

Schiff Bases from 4-(Dichloromethyl)-4-methyl-2,5-cyclohexadien-1-one. Thermal Decomposition and Reaction with Amines¹

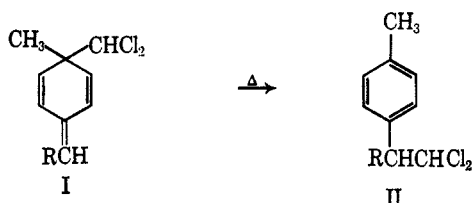
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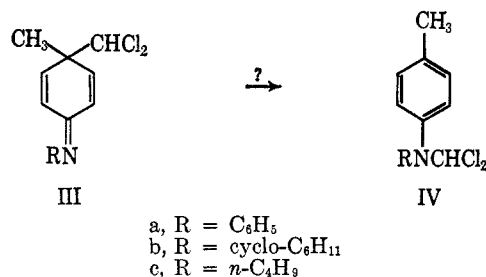
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Schiff bases prepared from 4-(dichloromethyl)-4-methyl-2,5-cyclohexadien-1-one and the alkylamines cyclohexylamine and butylamine react at elevated temperatures with the corresponding primary amine to give N-alkyl-*p*-toluidines, and N,N'-dialkylformamidines. If traces of water are present, the N,N'-dialkylformamidines are partly hydrolyzed to N-alkylformamides. Reaction of the Schiff base from butylamine with dibutylamine is very slow and the product is ill defined and tarry. The Schiff base prepared from the dienone and aniline reacts with aniline to give N-phenyl-*p*-toluidine, no N,N'-diphenylformamidines being formed. It is concluded that the reaction with primary amines is not preceded by a rearrangement of the cyclohexadiene structure to a reactive N-alkyl- (or -aryl-) N-(dichloromethyl)-*p*-toluidine intermediate. When the Schiff bases are heated alone they undergo a highly exothermic reaction resulting in complete carbonization.

1-Alkylidene-4-(dichloromethyl)-4-methyl-2,5-cyclohexadienes (I) undergo a facile thermal rearrangement to II in which the ring is aromatized and the dichloromethyl group is transferred to the α -carbon atom of the alkylidene side chain.²



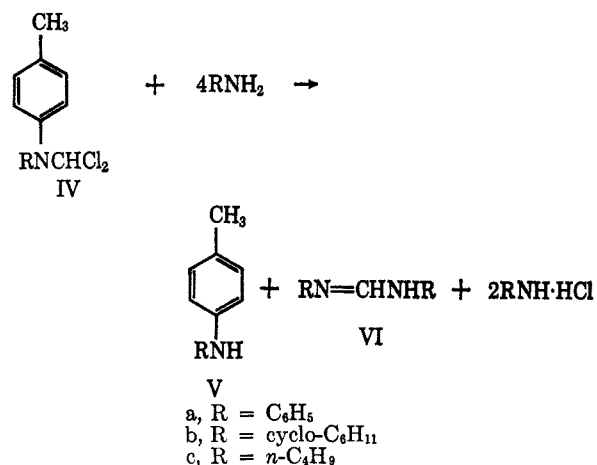
Nitrogen analogs of I (III) have been found, when heated, to undergo a vigorous, highly exothermic reaction which suggested that a similar rearrangement might be occurring, *i.e.*, the following equation.



In all cases examined the temperature required for rapid onset of the reaction was higher than would be required for rearrangement of the corresponding alkylidene compound,² 170° for IIIa, 180° for IIIb, and 155° for IIIc. Complete carbonization of the reaction product occurs whether the compounds are heated in bulk or in indifferent solvents, and a large amount of hydrogen chloride is evolved. In the examples studied the only products which could be isolated were traces of N-substituted-*p*-toluidine hydrochlorides, *p*-CH₃-C₆H₄NHR·HCl, which sublimed out of the reaction mixture and which were identified by comparison of their infrared spectra with those of authentic samples.

In the event that III did rearrange to give IV, extensive decomposition of the product at the temperatures extent would be expected in view of the known

thermal instability of compounds of structure IV.³ In order to obviate this difficulty an attempt was made to allow the thermal reaction of III to proceed in the presence of a trapping solvent which could react with IV, if it were indeed formed, before decomposition could occur. For this purpose the primary amines corresponding to R in III were chosen in order to minimize side reactions and because primary amines are known to react smoothly and completely with compounds such as IV to give readily identifiable secondary amines and formamidines.⁴ We have found that, instead of the reaction path visualized (III → IV → V and VI), primary amines react directly with III at elevated temperatures and that a prior rearrangement of III to IV is not involved.



The Schiff bases (III) were prepared in good yields from 4-(dichloromethyl)-4-methyl-2,5-cyclohexadien-1-one and the appropriate primary amine with the amine acetate serving as catalyst. Elemental analysis, the presence of a characteristic C=N band in the infrared spectra, and the ultraviolet spectra serve to confirm the assigned structures.

(3) H. H. Bosshard and H. Zollinger, *Helv. Chim. Acta*, **42**, 1659 (1959). The authors assign the ion-pair structure (R₂N=CHCl)⁺Cl⁻ to the so-called amide chlorides on the basis of their low solubility in nonpolar solvents and the presence of a strong absorption band in the C=N region, specifically 5.95 μ for [C₆H₅(CH₃)N=CHCl]⁺Cl⁻. *Chemical Abstracts* indexes these compounds as chloromethyleneammonium compounds or as dichloromethylamines according to the author's usage. We have chosen the latter nomenclature because it makes clearer the relation between these compounds and their precursors.

