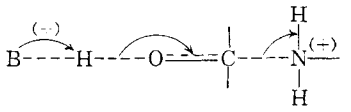
is thought to be rate determining. (4) The rate follows the activity of water to about the third power, implying that several (but not necessarily three[30]) molecules of water are involved in the transition state. Only one water molecule can be accounted for on the basis of water acting as a nucleophilic reagent alone. Thus, a reasonable transition state for Schiff base hydrolysis in acidic solution is that shown below, and the rate decrease in acidic solution is a consequence of the retardation of proton removal from the hydroxyl group of the carbinolamine, as well as a lower equilibrium concentration of carbinolamine because of the decreased availability of water in moderately concentrated acid solutions. This explanation requires that the reverse reaction, specific acid-catalyzed attack of aniline on the aldehyde be, in fact, general acid catalysis of aniline addition by the hydrated proton. The hypothesis[32] that the rate retardation observed for the hydrolysis of



4-(2,3-dimethylanilino)-pent-3-en-2-one in concentrated sulfuric acid is a consequence of the slower rate of addition of water to the protonated than to the free Schiff base seems unlikely on chemical grounds, particularly in view of the acid catalysis of the present reaction in dilute acid.

The hydrolysis of more basic Schiff bases, including retinylidenemethylamine[35] and 2-methyl-Δ^2-thiazoline,[36] is also retarded in acidic solution. However, the cause of the rate retardation in these cases is quite different from that with the less basic compounds. The hydrolysis of retinylidenemethylamine, for instance, is very slow even at *p*H 1,[35] where the rate of proton transfer is unaffected by variations in the acidity. In this case, the attack of the more basic amine is probably not subject to acid catalysis, and the *p*H-rate maximum may be explained by a change in rate-determining step somewhat similar to that described above for Schiff base formation; *i.e.*, the rate maximum in these reactions corresponds to the break near *p*H 4 in benzylideneaniline hydrolysis.

The pK_a' of N-*p*-chlorobenzylideneaniline is approximately 1.8 *p*H units lower than that of aniline. This decreased basicity may be ascribed to two competing factors: the rehybridization of the orbital containing the unshared electron pair on the nitrogen atom and the loss of conjugation of the unshared electron pair with the aromatic ring. Formation of semicarbazones of aromatic aldehydes, in which only the first factor is present, yields products having pK_a values about five *p*H units lower than semicarbazide itself.[22] Therefore, the loss of conjugation with the ring of the unshared electron pair on nitrogen must raise the pK_a of the Schiff base about three units relative to aniline, a value which seems reasonable since it has been estimated that the decreased basicity of aniline relative to ammonia (about 5 *p*H units) is due about equally to the electron-withdrawing power of the aromatic ring and to conjugation of the unshared electron pair with the ring.[37] Ricketts and Cho have observed that protonated water-stable Schiff bases formed from *p*-aminoazobenzene have pK_a values which are about 0.5 *p*H unit below the pK_a of the parent amine,[38] in general agreement with the result found in the present case.

(35) R. A. Morton and G. A. J. Pitt, *Biochem. J.*, **59**, 128 (1955).

(36) R. B. Martin, S. Lowey, E. L. Elson and J. T. Edsall, *J. Am. Chem. Soc.*, **81**, 5089 (1959).

(37) B. M. Wepster, *Rec. trav. chim.*, **71**, 1171 (1952).

(38) J. A. Ricketts and C. S. Cho, *J. Org. Chem.*, **26**, 2125 (1961).

[CONTRIBUTION FROM THE RESEARCH DEPARTMENT, CIBA PHARMACEUTICAL PRODUCTS, INC., SUMMIT, N. J.]

The Arylation of Enamines[1a]

BY MARTIN E. KUEHNE[1b]

RECEIVED AUGUST 28, 1961

Very reactive aryl halides attacked enamines by C-arylation to give α-aryl ketones on hydrolysis. With less reactive aryl halides, N-arylation and cleavage to N-arylated secondary amines was found. Aryliodonium salts and enamines produced α-aryl ketones in low yield after hydrolysis. Phenyldiazonium fluoroborate reacted primarily to form an α-phenylhydrazone imonium salt. The condensation of cyclohexanone enamines with quinone dibenzenesulfonimide led directly to an N,N'-dibenzenesulfonylaminotetrahydrocarbazole. Benzyne reacted with 1-pyrrolidinocyclohexene to produce, on hydrolysis, 2-phenylcyclohexanone and/or a benzocyclobutene derivative, depending on reaction conditions and the method of benzyne generation.

The Stork enamine reaction[2] is a convenient route for the alkylation and acylation of ketones. Conversion of a ketone to an enamine intermediate results not only in activation of an α-carbon to electrophilic attack but also provides selectivity with unequally substituted α- and α'-positions and usually allows termination of the reaction at the monoaddition stage.[3,4] A continued interest in

(1) (a) This paper was presented at the Enamine Symposium of the 140th National Meeting of the A.C.S., Chicago, Ill., September 6, 1961. (b) Present address: Chemistry Department, University of Vermont, Burlington, Vt.

