initiated with 3 drops of methyl iodide. To the resulting refluxing pale yellow Grignard solution was added dropwise over a 1-hr. period 8.5 g. (0.03 mole) of diphenylketene-*p*-tolylimine dissolved in 100 ml. of anhydrous ether. The resulting orange solution was then refluxed with rapid stirring for 24 hr. Decomposition was effected by the addition of 250 ml. of a cold slightly ammoniacal saturated solution of ammonium chloride. The ether layer was removed, the aqueous layer extracted twice with 100-ml. portions of ether, and the combined ether extracts washed with water and then dried over anhydrous magnesium sulfate. Evaporation of the solvent *in vacuo* gave a pale yellow solid. The solid was washed with 20 ml. of pentane to give 5.65 g. of white crystalline hydroperoxide, m.p. 112–113.5°. The pentane was evaporated from the filtrate and again treated in the above manner to give an additional 2.34 g. The total yield was 8 g. (68%).

Anal. Calcd. for $C_{27}H_{23}O_2N$: C, 82.42; H, 5.89. Found: C, 82.51; H, 6.10.

Acid-catalyzed Rearrangement.—One gram of the hydroperoxide was dissolved in 20.0 ml. of acetone containing 3 drops of 10% hydrochloric acid. The resulting mixture was allowed to stand at room temperature for two days, then evaporated to dryness under vacuum, dissolved in dry hexane and chromatographed on an alumina column. It was eluted first with hexane and then with a 90% hexane–10% acetone mixture. As previously shown, the benzophenone was isolated as the 2,4-dinitrophenylhydrazone, yield 0.78 g. (85%), m.p. 235–235.5°.

The benzoic acid *p*-toluide was isolated from the hexane–acetone-soluble fraction, m.p. 155–156°, 0.46 g. (92%).

Compound IV by Catalytic Reduction of α,α-Diphenyl-α-hydroperoxyacetophenone *p*-Tolylimine with Platinum in Ethyl Acetate.—Reduction of 30 mg. (0.13 millimole) of platinum oxide in 10 ml. of ethyl acetate in the microhydrogenation apparatus was completed in 1 hr., at which time 500 mg. (1.27 millimoles) of the hydroperoxide dissolved in 20 ml. of ethyl acetate was added and the reduction resumed. Very rapid uptake of 1 mole of hydrogen (31 ml.) was completed in 5 minutes. After the platinum was removed by filtration, the pale yellow ethyl acetate filtrate was evaporated to dryness under vacuum, yielding 0.44 g. (92%) of white crystalline α,α-diphenyl-α-hydroxyacetophenone *p*-tolylimine (IV) melting at 108–111°. Recrystallization from acetone–water gave 0.35 g. of white crystals melting at 113–114°. Infrared data showed bands characteristic of the OH (2.85 μ) and C═N— (6.10 μ) groups.

Anal. Calcd. for $C_{27}H_{23}NO$: C, 85.91; H, 6.14. Found: C, 86.07; H, 6.14.

Acid Hydrolysis of α,α-Diphenyl-α-hydroxyacetophenone *p*-Tolylimine (IV).—A mixture consisting of 230 mg. (0.006093 mole) of the above hydroxy Schiff base, m.p. 113–114°, 20.0 ml. of acetone, 10 drops of concentrated hydrochloric acid and sufficient water to produce a slight turbidity was refluxed for 15 hr. The resulting orange solution was evaporated to dryness, 10 ml. of water added and the aqueous layer extracted several times with ether. The combined ether extracts were washed once with water, dried over anhydrous magnesium sulfate and evaporated to dryness, yielding 210 mg. of impure white solid melting at 75–83°. Recrystallization from ligroin (90–120°) gave 160 mg. (91.2%) of a white solid melting at 81–83°. An infrared curve and a mixture melting point with an authentic sample of α-hydroxy-α,α-diphenylacetophenone prepared previously in this Laboratory[21] confirmed the structure.

The residual aqueous layer was made basic with dilute ammonia, extracted with 100 ml. of ether and the ether extract dried over anhydrous magnesium sulfate and finally evaporated to dryness. A pale yellow solid was obtained (65 mg.), which after recrystallization from petroleum ether gave 50 mg. (77%) of white crystalline plates melting at 43–45° and having an infrared curve and mixture melting point identical with those of *p*-toluidine.