(4) H. Eillingsfeld, M. Seefelder, and H. Weidinger, *Angew. Chem.*, **72**, 836 (1960).

(1) The author gratefully acknowledges financial support of this investigation by the National Science Foundation (G-20084) and the Petroleum Research Fund (1905-B).

(2) K. Auwers, *Ann.*, **352**, 219 (1907); K. Auwers and K. Ziegler, *ibid.*, **425**, 217 (1921); K. Auwers and W. Julicher, *Chem. Ber.*, **55**, 2167 (1922); R. C. Fuson and T. G. Miller, *J. Org. Chem.*, **17**, 316 (1952).

4-(Dichloromethyl)-4-methyl-1-(phenylimino)-2,5-cyclohexadiene (IIIa) reacts rapidly with boiling aniline, forming considerable tar and evolving chloride ion. From the reaction mixture 48% of the theoretical amount of *N*-phenyl-*p*-toluidine (Va) was isolated; however, in spite of repeated attempts using varying methods for the work-up, none of the expected *N,N'*-diphenylformamidine (VIa) could be found. This indicates that IVa is not an intermediate in the reaction, since IVa, prepared from *N*-phenyl-*p*-formotoluidine and phosgene, reacts as predicted⁴ with aniline, either at moderate or at elevated temperatures, to form both Va and VIa.

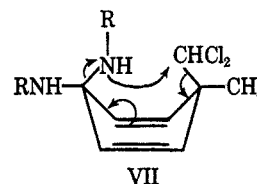
When 1-(cyclohexylimino)-4-(dichloromethyl)-4-methyl-2,5-cyclohexadiene (IIIb) is heated with cyclohexylamine to 190° in a glass-lined bomb, a smooth reaction occurs accompanied by almost no tarring. Cyclohexylamine hydrochloride is highly insoluble in the reaction mixture, and recovered yields of the salt account for approximately 95% of the theoretical amount of chloride ion. The product was found by thin layer and column chromatography and infrared and ultraviolet methods to consist of *N*-cyclohexyl-*p*-toluidine (Vb), *N,N'*-dicyclohexylformamidine (VIb), and *N*-cyclohexylformamide. Separate experiments demonstrated that the latter compound originated from the hydrolysis of *N,N'*-dicyclohexylformamidine by small amounts of water present in the cyclohexylamine used. Yields of the three products in a typical reaction and the method of determination are as follows: *N*-cyclohexyl-*p*-toluidine, 52% by isolation of the hydrochloride, 88% by column chromatography and infrared analysis of the appropriate fraction; *N,N'*-dicyclohexylformamidine, 20% by isolation, 49% by column chromatography; *N*-cyclohexylformamide, 36% by column chromatography and infrared analysis of the appropriate fraction. Thus, it appears that *N*-cyclohexyl-*p*-toluidine is formed almost quantitatively, and the dichloromethyl groups in the reactant are essentially all accounted for either as *N,N'*-dicyclohexylformamidine or as *N*-cyclohexylformamide.

1-(Butylimino)-4-(dichloromethyl)-4-methyl-2,5-cyclohexadiene (IIIc) is a liquid compound which undergoes thermal decomposition too readily to permit its distillation, even under reduced pressures. The crude material used in these experiments was believed to be essentially pure since the analysis checked reasonably well with predicted values, bands characteristic of the starting materials were absent from the infrared spectrum, and thin layer chromatograms under conditions which separate the Schiff base from the reactants showed only the former. When the imine (IIIc) was allowed to react with butylamine in a glass-lined bomb at 150–155° the product was found to consist of *N*-butyl-*p*-toluidine (Vc) and *N,N'*-dibutylformamidine (VIc), along with a small amount of a compound thought to be *n*-butylformamide. The latter compound has its C=O absorption band coincident with the C=N band of *N,N'*-dibutylformamidine and its presence in the reaction mixture could not be detected by infrared means. Thin layer chromatograms of the reaction product, however, show the presence of a third compound identical in its R_f value and behavior toward the potassium permanganate spray with an authentic sample of *N*-butylformamide. The isolated

product mixture was found to contain 92% of the theoretical amount of *N*-butyl-*p*-toluidine (ultraviolet analysis at 304 $m\mu$) and 65% of theory of *N,N'*-dibutylformamidine (estimated using the 5.91- μ band in the infrared). The latter figure is an approximation because the contribution of *N*-butylformamide to the sample weight and to the 5.91- μ band was ignored.

The reaction of 1-(butylimino)-4-(dichloromethyl)-4-methyl-2,5-cyclohexadiene (IIIc) with dibutylamine was also investigated as another means of determining whether or not the imine rearranges to IVc. If such a rearrangement did occur, then the IVc formed would react very rapidly with dibutylamine to give chloride ion. Instead, at conditions under which the reaction proceeds rapidly with butylamine, IIIc reacts very slowly with dibutylamine, as measured by the rates of formation of chloride ion and disappearance of starting material. A small quantity of butylamine is evolved during the course of the reaction and considerable tarring occurs. Some *N*-butyl-*p*-toluidine was formed, but whether it resulted from reaction of the butylamine liberated or dibutylamine with the imine is not known. Again, the evidence indicates that a rearrangement to IVc does not occur and that if the more hindered secondary amine reacts directly with the imine it does so at an understandably slower rate.