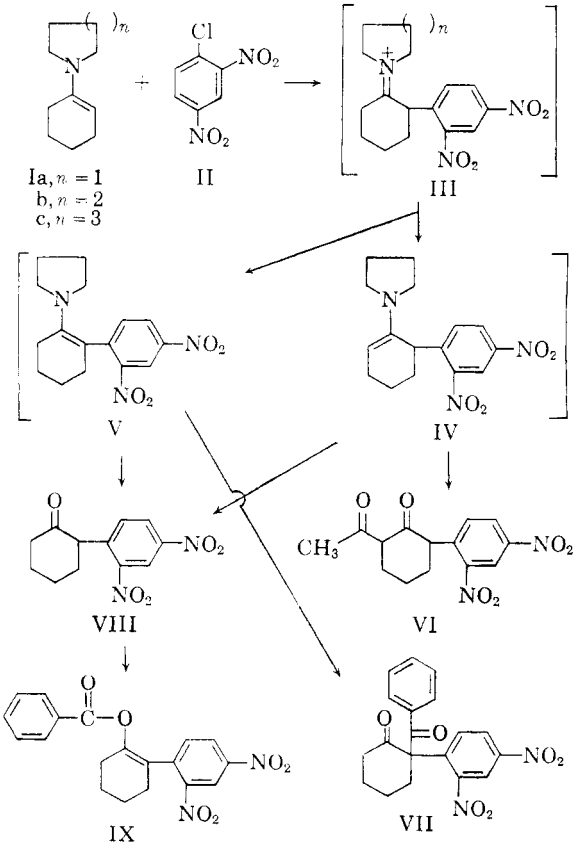
(2) A. R. Surrey, "Name Reactions in Organic Chemistry," Academic Press, Inc., New York, N. Y., 1961.

(3) G. Stork, R. Terrell and J. Szmuszkovicz, *J. Am. Chem. Soc.*, **76**, 2029 (1954); G. Stork and H. K. Landesman, *ibid.*, **78**, 5128, 5129 (1956); G. Stork, Abstr. 16th National Organic Symposium, June, 1959, pp. 44–52; S. Hünig, E. Benzig and E. Lücke, *Ber.*, **90**, 2833 (1957); S. Hünig, E. Benzig and E. Lücke, *ibid.*, **91**, 129 (1958); S. Hünig and E. Lücke, *ibid.*, **93**, 652 (1959); S. Hünig and W. Lendle, *ibid.*, **92**, 909, 913 (1960).

(4) M. E. Kuehne, *J. Am. Chem. Soc.*, **83**, 1492 (1961).

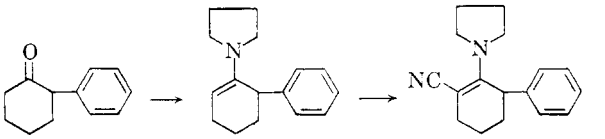
extensions of this method for C–C bond formation led to a study of enamines as intermediates for the α-arylation of ketones. This report describes the reactions of enamines with aryl halides in nucleophilic aromatic substitutions, reactions with diaryliodonium salts, with phenyldiazonium fluoroborate with quinone dibenzenesulfonimide and with benzyne.

Reactions with Very Reactive Aryl Halides.—2,4-Dinitrochlorobenzene reacted spontaneously with the pyrrolidino and hexamethylenimino enamines of cyclohexanone, Ia, c, to give excellent yields of 2-[2,4-dinitrophenyl]-cyclohexanone on hydrolysis of the reaction mixture. With the piperidine enamine a somewhat lower yield was found and the morpholine enamine did not lead to the desired arylation product. For completion of the reaction at least one equivalent of an auxiliary base, such as triethylamine, was required. This observation indicates the loss of hydrogen chloride from the intermediate imonium salt III and consequent generation of the arylated enamines IV and V, which were not isolated from the intensely colored mixture of complexes of enamines with dinitrobenzene compounds, but characterized by subsequent reactions.



That both possible enamines IV and V were formed could be seen from isolation of the enolic acylation product VI (strong ferric chloride reaction, solubility in dilute base, formation of a crystalline cupric salt) and the neutral benzoylation product VII, after treatment of the reaction mixture with acetyl chloride or benzoyl chloride and hydrolysis. The dinitrophenylcyclohexanone VIII did not react with benzoyl chloride even on prolonged standing and in the presence of pyridine it gave only the enol benzoate IX.

Formation of the enamines IV and V may be contrasted with the conversion of 2-phenylcyclohexanone (X), through an analogous imonium stage, to the single enamine XI, which reacted instantaneously with cyanogen chloride, at low temperature, to give only the vinylogous cyanamide XII.[5]



Apparently, formation of the enamine double bond toward the aryl substituent is thus favored somewhat by introduction of nitro groups onto the benzene ring. While the enamine XI formed from 2-phenylcyclohexanone and pyrrolidine with *p*-toluenesulfonic acid as catalyst, in refluxing benzene, must be an equilibrium product, this is not as certain for the enamines IV and V. These were generated at room temperature with some precipitation of hydrochloride salts and could thus represent a mixture of kinetic and equilibrium products. In any event, steric compression prohibits coplanar pyrrolidine and dinitrophenyl rings in either the imonium salt III or the enamine V. Activation of the tertiary hydrogen in III can thus not arise from an electronically ideal transition state but may be ascribed to structures which have only partial overlap of the breaking C–H orbital with the π-orbitals of the imonium or aryl groups, or to an inductive effect of the dinitrophenyl system. Similarly, resonance stabilization in V can only be partially realized by structures which have the pyrrolidine and benzene rings twisted out of the plane.[6]

The exothermic reaction of 1-pyrrolidinocyclohexene with 2,4-dinitrochlorobenzene was advantageously carried out in methylene chloride or dioxane. With not entirely anhydrous solvents, small amounts of water led to contamination of the ketonic product with N-2,4-dinitrophenylpyrrolidine, due to hydrolytic liberation of pyrrolidine. In benzene, a slower reaction rate was found. Addition of a very large excess of triethylamine lowered the yield, although 2,4-dinitrochlorobenzene reversibly complexes, but does not undergo a permanent transformation with triethylamine under these conditions. With the more reactive 2,4-dinitrofluorobenzene only tars were obtained in the absence of triethylamine, but addition of this base gave satisfactory yields of 2-[2,4-dinitrophenyl]-cyclohexanone.