Compound V by Catalytic Reduction of the Hydroperoxide III with Platinum in Ethyl Acetate and Glacial Acetic Acid.—Reduction of 500 mg. of the hydroperoxide was carried out as in the above procedure with 30 mg. of platinum oxide in ethyl acetate. After the uptake of 1 mole of hydrogen, the platinum was removed by filtration and the yellow filtrate evaporated to dryness. Without further purification, the resulting pale yellow α-hydroxy Schiff base IV was dissolved in 20 ml. of glacial acetic acid and the reduction continued using a new 50-mg. portion of reduced platinum oxide. After 2 hr., the addition of a second mole of hydrogen was complete and a white insoluble precipitate had formed. The reduction was stoppered, 20 ml. of acetone was added to dissolve the precipitate and the platinum was removed by filtration. The resulting solution was evaporated to dryness *in vacuo*. Yield of crude white 2-(N-*p*-toluino)-1,1,2-triphenylethanol (V) was 0.51 g., m.p. 204–212°. Three recrystallizations from acetone-water gave white crystals, 0.45 g. (93%), melting at 213-216°.

The infrared curve was identical with the one obtained for the product of the lithium aluminum hydride reduction of the hydroperoxide III and with that obtained for the compound which was synthesized from phenylmagnesium bro-

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[18] These are the experimental results referred to in footnote 9 of reference 17.

[19] Aluminum Company of America, Alcoa Activated Alumina, Grade F-20, minus 80 mesh, prepared according to the procedure of O. Mancera, D. H. R. Barton, G. Rosenkranz and C. Djerassi, *J. Chem. Soc.*, 1025 (1952), except that after being washed with methanol followed by petroleum ether, the alumina was dried in a vacuum dessicator and not reactivated by heat.

[20] Experimental results of J. C. French.

[21] C. L. Stevens and J. J. DeYoung, THIS JOURNAL, **76**, 718 (1954).

mide and N-*p*-tolyldesylamine. A mixture melting point with the latter compound was not depressed.

Anal. Calcd. for $C_{27}H_{25}NO$: C, 85.46; H, 6.64. Found: C, 85.61; H, 6.69.

Compound V by Reduction of the Hydroperoxide III with Lithium Aluminum Hydride.—The hydroperoxide (1.00 g., 0.00255 mole) was dissolved in 40 ml. of dry ether, and this solution was added dropwise over a 30 min. period to a slurry of 0.20 g. (0.00528 mole) of lithium aluminum hydride in 50 ml. of dry ether. After 6 hr., 0.94 g. of a pale yellow solid melting at 205–212° was isolated. Three recrystallizations from acetone–water gave 0.75 g. (78%) of a white crystalline solid melting at 213–216°. Infrared data on this compound were identical with those on the compounds obtained by catalytic reduction and independent synthesis; mixture melting points were not depressed.

Independent Synthesis of V.—N-*p*-Tolyldesylamine, m.p. 145–146°, was obtained in 84% yield from benzoin and *p*-toluidine. A Grignard reagent was prepared from 6.08 g. (0.25 g. at.) of magnesium turnings, 39.25 g. (0.25 mole) of bromobenzene and 100 ml. of ether under nitrogen. To this was added dropwise over a 1-hr. period a solution of 15.07 g. (0.05 mole) of N-*p*-tolyldesylamine in 400 ml. of dry benzene. The resulting mixture was refluxed for 6 hr. and finally decomposed by the addition of a cold saturated ammonium chloride solution. The benzene layer was separated and the aqueous layer extracted twice with 200 ml. of ether. The combined extracts were washed with water, dried over anhydrous $MgSO_4$ and evaporated to dryness *in vacuo*. The yield of crude white solid melting at 190–207° was 21.01 g. Three recrystallizations from acetone–water gave 16.94 g. (89.4%) of small white needles melting at 213–216°. Infrared curves of this and the compounds resulting from the catalytic and lithium aluminum hydride reductions of the hydroperoxide were identical and mixture melting points were undepressed.

Compound VI from the Grignard Reaction between Diphenylketene-*p*-tolylimine and Mesitylmagnesium Bromide.—A Grignard reagent was prepared from 4.98 g. (0.025 mole) of dry bromomesitylene in 10.0 ml. of anhydrous ether and 0.49 g. (0.02 g. at.) of magnesium ribbon cut into small pieces. To this was added dropwise, over a period of 1 hr., 2.83 g. (0.01 mole) of diphenylketene-*p*-tolylimine dissolved in 50.0 ml. of anhydrous ether. The resulting mixture was refluxed under nitrogen with vigorous stirring for 15 hr. After cooling in an ice-bath, the mixture was decomposed by the addition of 50.0 ml. of ice-cold saturated ammonium chloride solution made just basic to litmus with ammonium hydroxide. The ether layer was removed and the aqueous layer extracted three times with 100-ml. portions of ether. The combined ether extracts were dried over anhydrous sodium sulfate, filtered and evaporated to dryness *in vacuo* by warming on a 30–40° water-bath. The resulting residual oil was covered with about 10 ml. of dry pentane and cooled in a Dry Ice–acetone-bath with vigorous scratching. A white solid, m.p. 93–96° with evolution of gas and decomposition, was obtained in the amount of 1.82 g. After treating with carbon, recrystallization from warm hexane and drying in a vacuum desiccator gave 1.52 g. (35%) of the solid 2,4,6-trimethyl-α,α-diphenyl-α-hydroperoxyacetophenone *p*-tolylimine (VI) with a m.p. of 98–100°.