The mechanism of the reaction between primary amines and 1-(alkyl- or arylimino)-4-(dichloromethyl)-4-methyl-2,5-cyclohexadienes can only be speculated upon. A direct displacement by amine on the dichloromethyl group is one possibility. A less obvious path may involve the internal displacement of the dichloromethyl group from the amine-Schiff base adduct (VII). That such a mechanism is sterically



possible is indicated by the comparative lack of strain in the similar carbon-bridged molecule, bicyclo[2.2.2]-octa-2,5-diene.⁵

The nature of the thermal self-reaction of 1-(alkyl- or arylimino)-4-(dichloromethyl)-4-methyl-2,5-cyclohexadienes remains obscure.

Experimental Section

All melting points were determined on a Fisher-Johns melting point apparatus and are corrected. Infrared spectra were taken on a Beckman IR-5, and ultraviolet spectra were recorded on a Warren spectracord or a Beckman DK-2A.

4-(Dichloromethyl)-4-methyl-1-(phenylimino)-2,5-cyclohexadiene (IIIa).—A mixture of 5.00 g (0.0262 mole) of 4-(dichloromethyl)-4-methyl-2,5-cyclohexadien-1-one,⁶ 2.44 g (0.0262 mole) of aniline, and 1 drop of glacial acetic acid was warmed under nitrogen for 17 hr in an 80° oil bath. The amber product, which slowly solidified on standing, was crystallized from a methanol-water mixture to give 3.8 g (53%) of yellow needles, mp 88–88.5°. The analytical sample melted at 89.5–90.5°: $\lambda_{\text{max}}^{\text{CCl}_4}$ 6.01 (C=N), 6.26 and 6.71 (aryl C=C), 8.16, 10.96, 12.00 (monosubstituted phenyl), and 14.33 μ (*cis*-CH=CH); $\lambda_{\text{max}}^{\text{CH}_3\text{OH}}$ 251 $m\mu$ (ϵ 2.32 \times 10⁴) and 343 $m\mu$ (ϵ 4.53 \times 10³).

(5) R. B. Turner, W. R. Meador, and R. E. Winkler, *J. Am. Chem. Soc.*, **79**, 4116 (1957).

(6) K. Auwers and G. Keil, *Chem. Ber.*, **35**, 4207 (1902).

Anal. Calcd for $C_{14}H_{13}Cl_2N$: C, 63.17; H, 4.92; N, 5.26. Found: C, 63.05; H, 5.06; N, 5.37.

1-(Cyclohexylimino)-4-(dichloromethyl)-4-methyl-2,5-cyclohexadiene (IIIb).—A mixture of 5.00 g (0.0262 mole) of 4-(dichloromethyl)-4-methyl-2,5-cyclohexadien-1-one,⁸ 3.00 g (0.0303 mole) of cyclohexylamine, and 2 drops of glacial acetic acid was warmed under nitrogen at 50–60° for 18 hr. The pale yellow product, which solidified on standing, was crystallized from 30–60° petroleum ether to give 6.0 g (84% of theory) of white needles melting at 77.5–78.5°. An analytical sample melted at 80–80.5°: $\lambda_{max}^{CCl_4}$ 5.99 (C=N), 6.29 (C=C), 6.87 (CH₂), 10.99, 12.05, and 14.76 μ (*cis* CH=CH); $\lambda_{max}^{cyclohexane}$ 242 (ϵ 2.08 \times 10⁴) and 311 m μ (ϵ 246).

Anal. Calcd for $C_{14}H_{13}Cl_2N$: C, 61.77; H, 7.03; N, 5.15. Found: C, 62.02; H, 6.97; N, 4.85.

1-(Butylimino)-4-(dichloromethyl)-4-methyl-2,5-cyclohexadiene (IIIc).—A mixture of 4.00 g (0.0209 mole) of 4-(dichloromethyl)-4-methyl-2,5-cyclohexadien-1-one,⁸ 1.65 g (0.0220 mole) of butylamine, and 2 drops of glacial acetic acid was allowed to stand at room temperature for 3 days. A yellow color developed and water began to separate from the mixture almost immediately. The crude product was dissolved in 30–60° petroleum ether and the solution was washed four times with small portions of water and dried over potassium carbonate. Evaporation of the petroleum ether under a current of nitrogen and evacuation of the residue at 1 mm for several hours gave a yellow liquid (4.6 g 90% of theory): n_D^{20} 1.5418; $\lambda_{max}^{CCl_4}$ 5.99 (C=N), 6.29 (C=C), 6.87 (CH₂), 8.17, 11.00, 11.61, 13.71, and 14.80 μ ; $\lambda_{max}^{cyclohexane}$ 239 m μ (ϵ 1.88 \times 10⁴) and 307 m μ (ϵ 350).

Anal. Calcd for $C_{12}H_{17}Cl_2N$: C, 58.54; H, 6.96; N, 5.69. Found: C, 57.98; H, 7.08; N, 5.10.