While the arylation of the pyrrolidine enamine of cycloheptanone, XIIIc, with 2,4-dinitrochlorobenzene led only to a small yield of 2-[2,4-dinitrophenyl]-cycloheptanone (XIVc) and much tarry and acid-soluble material, the analogous reactions with the enamines of cyclopentanone, N-methyl-4-

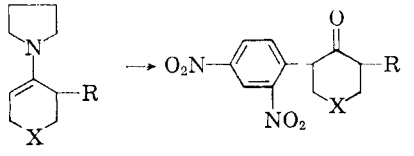
(5) M. E. Kuehne, *J. Am. Chem. Soc.*, **81**, 5400 (1959).

(6) The enhancement by a *p*-nitro group can be estimated by comparison with ultraviolet absorption measurements and calculations on *cis*-stilbene and nitrostilbene: G. Riezebos and E. Havinga, *Rec. trav. chim.*, **80**, 446 (1961).

piperidone and α-methylcyclohexanone proceeded satisfactorily. Acid hydrolysis of the α-arylated cyclohexane imonium intermediates, *i.e.* III, occurred at room temperature, but the cyclopentane derivative required prolonged heating.

Although steric hindrance to α′-substitution by an already present α-substituent requires enhanced activation in the alkylation of cyclohexanone enamines,[3] the pyrrolidine enamine of α-methylcyclohexanone reacted readily with 2,4-dinitrochlorobenzene at room temperature. Proof of the expected[3,5] arylation at the α′-methylene side was obtained by reductive cyclization of the product XIVd to the aminocarboline XVIIb.

Analogous condensations of polynitro aryl chlorides with 1,3,3-trimethyl-2-methyleneindoline have been reported in addition to its acylation and alkylation.[7]



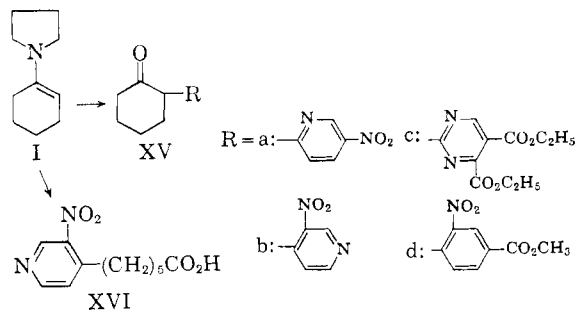
XIII XIV

a, X = —, R = H
b, X = NCH_3, R = H
c, X = CH_2CH_2, R = H
d, X = CH_2, R = CH_3

C-Arylation of 1-pyrrolidinocyclohexene could also be achieved with the heterocyclic halides 2-chloro-5-nitropyridine, 4-chloro-3-nitropyridine and 2-chloro-4,5-dicarbethoxypyrimidine. The first compound gave a completely enolic product (XVa), which showed no carbonyl absorption in the infrared but formed a crystalline 2,4-dinitrophenylhydrazone. The reaction of 2-chloro-5-nitropyridine is also of special interest because complexing of this reagent with a reaction product could be demonstrated by its partial recovery, even when a large excess of triethylamine or enamine were used. The formation of charge transfer complexes was always evident in these reactions by an intense coloration, which was also seen on addition of enamines to unreactive aromatic nitro compounds.

Hydrolysis of the imonium salt obtained with 4-chloro-3-nitropyridine gave the expected pyridyl ketone XVb and its cleavage product, the nitropyridylhexanoic acid XVI.

C-Arylation of I with 4-chloro-2-nitromethylbenzoate proceeded at a very slow rate at room temperature. A change to refluxing dioxane did not improve the preparative yield of aryl ketone XVd, but led to a small amount of 4-carbomethoxy-2-nitro-N-pyrrolidinobenzene. No significant reaction was found with 2-benzoyl-4-nitro-chlorobenzene at room temperature for thirty days or in refluxing dioxane.

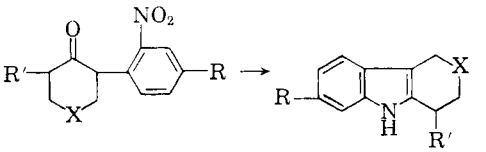


I XV XVI

R = a: b: c: d:

(7) M. Coenen, *Angew. Chem.*, **61**, 11 (1949).

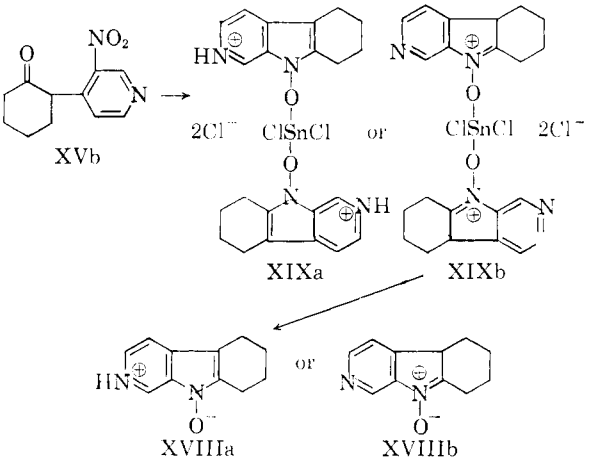
The *o*-nitroaryl ketones obtained in the preceding reactions were subjected to reductive cyclization. Catalytic or tin and hydrochloric acid reduction of 2-[2,4-dinitrophenyl]-cyclohexanone (VIII) readily yielded the aminotetrahydrocarbazole XVIIa and catalytic reduction of the corresponding 6-methyl ketone XIVd and the carbomethoxy nitroaryl ketone XVd gave the amino and carbomethoxytetrahydrocarbazoles XVIIb and c.