Anal. Calcd. for $C_{30}H_{29}NO_2$: C, 82.73; H, 6.71. Found: C, 82.99; H, 6.99.

The mother liquors from the above recrystallizations were evaporated to dryness under vacuum, then dissolved in hexane and passed through a column of alumina. Upon elution with hexane, followed by evaporation of the fraction, a pale yellow oil was obtained which showed a carbonyl group in the infrared and proved to be benzophenone. The 2,4-dinitrophenylhydrazone, m.p. 235–236°, gave no depression in m.p. when mixed with an authentic sample.

Elution of the column with a hexane–acetone mixture gave a third compound having a m.p. of 172–173°. The latter gave no depression in m.p. when mixed with a known sample of mesitoic acid *p*-toluide, but did give a depression in m.p. when mixed with a sample of diphenylacetic acid *p*-toluide. The mesitoic acid *p*-toluide and the benzophenone apparently result from the acid-catalyzed decomposition of the vinylamine hydroperoxide.

Acid-catalyzed Rearrangement of the Hydroperoxide VI.—One gram of the above hydroperoxide, m.p. 98–100°, was dissolved in 20.0 ml. of acetone containing 3 drops of 10% hydrochloric acid. The solution was allowed to stand for 2 days at room temperature and was then evaporated to dryness *in vacuo*. The pale yellow residual oil was dissolved in hexane and chromatographed on an alumina column, being eluted first with hexane and finally with a 90% hexane–10% acetone mixture. The hexane solutions, after evaporation, yielded benzophenone which was characterized as its 2,4-dinitrophenylhydrazone, m.p. 235–236°, 0.52 g. (62.5%).

The mesitoic acid *p*-toluide was isolated from the hexane–acetone-soluble fraction in a yield of 0.52 g. (89%), m.p. 174–175°.

Mesitylphenylketene-*p*-tolylimine (IX).—The ketene was prepared in 83% yield by the method of Fuson[22] starting with 51 g. of mesitylphenylacetic acid. The ketene (39 g., 0.166 mole) was dissolved in 100 ml. of dry ether, and a solution of 43 g. (0.40 mole) of *p*-toluidine dissolved in 200 ml. of ether was added dropwise. The initial exothermic reaction was controlled by an ice-bath, and the solution was then refluxed for 4.5 hr. A small amount of *p*-toluidine hydrochloride resulting from free acid chloride in the ketene was removed by filtration and the filtrate was washed with water, 5% hydrochloric acid, 5% sodium hydroxide and again with water. After drying overnight with anhydrous magnesium sulfate, the ethereal solution was filtered and then evaporated *in vacuo*. The residue was recrystallized twice from methanol–water to yield 34.3 g. of white needles melting at 124.5–125.5°. Concentration and recrystallization of the mother liquors led to an additional 9.0 g. of the amide. The total yield was 43.0 g. (84%). This procedure gave a much better yield of purer mesitylphenylacetic acid *p*-toluide than that obtained *via* the acid chloride and *p*-toluidine.

Anal. Calcd. for $C_{24}H_{25}NO$: C, 83.92; H, 7.34. Found: C, 84.17; H, 7.61.

The amide was converted to the crude ketenimine *via* the imino chloride using the procedure described above. Chromatographic purification of the crude ketenimine resulting from 0.1 mole of the amide was accomplished with 300 g. of neutral alumina and produced a 65% yield of the pure ketenimine, m.p. 106–108°, after elution with petroleum ether. The ketenimine had ultraviolet absorption maxima at 267 mμ (ε 29,400) and 348 mμ (ε 1010); it was characterized by hydrolysis to the amide for which characteristic infrared absorption bands were observed at 3.36(CH), 4.99(C=C=N), 6.26, 6.33, 6.65 (phenyl conjugation), 7.27, 11.71, 11.96 and 12.16 (mesityl conjugation).