Thin layer chromatography on the product (Eastman chromatogram sheet K301R, 95-5 benzene-methanol, ultraviolet, and KMnO₄ spray) showed only one spot at R_f 0.47, due to the imine. Under these conditions the ketone has an R_f of 0.6, and butylamine remains at the origin.

N-Phenyl-*p*-formotoluidide.—A mixture of 13.7 g (0.076 mole) of *N*-phenyl-*p*-toluidine⁷ and 100 ml of 90% formic acid solution was heated at reflux for 7 hr then allowed to stand at room temperature for 1 day. Addition of 250 ml of water precipitated an oily phase which solidified when the mixture was chilled overnight. The solid was collected by filtration, washed with water, and crystallized twice from an ethanol-water mixture to give 12.0 g (75% of theory) of shining, white plates: mp 86.5–87°; $\lambda_{max}^{CCl_4}$ 5.89 (C=O), 6.26, 6.61, 6.69 (all aromatic C=C), 7.53, 7.68, 7.88, 8.79, 13.70, and 14.30–14.42 μ (doublet).

Anal. Calcd for $C_{14}H_{13}NO$: C, 79.59; H, 6.20; N, 6.63. Found: C, 79.38; H, 6.58; N, 6.66.

This compound was also prepared in 48% yield by the phenylation of *p*-formotoluidide⁹ with bromobenzene in the presence of potassium carbonate and cuprous iodide, the procedure used by Weston and Adkins for the acetyl analog.⁹

N-(Dichloromethyl)-*N*-phenyl-*p*-toluidine (IVa) and Reaction with Aniline.—Phosgene was bubbled into a solution of 1.00 g of *N*-phenyl-*p*-formotoluidide in 25 ml of dry ether, with simultaneous cooling in an ice bath, until a large excess was present. The solution was allowed to warm slowly to room temperature and stand overnight. Removal of the ether and excess phosgene under water-pump vacuum left a pale yellow solid which when exposed to air evolved HCl strongly and turned orange then red. A sample of the product was found to evolve 63% of the theoretical amount of hydrochloric acid when hydrolyzed in aqueous alcoholic sodium hydroxide at room temperature. Longer reaction times in the preparation and in the hydrolysis did not change these results appreciably. For comparison, 90% of the theoretical amount of hydrochloric acid was accounted for by the hydrolysis of a sample of 1,1-dichlorotrimethylamine prepared by the above method, which, if the product is isolated by filtration, is reported to give analytically pure material.¹⁰

Because of its extreme sensitivity to moisture the crude *N*-(dichloromethyl)-*N*-phenyl-*p*-toluidine (IVa) was not purified but was treated with aniline directly. One-half gram of the crude dichloroamine was stirred at room temperature with 5 ml

of aniline. The mixture was then warmed to 50° and poured into 75 ml of 3 *N* hydrochloric acid. The mixture was saturated with salt and filtered, and the solids were warmed with 25 ml of water. The undissolved solid was removed by filtration and crystallized from ethanol and water to give 45% of the theoretical amount of *N*-phenyl-*p*-toluidine, characterized by its melting point and the identity of its infrared spectrum with that of an authentic sample.⁷ *N,N'*-Diphenylformamidine in 36% yield, identified by comparison of its infrared spectrum with that of an authentic sample,¹¹ was isolated from the filtrate by making the solution basic with sodium hydroxide, filtering, and recrystallizing the solid from alcohol and water.

Similar results were obtained when the crude IVa was dropped into boiling aniline, although in this case the products do not necessarily represent the reaction of IVa with aniline, because under these conditions *N*-phenyl-*p*-formotoluidide itself reacts with aniline in the presence of aniline hydrochloride to form *N*-phenyl-*p*-toluidine and *N,N'*-diphenylformamidine.

N-Cyclohexyl-*p*-toluidine (Vb).¹²—A mixture of 19.6 g (0.20 mole) of cyclohexanone, 21.4 g (0.20 mole) of *p*-toluidine, 40.8 g (0.60 mole) of sodium formate, and 160 ml of glacial acetic acid was heated at reflux for 22 hr, then poured into 400 ml of cold water. The organic layer was separated and the aqueous layer was extracted twice with 50-ml portions of benzene. The combined organic layers were mixed with 400 ml of 20% hydrochloric acid and the mixture was distilled until no more water-insoluble material came over. The mixture was refluxed for 18 hr, then diluted with an equal volume of hot water. Activated charcoal was added, the solution was filtered, and the filtrate was salted and chilled to give the amine hydrochloride, mp 205–207° after recrystallization from 3 *N* hydrochloric acid. The hydrochloride was slurried with 400 ml of cold water, the slurry was made basic with sodium hydroxide, and the precipitated free amine was collected on a filter, washed with water, and dried in a vacuum desiccator, yield 19.0 g (50% of theory): mp 41–41.5°; $\lambda_{max}^{CCl_4}$ 2.93 (NH), 6.18 and 6.60 (aromatic C=C), 6.88 (CH₂), 7.67 (PhNH), 7.95, and 12.40 (Nujol, p -C₆H₄) μ ; $\lambda_{max}^{cyclohexane}$ 306 m μ (ϵ 2.10 \times 10³) and 252 m μ (ϵ 1.4 \times 10⁴).