VIII, R = NO_2, R′ = H, X = CH_2
XIVd, R = NO_2, R′ = CH_3, X = CH_2
XVd, R = CO_2CH_3, R′ = H, X = CH_2
XIVb, R = NO_2, R′ = H, X = NCH_3

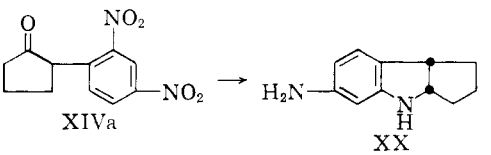
XVIIa, R = NH_2, R′ = H, X = CH_2
b, R = NH_2, R′ = CH_3, X = CH_2
c, R = CO_2CH_3, R′ = H, X = CH_2
d, R = NH_2, R′ = H, X = NCH_3

Both catalytic and chemical reduction of the α-nitropyridyl ketone XVb did not proceed beyond the hydroxylamine stage, which cyclized to an amphoteric, polar compound with the internal salt structure XVIIIa or the imine oxide structure XVIIIb. A crystalline chlorostannate XIXa or b could be isolated from the tin reduction and hydrolyzed to the oxide XVIII with aqueous sodium bicarbonate.



XVb XIXa XIXb XVIIIa XVIIIb

On the other hand, catalytic reduction of 2-[2,4-dinitrophenyl]-cyclopentanone (XIVa) could not be stopped before the dihydroindole XX, presumably because of preferential dehydration of the intermediate carbinolamine to an imine rather than an indole.

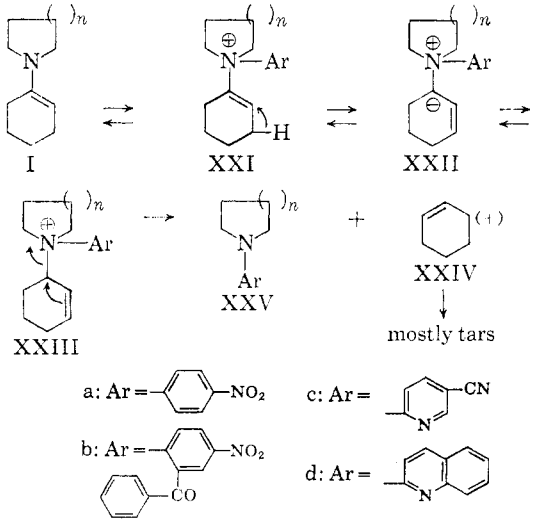


XIVa XX

Reactions with Less Reactive Aryl Halides.—While the more reactive aryl halides, above, were found to attack enamines on carbon, less reactive compounds gave only products which were derived from nitrogen arylation. Thus, 4-nitrochlorobenzene did not react with 1-pyrrolidinocyclohexene to an appreciable extent at 100°, but above that temperature N-4-nitrophenylpyrrolidine was formed. The same course was observed with the somewhat more reactive 4-fluoronitrobenzene, with 2-benzoyl-4-nitrochlorobenzene, with 2-chloro-5-cyanopyridine and with 2-chloroquinoline. Analogous results were also obtained with the hexamethyleneimino enamine.

4-Chloronitrobenzene does not react with simple tertiary amines under the conditions which gave N-arylation of the cyclohexanone enamines. With secondary amines such as pyrrolidine, however, nucleophilic substitution proceeded readily at 100°. A reaction path for the formation of N-nitrophenylpyrrolidine, which involves liberation and subsequent arylation of pyrrolidine, could conceivably arise from an initial addition of a nitro group to the enamine double bond. However, this course, or its equivalents, are rendered unlikely by the observations that with one equivalent of 4-chloronitrobenzene the yield of N-4-nitrophenylpyrrolidine is above the required maximum of 50% and that no increase is found with two equivalents of 4-chloronitrobenzene or when the reaction is carried out with nitrobenzene as solvent.

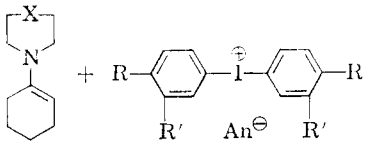
A more general route for the N-arylation and cleavage of enamines can be visualized in a double bond migration from the vinyl ammonium salt XXI through the stabilized allylic ylid XXII, to the allylic ammonium salt XXIII and subsequent elimination of the respective arylamines. Further evidence for this sequence was found in the isolation of 3-pyrrolidinocyclohexene (18% yield) from the reaction of 1-pyrrolidinocyclohexene with diphenyliodonium fluoroborate (below).



Reactions with Diaryliodonium Salts.—Diaryliodonium salts have been reported to act at elevated temperatures as sources of either phenyl radicals or phenyl cations, depending on the accompanying anion,[8] and the facile solvolytic cleavage of these compounds has been examined.[9,10] It could thus be anticipated that diaryliodonium salts would react with enamines either by C- or N-arylation.

Diphenyliodonium chloride and tosylate, *p,p'*-dichlorodiphenyliodonium chloride and *m,m'*-dinitrophenyliodonium bromide were cleaved at room temperature by 1-pyrrolidino, 1-piperidino and 1-morpholinocyclohexene. Hydrolysis of the reaction mixtures yielded 2-phenylcyclohexanone and 2-[3-nitrophenyl]-cyclohexanone, but the yields were disappointingly small. Attempts to enhance the formation of arylcyclohexanones by variations of solvents and temperature or the use of the boron tetrafluoride salt were essentially without success.