Anal. Calcd. for $C_{24}H_{23}N$: C, 88.57; H, 7.12. Found: C, 88.31; H, 7.22.

The ketenimine (0.304 g.) was hydrolyzed in an acetone–water solution containing a few drops of concentrated hydrochloric acid. The yield of amide was 96%, m.p. 124–125°.

Compound V by Reduction of Mesitylphenylketene-*p*-tolylimine with Lithium Aluminum Hydride.—From 1.63 g. of ketenimine IX and 1.90 g. of lithium aluminum hydride in 50 ml. of ether 1.84 g. of a pale yellow solid melting at 146–147.5° was obtained. Recrystallization from acetone–water gave 0.82 g. (50%) of 2-mesityl-2-phenyl-N-*p*-tolylvinylamine (X) as white platelets melting at 148–149°.

Anal. Calcd. for $C_{24}H_{25}N$: C, 88.02; H, 7.70. Found: C, 87.93; H, 7.40. Characteristic infrared absorption occurred at 2.88 (NH)k 3.25, 3.36 (CH), 6.12 (C=C), 6.19, 6.28, 6.59 (phenyl conjugation), 11.53, 11.68 and 12.39 (mesityl group).

Compound XII by Catalytic Reduction of Vinylamine X with Platinum in Ethyl Acetate.—Catalytic reduction of 200 mg. (6.12 millimoles) of the vinylamine in 25 ml. of ethyl acetate was carried out at 25°, using 50 mg. of platinum oxide in 10 ml. of ethyl acetate. The reduction was allowed to continue overnight, after which time 15.0 ml. of hydrogen uptake had occurred. Theoretical uptake for 1 mole was 14.9 ml. The resulting suspension was filtered from the platinum and the bright green filtrate evaporated to dryness *in vacuo*. A pale green solid, 200 mg., melting at 152–154°, was obtained. Recrystallization from acetone–water gave 175 mg. (87.5%) of 2-mesityl-2-phenyl-N-*p*-tolylethylamine (XII) as white platelets melting at 153–154°. The infrared spectrum showed characteristic bands at 2.94 (NH); 3.38, 3.42, 3.46 (CH); 6.15, 6.26 and 6.58 (phenyl conjugation).

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[22] R. Fuson, L. Armstrong, J. Kneisley and W. Shenk, THIS JOURNAL, 66, 1464 (1944).

Anal. Calcd. for $C_{24}H_{27}N$: C, 87.49; H, 6.56. Found: C, 87.39; H, 6.66.

Compound XII by Reduction of Phenylmesitylacetic Acid *p*-Toluide with Lithium Aluminum Hydride.—A solution of 3.43 g. (0.01 mole) of the amide in 50 ml. of anhydrous tetrahydrofuran was reduced with 3.80 g. (0.10 mole) of lithium aluminum hydride. From this reaction 3.43 g. of crude product melting at 128–160° was obtained. Three recrystallizations from acetone–water gave 2.93 g. (89%) of white solid melting at 153–154°. The infrared curve of this compound was identical to that obtained for the product from catalytic reduction. A mixture melting point was not depressed. Lithium aluminum hydride reduction of the amide could not be effected in ethyl ether solution.

Anal. Calcd. for $C_{24}H_{27}N$: C, 87.49; H, 6.56. Found: C, 87.49; H, 6.68.

Preparation of 1,2-Dimesityl-2-phenyl-N-*p*-tolylvinylamine (XI).—Lithium metal (1.39 g., 0.20 g. at.), cut into small pieces under ether and nitrogen and weighed into a beaker of ether, was placed in a 500-ml. three-necked flask equipped with a stirrer, condenser, drying tube, dropping funnel and nitrogen inlet tube and covered with 50 ml. of ether. A solution of 19.91 g. (0.1 mole) of bromomesitylene in 30 ml. of ether was then added dropwise over a 1-hr. period to the vigorously stirred lithium–ether suspension. The resulting suspension was stirred and refluxed for 24 hr. Ether was added occasionally to compensate for losses through evaporation. At the end of this period, a solution of 3.25 g. (0.01 mole) of mesitylphenylketene-*p*-tolylimine, m.p. 106–108°, in 50 ml. of dry ether was added dropwise over a 1-hr. period to the stirred lithium aryl suspension at the reflux temperature while a slow stream of nitrogen was passed through the mixture. The resulting suspension was refluxed an additional hour and then stirred at room temperature for two days after the addition of 100 ml. of ether. Decomposition was effected by the dropwise addition of 100 ml. of cold water. The ether layer was removed, the aqueous layer extracted twice with 100-ml. portions of ether and the combined ether extracts washed with cold water, dried over anhydrous magnesium sulfate, filtered and finally evaporated to dryness under vacuum. The resulting pale yellow residue was washed thoroughly with pentane and then recrystallized from isopropyl alcohol. The yield of white platelets melting at 195–196.5° was 2.72 g. (61%).