N-Cyclohexyl-*p*-formotoluidide.—A mixture of 77 g (0.45 mole) of *p*-bromotoluene, 57 g (0.45 mole) of *N*-cyclohexylformamide,¹³ 45 g (0.24 mole) of cuprous iodide, and 45 g (0.33 mole) of potassium carbonate was heated at reflux for 10 hr. The mixture was cooled and filtered, and the residues were washed with ether. Distillation of the ether from the combined organic solutions followed by vacuum distillation of the residue gave 46 g of *p*-bromotoluene, bp 80° (22 mm); 35 g of *N*-cyclohexylformamide, bp 75–95° (0.05 mm); and 9.0 g (9.2% of theory) of *N*-cyclohexyl-*p*-formotoluidide, bp 103–112° (0.05–0.1 mm). The distillate, which solidified on standing, was crystallized from 30–60° petroleum ether to give 8.5 g (8.7% of theory) of white needles: mp 48.5–49°, $\lambda_{max}^{CCl_4}$ 5.95 (C=O), 6.19 and 6.60 (Ar C=C), 6.87 (CH₂), 7.23 (CCH₃), 7.41, 7.71, 7.89, 8.08, and 12.07 μ (*p*-C₆H₄).

Anal. Calcd for $C_{14}H_{19}NO$: C, 77.38; H, 8.81; N, 6.45. Found: C, 77.51; H, 8.78; N, 6.60.

***N,N'*-Dicyclohexylformamidine (VIb).**—To the 1,1-dichlorotrimethylamine prepared from 4.0 g (0.055 mole) of *N,N*-dimethylformamide¹⁰ and isolated by evaporating the excess phosgene and ether was added 35 g of cyclohexylamine. The mixture was stirred at ambient temperature for 1 hr then heated to reflux for 10 min. The solution was poured into 150 ml of water and 10% sodium hydroxide solution was added until an organic layer separated. Repeated washing of the organic layer with water caused the product to solidify. This was filtered, dried under vacuum, and recrystallized from 30–60° petroleum ether to give 5.0 g (44% of theory) of *N,N'*-dicyclohexylformamidine, mp 103–104° (lit.¹⁴ mp 102–104°), hydrochloride mp 228–230° dec (lit.¹⁵ mp 229–230° dec). Adsorption maxima in the infrared for the free base and the hydrochloride corresponded to reported values.¹⁵

(11) J. B. Shoemith and J. Haldane, *J. Chem. Soc.*, **124**, 2704 (1923).

(12) The procedure used is essentially method C of R. Baltzly and O. Kauder [*J. Org. Chem.*, **16**, 173 (1951)] who reported a 29% yield of the free amine as the product of the first step in the reaction sequence. We found the product to be entirely the acetyl derivative, however, necessitating the hydrolysis step described above.

(13) O. Hromatka and E. Eiles, *Monatsch. Chem.*, **75**, 129 (1948).

(14) E. C. Taylor and W. A. Ehrhart, *J. Org. Chem.*, **28**, 1108 (1963).

(15) M. T. Leplawly, *et al.*, *Tetrahedron*, **11**, 39 (1960).

(7) F. Scardiglia and J. D. Roberts, *J. Org. Chem.*, **23**, 629 (1958).

(8) M. D. Farrow and C. K. Ingold, *J. Chem. Soc.*, **125**, 2543 (1924).

(9) P. E. Weston and H. Adkins, *J. Am. Chem. Soc.*, **50**, 859 (1928).

(10) H. H. Bosshard, R. Mory, M. Schmid, and H. Zollinger, *Helv. Chim. Acta*, **42**, 1653 (1959).

N-Cyclohexyl-N-(dichloromethyl)-*p*-toluidine (VIb) and Reaction with Cyclohexylamine.—A solution of 1.02 g (0.0047 mole) of N-cyclohexyl-*p*-formotoluidide in 40 ml of anhydrous ether was cooled in an ice bath and phosgene was bubbled in rapidly until a large excess was present (1 hr). After the first 30 min a precipitate of yellowish white needles appeared. The mixture was stirred at ice-bath temperature for 1.5 hr, then at room temperature for 4 hr. Excess phosgene and ether were removed under water-pump vacuum, leaving a yellowish white residue of crude IVb.¹⁶ When the crude IVb was heated to 195° with cyclohexylamine in a glass-lined bomb the product mixture was the same as that obtained by the reaction of IIIb with cyclohexylamine (see below).

N,N'-Dibutylformamidine (VIc).—To the 1,1-dichlorotrimethylamine prepared from 4.0 g (0.055 mole) of N,N-dimethylformamide¹⁰ and isolated by evaporating the excess phosgene and ether was added with cooling 30 ml of butylamine. The mixture was allowed to stand at room temperature for 18 hr then heated to reflux for 1 hr. The solution was extracted once with 50 ml of 10% sodium hydroxide solution then, after addition of 100 ml of ether, twice with 2% sodium hydroxide solution. The ethereal solution was dried over potassium carbonate then distilled to give 3.0 g (35% of theory) of the formamidine: bp 50–55° (0.05 mm) [lit.¹⁷ bp 103–104° (4 mm)]; picrate mp 114–115° (lit.¹⁸ mp 114.5–116.5°); $\lambda_{\text{max}}^{\text{CHCl}_3}$ 2.91 (NH), 5.91 (C=N), 6.60, and 7.17 μ . In the ultraviolet region VIc begins to absorb at ca. 255 m μ , the absorption increasing gradually to a maximum somewhere below 220 m μ .