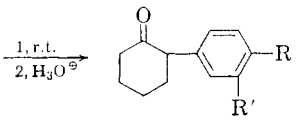
Subsequent to this work, some O- and C-arylations of β-dicarbonyl enolate salts with diphenyliodonium chloride have been reported.[11]



XXVI

X = —, CH_2, O

a, R = R' = H, An^- = Cl^-, Tos^-, BF^-
b, R = H, R' = NO_2, An^- = Br^-
c, R = Cl, R' = H, An^- = Cl^-



X, R = R' = H
XXVII, R = H, R' = NO_2

Reaction of Quinone Dibenzenesulfonimide.—Quinone imides are known as electrophiles which form C–C bonds on condensation with sodium enolates.[12,13] The products thus obtained from β-diketones and β-ketoesters can be cyclized with hot acid to N,N'-diacylindoles.[13,14]

1-Pyrrolidinocyclohexene reacted exothermically with quinone dibenzenesulfonimide (XXVIII). On addition of methanol and aqueous hydrochloric acid to the reaction mixture, the tetrahydrocarbazole XXXII was obtained directly. The same product was also obtained from the reaction of 1-hexamethyleneiminocyclohexene. However, here much of the dibenzenesulfonimide was reduced to the dibenzenesulfonamide.

Reaction with Phenyldiazonium Fluoroborate.—In the Schiemann reaction[15] phenyldiazonium fluoroborate decomposes to give fluorobenzene, and if nitrobenzene is used as solvent, *m*-phenyl-

(8) I. G. Makarova and A. N. Nesmeyanov, *Izvest. Akad. Nauk SSSR Otdel. Khim. Nauk*, 617 (1945); *Org. Kim.*, **7**, 109 (1950).

(9) M. C. Caserio, D. L. Glusker and J. D. Roberts, *J. Am. Chem. Soc.*, **81**, 336 (1959).

(10) F. M. Beringer, E. M. Gindler, M. Rapoport and R. J. Taylor, *ibid.*, **81**, 351 (1959).

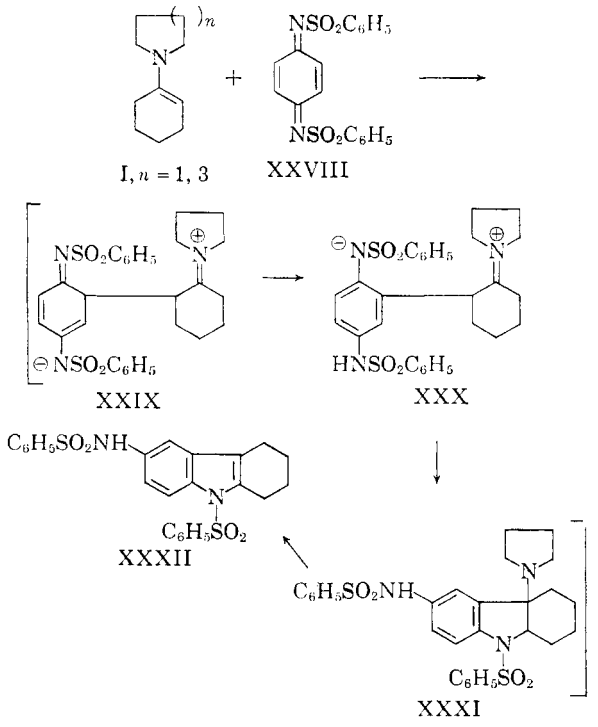
(11) F. M. Beringer, P. S. Forgione and M. D. Yuds, *Tetrahedron*, **8**, 49 (1960).

(12) R. Adams and D. C. Blomstrom, *J. Am. Chem. Soc.*, **75**, 3403 (1953).

(13) R. R. Holmes, K. G. Untch and H. D. Benson, *J. Org. Chem.*, **26**, 439 (1961).

(14) R. Adams and W. P. Samuels, *J. Am. Chem. Soc.*, **77**, 5375, 5383 (1955).

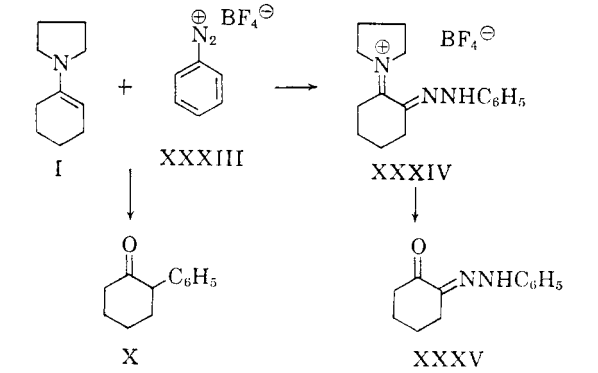
(15) A. Roe in "Organic Reactions," Vol. 5, J. Wiley and Sons, Inc. New York, N. Y., 1949.



I, $n = 1, 3$ XXVIII XXIX XXX XXXII XXXI

nitrobenzene is formed by arylation of the nitrobenzene with phenyl cations.[16] However, phenyldiazonium chloride and base arylates nitrobenzene through generation of phenyl radicals to form *o*- and *p*-nitrobiphenyl.[17-19] From the reaction of aldehyde enamines with aryldiazonium chlorides, conjugated phenylazoenamines were obtained.[20]

In order to determine if enamines of ketones might undergo a partial C-arylation, phenyldiazonium fluoroborate was added to 1-pyrrolidinocyclohexene. The only crystalline product, imonium salt XXXIV, was hydrolyzed to 1,2-cyclohexanedione monophenylhydrazone (XXXV). Acid hydrolysis and subsequent vapor phase chromatography of the total reaction mixture indicated the formation of some phenylcyclohexanone, but the amount was not sufficient for isolation.



I XXXIII XXXIV X XXXV

(16) A. W. Nesmeyanov and L. G. Makarova, *Izvest. Akad. Nauk SSSR. Otdel. Khim. Nauk.*, 213 (1947).

(17) M. Gomberg and J. C. Pernert, *J. Am. Chem. Soc.*, **48**, 1372 (1926).

(18) M. Gomberg and W. E. Bachmann, *ibid.*, **46**, 2342 (1924).