Anal. Calcd. for $C_{33}H_{35}N$: C, 88.94; H, 7.92. Found: C. 88.62; H, 8.26.

A mixture consisting of 1.00 g. of the vinylamine XI, 50 ml. of methanol, 1.00 ml. of 20% sodium hydroxide solution and 5 ml. of 30% hydrogen peroxide was stirred at room temperature for two days and then refluxed for 5 hr. The vinylamine was recovered (77%) unchanged. A mixture of 158 mg. of the vinylamine, 5 ml. of acetic anhydride and 2 ml. of dry pyridine was allowed to stand for two days at room temperature and was then refluxed for 1 hour from which 140 mg. of XI was recovered.

A mixture of 187 mg. of the compound melting at 191–192°, 20.0 ml. of acetone and 5 ml. of concd. HCl was refluxed for two days. Evaporation of the mixture to dryness under vacuum gave 170 mg. of the starting material.

Preparation of 2,2-Diphenyl-N-methyl-N-phenylvinylamine.—A homogeneous solution of 9.81 g. (0.05 mole) of diphenylacetaldehyde, 10.72 g. (0.1 mole) of N-methylaniline and 100 ml. of dry benzene was refluxed in a 200-ml. flask equipped with a Dean–Stark water separator, a condenser and a drying tube. The theoretical volume of water. 0.90 ml., had separated after 10 hr. The resultant pale yellow solution was evaporated to dryness *in vacuo* and the residual liquid distilled *in vacuo*. Three fractions were collected. The first boiled at 40–60° (0.3 mm.) and amounted to 5.11 g. of unreacted methylaniline. The second fraction, b.p. 100–150° (0.3 mm.), 2.80 g., was not identified but probably contained a small amount of the vinylamine. The third fraction, b.p. 150–160° (0.3 mm.), 8.53 g., was the vinylamine. Refractionation of the latter pale yellow viscous oil gave 6.55 g. (46%) of a pale yellow extremely viscous oil boiling at 173–176° (0.5–0.6 mm.).

Anal. Calcd. for $C_{21}H_{19}N$: C, 88.38; H, 6.71. Found: C, 88.18; H, 6.88.

The ultraviolet absorption of the following compounds was determined in absolute ethanol using a Cary automatic recording ultraviolet spectrophotometer.

Compound	Maxima, mμ	Extinction (ε)
1. 2,2-Diphenyl-N-methyl-N-phenylvinylamine (XIII)	337	21,400
2. 2-Phenyl-2-mesityl-N-*p*-tolylvinylamine (X)	334	27,500
3. 2-Phenyl-1,2-dimesityl-N-*p*-tolylvinylamine (XI)	332	15,000

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DETROIT 2, MICHIGAN

[CONTRIBUTION FROM THE LILLY RESEARCH LABORATORIES, ELI LILLY AND COMPANY]

Erythromycin. X.[1] Structure of Erythromycin

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Evidence for the complete structure of erythromycin is presented.

Previous papers in this series[2] have reported that the antibiotic, erythromycin, is a polyhydroxyketolactone having the molecular formula $C_{37}H_{67}NO_{13}$. In the molecule there are an aminosugar, desosamine and a nitrogen free sugar, cladinose. The structures of desosamine[2a,3] and cladinose[2c] and of dihydroerythronolide,[2d] the reduced aglycone portion of erythromycin, have been published. For the complete elucidation of the erythromycin structure there remains to be established the positions of the sugar moieties, the position of the ketonic carbonyl and the size of the lactone ring. The solutions of these problems are described in this paper, and I is shown to be the structure of erythromycin.

Oxidation of erythromycin N-oxide[2a] with sodium periodate followed by mild alkaline hydrolysis gave rise to a steam volatile product VI. This

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[1] Previous paper in this series: "Erythromycin. IX. Degradative Studies of Erythromycin B," K. Gerzon, R. Monahan, O. Weaver, M. V. Sigal, Jr., and P. F. Wiley, THIS JOURNAL, **78**, 6412 (1956).

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[3] R. K. Clark, *Antibiotics and Chemotherapy*, **3**, 663 (1953).