Reaction of 4-(Dichloromethyl)-4-methyl-1-(phenylimino)-2,5-cyclohexadiene (IIIa) with Aniline.—A solution of 2.0 g (0.0075 mole) of 4-(dichloromethyl)-4-methyl-1-(phenylimino)-2,5-cyclohexadiene (IIIa) in 6 ml of aniline was added over a period of 10 min to 8 ml of boiling aniline. Refluxing was continued for another 10 min, and the aniline was removed by distillation under water-pump vacuum. The tarry residue was treated with 75 ml of 3 *N* hydrochloric acid and the mixture was extracted with 75 ml of ether. The ether solution was washed with water and dried over potassium carbonate, and the solvent was evaporated to give 0.66 g (48% of theory) of a tan solid shown by its infrared spectrum to consist only of N-phenyl-*p*-toluidine. Recrystallization of the solid from alcohol and water gave 0.45 g of the purified amine, mp 88–89°.

The hydrochloric acid solution was made strongly basic with 50% sodium hydroxide, then extracted with ether. Evaporation of the ether left a small amount of tarry residue whose infrared spectrum showed no bands attributable to the C=N grouping.

Reaction of 1-(Cyclohexylimino)-4-(dichloromethyl)-4-methyl-2,5-cyclohexadiene (IIIb) with Cyclohexylamine.—A solution of 2.0 g (0.0074 mole) of 1-(cyclohexylimino)-4-(dichloromethyl)-4-methyl-2,5-cyclohexadiene (IIIb) in 20 ml of cyclohexylamine, previously dried over potassium hydroxide, was heated in a nitrogen-flushed glass-lined bomb to 190–200° over a period of 45 min, then allowed to cool slowly and stand overnight at room temperature. The precipitated solid was collected by filtration, washed with ether, and dried to constant weight in a vacuum desiccator to give 1.89 g (95% of theory) of cyclohexylamine hydrochloride, identified by comparison of its infrared spectrum with that of an authentic sample.

The organic solution combined with the ether washings was washed several times with 1% potassium hydroxide solution then dried over solid potassium hydroxide. Distillation of the solution, first at atmospheric pressure to remove ether, then under water-pump vacuum to remove cyclohexylamine, left 2.47 g of crude product, a deep amber oil.

From a crude product thus obtained was isolated 52% of the theoretical amount of N-cyclohexyl-*p*-toluidine as the hydrochloride by dissolving the oil in 3 *N* HCl and salting and chilling the solution. The filtrate, made basic with sodium hydroxide, yielded 20% of the theoretical amount of N,N'-dicyclohexylformamidine after crystallization of the precipitated solid from 30–60° petroleum ether. Both the amine and the formamidine were identified by comparison of their infrared spectra with those of authentic samples.

(16) A portion of a similar preparation released 97% of the theoretical amount of hydrochloric acid when hydrolyzed at room temperature in 0.1 *N* aqueous alcoholic sodium hydroxide.

(17) C. Grundmann and A. Kreutzberger, *J. Am. Chem. Soc.*, **77**, 6559 (1955).

(18) T. L. Davis and W. E. Yelland, *ibid.*, **59**, 1998 (1937).

The infrared spectrum of the crude product in chloroform solution was similar to that of a mixture of N-cyclohexyl-*p*-toluidine and N,N'-dicyclohexylformamidine except for a band at 5.93 μ due to N-cyclohexylformamide. Yields of 90–98% for N-cyclohexyl-*p*-toluidine and 60–65% for N,N'-dicyclohexylformamidine were estimated by a quantitative comparison of the strengths of the 6.19- and 6.01- μ bands, respectively, with those of known chloroform solutions of the pure compounds. The yield thus obtained for the formamidine derivative is particularly subject to error since possible contributions at 6.01 μ from N-cyclohexylformamide and water were ignored.

Ultraviolet analysis on the crude product in cyclohexane solution using the 306-m μ band gave a yield of 103% for N-cyclohexyl-*p*-toluidine, a figure enhanced somewhat, no doubt, by contributions of minor impurities revealed by shoulders at 291, 285, and 281 m μ .

Thin layer chromatography (silica gel G, 95% benzene–5% methanol, neutral KMnO₄ developer) showed the crude product to contain three compounds whose *R_f* values (0, 0.2, 0.9) and behavior towards the developer corresponded to N,N'-dicyclohexylformamidine, N-cyclohexylformamide, and N-cyclohexyl-*p*-toluidine, respectively.

Column chromatography (Fisher thin layer alumina, CHCl₃¹⁹ eluent for Vb and N-cyclohexylformamide, pyridine for VIb) on the crude product permitted isolation of N-cyclohexylformamide and its identification by means of its infrared spectrum. Yields for the three components thus separated, obtained by infrared analysis of the appropriate fractions, were 88% for Vb, 49% for VIb, and 36% for N-cyclohexylformamide.

When the reaction was carried out with cyclohexylamine that had been dried over barium oxide only a trace of N-cyclohexylformamide was formed. When 1% water was added to the reaction mixture thus obtained and the mixture was reheated to 195°, all of the N,N'-dicyclohexylformamidine was converted to N-cyclohexylformamide.