(19) W. S. M. Grieve and D. H. Hey, *J. Chem. Soc.*, 1797 (1934).

(20) J. W. Crary, O. R. Quayle and C. T. Lester, *J. Am. Chem. Soc.*, **78**, 5584 (1956).

Reactions with Benzyne.—The demonstrated electrophilic character of benzyne[21-24] suggested the condensation of this very reactive compound with enamines. In this addition, the isolated final products were found to depend upon the reaction conditions and the methods employed in the generation of benzyne.

Formation of benzyne from fluorobenzene and piperidyllithium in the presence of 1-pyrrolidinocyclohexene and subsequent hydrolysis led to some 2-phenylcyclohexanone and much N-phenylpiperidine. While piperidine, which is generated in the initial benzyne formation, could protonate the zwitterionic intermediate XXXVII, it can also compete with the enamine in its condensation with benzyne and thus lead to N-phenylpiperidine.

When butyllithium was used in place of piperidyllithium, the competing addition to benzyne was eliminated. In the absence of a proton source, the zwitterionic intermediate XXXVII now collapsed to give the benzocyclobutene XXXIX. The structure of this compound followed from its empirical composition, resistance to catalytic hydrogenation on a palladium catalyst, stability to dilute acid and its ultraviolet spectrum. It was readily purified by distillation, picrate formation and chromatographic regeneration and could be converted to a crystalline N-oxide hydrate. (Further definitive transformations will be described with a study of aminocyclobutenes.)

Benzyne formed from *o*-bromofluorobenzene and lithium amalgam reacted with 1-pyrrolidinocyclohexene to give, again, only the benzocyclobutene XXXIX; but when magnesium was used, both possible routes were followed. When the reaction was carried out in ether and only part of the required magnesium was consumed, a low yield of 2-phenylcyclohexanone and traces of the benzocyclobutene XXXIX were obtained after hydrolysis. In refluxing tetrahydrofuran a vigorous reaction produced 2-phenylcyclohexanone in 17% yield and the benzocyclobutene XXXIX in 20% yield.

In a control experiment it was found that phenylmagnesium bromide does not add to 1-pyrrolidinocyclohexene. Addition of Grignard reagents to enamines requires the prior formation of an imonium salt, such as a perchlorate.[25] Since the preceding condensations involved the generation of metal salts in the benzyne formation and the results indicated cationic participation, presumably by association of the cation with the charged intermediate XXXVII, it was of interest to examine the reaction of benzyne formed by an alternative method. Decomposition of *o*-benzenediazonium carboxylate[26] at 40° in 1-pyrrolidinocyclohexene resulted, however, in a violent detonation.

(21) G. Wittig, *Angew. Chem.*, **69**, 245 (1957).

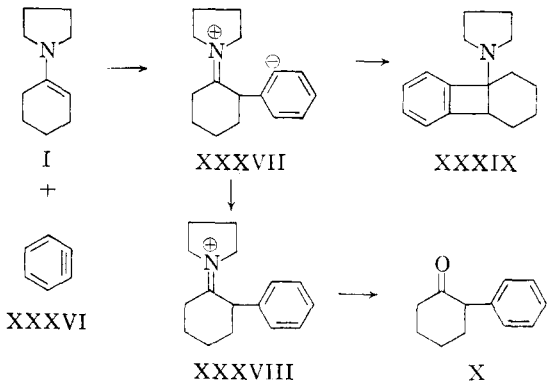
(22) E. F. Jenny, M. C. Caserio and J. D. Roberts, *Experientia*, **14**, 349 (1958).

(23) J. F. Bunnett, *Quart. Revs.*, **12**, 1 (1958).

(24) R. Huisgen and J. Sauer, *Angew. Chem.*, **72**, 91 (1960).

(25) R. Lukes, V. Dienstbierova and O. Cervinka, *Coll. Czechoslov. Chem. Comm.*, **24**, 429 (1959).

(26) (a) M. Stiles and R. G. Miller, *J. Am. Chem. Soc.*, **82**, 3802 (1960); (b) R. S. Berry, G. N. Spokes and M. Stiles, *ibid.*, **82**, 5241 (1960).



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Experimental

2-[2,4-Dinitrophenyl]-cyclohexanone (VIII).—To a cooled solution of 6.70 g. (0.033 mole) of 1-chloro-2,4-dinitrobenzene and 3.50 g. (0.034 mole) of triethylamine in 50 ml. of methylene chloride, under nitrogen, was added 5.00 g. (0.033 mole) of 1-pyrrolidinocyclohexene.[3,5] After standing for 24 hr. at room temperature, the suspension was concentrated under vacuum and the residue stirred into 200 ml. of 3% hydrochloric acid. Separation of the crude product was essentially complete after 24 hr. Filtration and recrystallization from methylene chloride–methanol gave 8.0 g. (92% yield) of 2-[2,4-dinitrophenyl]-cyclohexanone, m.p. 99–100°.

Anal. Calcd. for $C_{12}H_{12}N_2O_5$: C, 54.54; H, 4.58; N, 10.60. Found: C, 54.15; H, 4.62; N, 10.57.

Variations of Reaction Conditions.—**a:** The reaction was carried out as above but terminated after 4 hr. in methylene chloride with one equivalent of triethylamine; 7.0 g. (80% yield) of product. **b:** Reaction terminated after 4 hr. in 50 ml. of benzene with one equivalent of triethylamine; 4.7 g. (53% yield) of product and 1.7 g. (25% recovery) of 1-chloro-2,4-dinitrobenzene. **c:** The reaction terminated after 24 hr. in 50 ml. of dry dioxane with 30.0 g. (0.30 mole) of triethylamine; 5.8 g. (66% yield) of product. **d:** Reaction terminated after 24 hr. in 50 ml. of dry dioxane with 3.50 g. (0.034 m.) of triethylamine; 8.0 g. (92% yield) of product. **e:** Reaction terminated after 24 hr. in 50 ml. of dry dioxane without triethylamine; 2.6 g. (30% yield) of product. When small amounts of water were introduced with the solvent or with triethylamine, N-2,4-dinitrophenylpyrrolidine was formed and could be separated from the product by fractional recrystallization from carbon tetrachloride. N-2,4-Dinitrophenylpyrrolidine, m.p. 98–99°, was formed quantitatively from 1-chloro-2,4-dinitrobenzene in ether with an excess of pyrrolidine.