Reaction of 1-(Butylimino)-4-(dichloromethyl)-4-methyl-2,5-cyclohexadiene (IIIc) with Butylamine.—A solution of 4.10 g (0.0167 mole) of 1-(butylimino)-4-(dichloromethyl)-4-methyl-2,5-cyclohexadiene (IIIc) in 30 ml of butylamine was placed in a nitrogen-flushed glass-lined bomb, and the bomb was heated at 150–155° for 1 hr then allowed to cool and stand overnight. The pale brown solution was mixed with twice its volume of ether, extracted twice with 10-ml portions of 50% sodium hydroxide solution, and dried over potassium hydroxide. Distillation of the ether and butylamine at reduced pressure left 4.39 g of a brownish oil whose infrared spectrum (chloroform solution) showed no bands due to the starting material and was qualitatively identical with the spectrum of a mixture of N-butyl-*p*-toluidine (Vc) and N,N'-dibutylformamidine (VIc). The N,N'-dibutylformamidine content of the crude product was estimated at 65% of theory, using the 5.91- μ band and ignoring the contribution of N-butylformamide.

Thin layer chromatography (silica gel G, 9:1 benzene–methanol, neutral KMnO₄ spray, heating to 100°) on the crude product showed three components whose *R_f* values (0, 0.3, and 0.9) and behavior toward the spray were identical with N,N'-dibutylformamidine, N-butylformamide, and N-butyl-*p*-toluidine, respectively.

The ultraviolet spectrum of the crude product (cyclohexane solvent) contained two peaks, at 249 and 304 m μ , whose location and relative strengths were identical with those of an authentic sample²⁰ of N-butyl-*p*-toluidine. Analysis for N-butyl-*p*-toluidine using the 304-m μ peak (ϵ 2260) where neither N,N'-dibutylformamidine nor N-butylformamide absorbs appreciably showed the crude product to contain 57% of the amine, representing a yield of 92% of theory.

The crude product was vacuum distilled, bp 69–78° (0.5 mm), to give an amber liquid which, when mixed with concentrated hydrochloric acid, gave an amine hydrochloride, melting at 149–151° after recrystallization from ethanol, which was identified as N-butyl-*p*-toluidine hydrochloride by comparison of its melting point and infrared spectrum (Nujol) with those of an authentic sample.²⁰ The acidic mother liquor was made basic with sodium hydroxide and extracted with ether, and the ether was distilled to give an oil from which was prepared the picrate of N,N'-dibutylformamidine.¹⁸

(19) The chloroform used as eluent was J. T. Baker Analyzed reagent grade containing 0.7% ethanol as a stabilizer.

(20) J. Reilly and W. T. Hickenbottom, *J. Chem. Soc.*, **118**, 974 (1918).

Reaction of 1-(Butylimino)-4-(dichloromethyl)-4-methyl-2,5-cyclohexadiene (IIIc) with Dibutylamine.—Dibutylamine hydrochloride is quantitatively insoluble in thea mine at room temperature; *i.e.*, a saturated solution does not give a test for chloride ion with silver nitrate. The reaction of dibutylamine with IIIc was followed by measuring the weight of the amine hydrochloride formed at intervals and by observation of the C=N band of the imine at 5.99 μ . A solution of 1.0 g (0.0046 mole) of IIIc in 10 ml of dibutylamine was thus found to contain 0.14 g (9.2% of theory) of dibutylamine hydrochloride after 1 hr at 150°. After another 5 hr at 150–155° an additional 0.28 g (18% of theory) of the amine hydrochloride had formed. During the heating period the solution became very dark and tarry, and the intensity of the C=N absorption band at 5.99 μ was noticeably diminished. A small quantity of butylamine which appeared was allowed to distil from the reaction flask as it formed.

After a total of 6 hr reaction time at 150–155°, the excess dibutylamine was evaporated under a current of nitrogen and the residue was dissolved in ether. Extraction of the ether solution with 10% HCl and salting the aqueous extract gave a small yield of *N*-butyl-*p*-toluidine hydrochloride, identified by comparing its infrared spectrum with that of an authentic sample.²⁰ No other identifiable products could be separated from the reaction mixture.

***N*-Butyl-*p*-formotoluidide.**—A mixture of 13.5 g (0.10 mole) of *p*-formotoluidide⁷ and 15.1 g (0.11 mole) of butyl bromide was warmed to 40° and a solution of 6.6 g of 85% potassium hydrox-

ide (0.10 mole) in 30 ml of absolute ethanol was added with stirring over a period of 10 min. The mixture was then heated to reflux until it was no longer basic (90 min). Water was added to dissolve precipitated potassium bromide, the mixture was extracted with ether, and the ether solution was dried over potassium carbonate. Distillation of the ether and fractionation of the residue through a small Vigreux column gave 9.8 g (51% of theory) of *N*-butyl-*p*-formotoluidide, bp 80–86° (0.05 mm). The analytical sample distilled at 86° (0.05 mm): n_D^{20} 1.5298; $\lambda_{\text{max}}^{\text{CHCl}_3}$ 5.99 (C=O), 6.19 and 6.59 (aryl C=C), 7.32, and 12.13 μ (*p*-C₆H₄).

Anal. Calcd for C₁₂H₁₇NO: C, 75.35; H, 8.96; N, 7.32. Found: C, 75.23; H, 8.68; N, 7.29.