Anal. Calcd. for $C_{10}H_{11}N_3O_4$: C, 50.63; H, 4.67; N, 17.72. Found: C, 50.88; H, 4.94; N, 17.80.

Use of 1-Fluoro-2,4-dinitrobenzene.—**a:** The reaction, initially cooled (very exothermic), was terminated after 24 hr. at room temperature in 50 ml. of dioxane and 3.5 g. (0.034 mole) of triethylamine; 7.0 g. (80% yield) of product. **b:** The same conditions without triethylamine produced less than 0.5 g. (6% yield) of product and formation of tars.

Use of Other Cyclohexanone Enamines.—The main procedure, repeated with **a**, 5.3 g. (0.033 mole) of 1-piperidinocyclohexene[3] gave 5.8 g. (66% yield) of product; with **b**:, 6.0 g. (0.033 mole) of 1-hexamethyleneiminocyclohexene, b.p. 114° (5 mm.) (formed in 74% yield in the usual way[5]), gave 8.1 g. (92% yield) of product; and with **c**: 5.3 g. (0.033 mole) of 1-morpholinocyclohexene[3] gave no product but a red, acid stable and insoluble oil which was not further investigated.

2-Acetyl-6-[2,4-dinitrophenyl]-cyclohexanone (VI).—To a solution of 10.1 g. (0.050 mole) of 2,4-dinitrochlorobenzene in 100 ml. of methylene chloride and 10.1 g. (0.10 mole) of triethylamine was added 7.5 g. (0.050 mole) of 1-pyrrolidinocyclohexene. After 48 hr. at room temperature, under nitrogen, 4.0 g. (0.050 mole) of acetyl chloride was added. The reaction was stirred for 3 days at room temperature, concentrated in vacuum and distributed between dilute hydrochloric acid and ether. A small amount of insoluble gum yielded 0.15 g. of 2-[2,4-dinitrophenyl]-cyclohexanone in the initial benzene eluate on chromatography over Florisil. Concentration of the ether extract and chromatography gave 0.70 g. of a crystalline mixture of 2-[2,4-dinitrophenyl]-cyclohexanone and N-2,4-dinitrophenylpyrrolidine in the benzene eluate. Later fractions eluted with methylene chloride, 10% methanol in methylene chloride and methanol all gave an intense ferric chloride color reaction, but only one fraction, eluted with 10% methanol, gave an appreciable amount of crystalline copper complex. On addition of methanolic cupric acetate, 0.10 g., m.p. 208–210°, crystallized. From the initial aqueous acid solution a gum precipitated over 48 hr. Extraction with methylene chloride and concentration was followed by solution in ether. The ether was washed once with dilute hydrochloric acid and then extracted with cold 0.5 *N* sodium hydroxide. On concentration, 2.8 g. of 2-[2,4-dinitrophenyl]-cyclohexanone was obtained. Acidification of the sodium hydroxide solution, extraction with ether and addition of methanolic cupric acetate gave 1.50 g. of crystalline cupric salt, m.p. 208–210°; recrystallized from acetone, m.p. 210–211°.

Anal. Calcd. for $C_{26}H_{26}N_4O_{12}Cu$: C, 49.89; H, 3.89; N, 8.31. Found: C, 49.51; H, 3.90; N, 8.44.

The free β-diketone, liberated with hydrogen sulfide, could not be crystallized. It gave an intense ferric chloride color reaction and had strong infrared absorption at 1610 (O=CR–CR=CR—OH), 1530 and 1350 cm.$^{-1}$ (NO_2).

2-Benzoyl-2-[2,4-dinitrophenyl]-cyclohexanone (VII). The benzoylation was carried out like the preceding acetylation with 7.0 g. (0.050 mole) of benzoyl chloride. The reaction concentrate was separated into ether-soluble and dilute acid-soluble fractions and 4.9 g. of an insoluble gum. Concentration of the ether and crystallization from ethanol gave 1.50 g. of crude product, recrystallized from methylene chloride and ethanol to 1.40 g., m.p. 176–178°. The compound was insoluble in dilute alkali, did not give a ferric chloride color reaction and had infrared absorption at 1710 (C=O cyclohexanone), 1685 (C=O benzoyl), 1530 and 1350 cm.$^{-1}$ (NO_2).

Anal. Calcd. for $C_{19}H_{16}N_2O_6$: C, 61.95; H, 4.38; N, 7.61. Found: C, 62.16; H, 4.59; N, 7.40.

Enol Benzoate of 2-[2,4-Dinitrophenyl]-cyclohexanone (IX).—A solution of 2.64 g. (0.10 mole) of 2-[2,4-dinitrophenyl]-cyclohexanone in 25 ml. of dry pyridine was combined with 1.7 g. (0.012 mole) of benzoyl chloride. After 24 hr. at room temperature the reaction mixture was concentrated in vacuum and 20 ml. of methanol added, causing 3.3 g. of crude product to crystallize. Recrystallization from methylene chloride and ethanol gave 3.0 g. (82% yield) of product, m.p. 137–138°; infrared absorption at 1730 (C=O enol benzoate), 1530 and 1350 cm.$^{-1}$ (NO_2).