***N*-Butyl-*N*-(dichloromethyl)-*p*-toluidine (IVc) and Reaction with Dibutylamine.**—A solution of 1.00 g (0.00524 mole) of *N*-butyl-*p*-formotoluidide in 25 ml of anhydrous ether was chilled in an ice bath and phosgene was bubbled in (45 min) until a large excess was present. The solution was stirred at ice-bath temperature for 2 hr then allowed to stand overnight at room temperature. Removal of the excess phosgene and ether under water pump vacuum left a yellowish oil which showed, in chloroform solution, a strong absorption band at 6.01 μ .³ Addition of 15 ml of dibutylamine to the crude dichloromethylamine resulted in an immediate exothermic reaction. The mixture was stirred for 0.5 hr and filtered, and the precipitate was washed with ether and dried to constant weight to give 1.44 g (83% of theory) of dibutylamine hydrochloride. The organic reaction product was not isolated.

Methylation Studies on Arylidene-5-tetrazolyhydrazones^{1a,b}

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Methylation of arylidene-5-tetrazolyhydrazones in basic medium occurs predominantly at the 1 position with much less, if any, occurring at the 2 and 6 positions. Dimethylation, *in situ* or independently, occurs at the 1 and 6 positions.

In a study of the alkylation of 5-aminotetrazole in a basic aqueous medium Henry and Finnegan² found the products to be a mixture of mono- and dialkylated isomers. Monoalkylation occurred at the 1 and 2 positions with the 1 isomer generally predominating. The dialkylated compounds isolated were the 1,3 and 1,4 isomers, and in less than 1% the 1- and 2-methyl-5-methylaminotetrazoles. Our work led to an investigation of the compounds formed when arylidene-5-tetrazolyhydrazones are treated with methylating agents under various conditions in basic aqueous and 50% aqueous ethanolic media. Table IV (Experimental Section) summarizes the results of this reaction with benzylidene-5-tetrazolyhydrazone (1a^{3a}) as substrate and dimethyl sulfate and methyl iodide as methylating agents. The main products isolated were the 1-monomethylated isomer (2a) and the 1,6-dimethylated^{3b} isomer (3a) along with a small quantity of the 6-methylated compound (4a).

(1) (a) Dedicated to the memory of the late Professor E. Lieber, Fulbright Professor at Cork, 1964–1965. (b) Part of this work has appeared previously in communication form; see F. L. Scott, R. N. Butler, and D. C. Cronin, *Angew. Chem. Intern. Ed. Engl.*, **4**, 950 (1965). (c) This author is grateful for a State Maintenance Grant for Research.

(2) R. A. Henry and W. G. Finnegan, *J. Am. Chem. Soc.*, **76**, 923 (1954). See also, K. R. Wilson, R. M. Herbst, and W. J. Haak, *J. Org. Chem.*, **24**, 1046 (1959); D. F. Percival and R. M. Herbst, *ibid.*, **22**, 925 (1957).

(3) (a) The letters a, b, c, d, and e are used to modify symbols throughout. These letters carry the following implications: where a is used X = H, for b, X = Cl, for c, X = Br, for d, X = CH₃, for e, X = (CH₃)₂CH. (b) For convenience throughout this paper we shall number substituents on the nitrogen atom of the exocyclic 5-amino (and 5-hydrazino) group as 6 substituents, *i.e.*, R' in the formula as drawn.

Assuming adequate methylating agent, dimethylation depends on the quantity of sodium hydroxide present. With a large excess of base, the ratio of dimethylated to monomethylated materials produced is approximately 2:1. With 1 equiv of base this ratio becomes *ca.* 1:7. The extent to which mono- or dimethylation occurs depends on both the nucleophilicity and concentration of the anions of the unmethylated (1) and monomethylated (2)^{4a} hydrazones. The population of the latter anion is low in the initial stages of the reaction. The effect of the methyl group on the system is to increase the nucleophilicity of this anion and to reduce its concentration by decreasing the acidity^{4b} of the hydrazone (2) from which it is derived. These factors can offset one another and the results obtained (Table I) indicate that the anion of the monomethylated hydrazone (2) becomes a serious competitor for methylating agent during the course of the reaction. The dimethylated materials (3) which were isolated from the methylation reactions of the arylidene-5-

(4) (a) While aromatic hydrazones are weakly acidic [L. E. Scoggins and C. K. Hancock, *J. Org. Chem.*, **26**, 3490 (1961)] with pK_a values of about 12 [N. V. Chugreeva, *Zh. Anal. Khim.*, **15**, 391 (1960)] they are much less so than aminotetrazoles (see part b). The acidity of arylidene-1-methyl-5-tetrazolyhydrazones is thus principally due to the stability conferred on the anion of these materials by delocalization of the ionic charge to the tetrazole nucleus. Disruption of the aromaticity in this monosubstituted tetrazole nucleus, a consequence of further alkylation at the 2 or 4 position, confers a predominance of reactivity at the 6 position of these amidant anions. (b) M. Charton, *J. Org. Chem.*, **30**, 3346 (1965); J. M. McManus and R. M. Herbst, *ibid.*, **24**, 1643 (1959); R. M. Herbst and W. L. Garbrecht, *ibid.*, **18**, 1286 (1953); E. Lieber, S. H. Patinkin and H. H. Tao, *J. Am. Chem. Soc.*, **73**, 1792 (1951).