Anal. Calcd. for $C_{19}H_{16}N_2O_6$: C, 61.95; H, 4.38; N, 7.61. Found: C, 61.90; H, 4.58; N, 7.74.

Repeated attempts at hydrolytic cleavage of the enol benzoate with aqueous acid, aqueous pyridine and aqueous sodium acetate led only to recovery of the compound. Sodium hydroxide or concd. sulfuric acid destroyed the material. However, hydrolysis was found after reduction of the nitro groups (below).

2-[2,4-Dinitrophenyl]-cyclopentanone (XIVa).—An exothermic reaction started on addition of 6.90 g. (7.4 ml., 0.050 mole) of 1-pyrrolidinocyclopentene[5] to a solution of 10.05 g. (0.050 mole) of 2,4-dinitrochlorobenzene in 80 ml. of methylene chloride and 5.5 g. (0.05 mole) of triethylamine. After 24 hr. at room temperature, under nitrogen, the solvent was removed in vacuum, the residue taken up in an excess of 3% hydrochloric acid and the solution washed

with ether. After 20 hr. at room temperature the clear solution was heated on a steam-bath. The crude product began to precipitate, giving after 2 hr., 4.2 g., m.p. 118–121°; after an additional 5 hr., 3.0 g., m.p. 115–120°; and after further 8 hr., 3.0 g., m.p. 110–115°. Recrystallization of the combined material from methylene chloride and methanol resulted in 9.2 g. (74% yield), m.p. 122–123°.

Anal. Calcd. for $C_{11}H_{10}N_2O_5$: C, 52.80; H, 4.03; N, 11.20. Found: C, 52.37; H, 4.22; N, 11.13.

Alternatively, the reaction was worked up by dissolving the residue in 250 ml. of ice-water containing 12.5 ml. of concd. hydrochloric acid. After washing with ether, 30.0 g. of sodium acetate was added and the solution heated for 4 hr. on a steam-bath, to give 12.0 g. of crude product, recrystallized from methylene chloride and methanol to 11.6 g. (93% yield). Hydrolysis of the reaction mixture with concentrated hydrochloric acid led mostly to destruction.

2-[2,4-Dinitrophenyl]-cycloheptanone (XIVc).—The exothermic reaction of 8.3 g. (8.7 ml., 0.050 mole) of 1-pyrrolidinocycloheptene[5] with 10.05 g. (0.050 mole) of 2,4-dinitrochlorobenzene was carried out as with 1-pyrrolidinocyclopentene. On addition of 3% hydrochloric acid to the reaction concentrate, about 1 g. of a dark gum separated. The gum was heated with an excess of 3% hydrochloric acid for 5 hr. and then extracted with carbon tetrachloride. Concentration and crystallization from methanol gave 0.55 g. of crude product, m.p. 117–118°. Heating of the clear initial acidic solution for 5 hr. on a steam-bath did not yield a precipitate. However, when the solution was made strongly basic and then reacidified after 10 min., 0.70 g. of material separated. Crystallization from methanol gave 0.40 g., m.p. 117–119°. Repeated recrystallization of the combined fractions from carbon tetrachloride led to 0.75 g. (5.4% yield) of pure product, m.p. 120–121°.

Anal. Calcd. for $C_{13}H_{14}N_2O_5$: C, 56.11; H, 5.07; N, 10.07. Found: C, 56.14; H, 5.28; N, 10.37.

In other experiments hydrolytic workup with ammonium hydroxide, sodium acetate or concd. hydrochloric acid failed to give the desired product.

1-Methyl-4-N-pyrrolidino-3-piperideine (XIIIb).—A solution of 113 g. (2.0 moles) of N-methyl-4-pyridone and 156 g. (2.2 moles) of pyrrolidine were refluxed in 600 ml. of toluene, under nitrogen, for 3 hr. with a Dean–Stark water separator. The solvent was distilled off and the residue distilled, giving 9.0 g., b.p. about 80° (0.2 mm.), and 131 g. (40% yield) of product, b.p. 87–91° (0.2 mm.).

3-[2,4-Dinitrophenyl]-1-methyl-4-piperidone (XIVb).—An exothermic reaction was found on addition of 8.3 g. (0.050 mole) of the enamine XIIIb to 10.1 g. (0.050 mole) of 2,4-dinitrochlorobenzene in 100 ml. of methylene chloride and 5.0 g. (0.050 mole) of triethylamine. After 40 hr. at room temperature, under nitrogen, the reaction was concentrated in vacuum and the residue taken up in an excess of 3% hydrochloric acid. Extraction with ether yielded 1.2 g. of N-2,4-dinitrophenylpyrrolidine. After 3 days at room temperature an excess of solid sodium bicarbonate was added to the clear acidic solution. Extraction with ether, concentration and recrystallization from methanol gave 1.95 g. (14% yield) of product, m.p. 125–126°; infrared peaks at 1725 (C=O), 1540, 1350 cm.$^{-1}$ (NO_2).

Anal. Calcd. for $C_{12}H_{13}N_3O_5$: C, 51.61; H, 4.69; N, 15.05. Found: C, 51.82; H, 4.90; N, 1517.

2-[4-Carbomethoxy-2-nitrophenyl]-cyclohexanone (XVd).—A solution of 12.9 g. (0.060 mole) of 4-carbomethoxy-2-nitrochlorobenzene, m.p. 82–83° (reported[27] m.p. 83°) (prepared by refluxing the chloronitro acid for 2 hr. in methanol containing 10% sulfuric acid), 18.0 g. (0.12 mole) of 1-pyrrolidinocyclohexene and 1 ml. of triethylamine in 100 ml. of methylene chloride was stored at room temperature for 12 days under nitrogen. The reaction was concentrated under vacuum, taken up in an excess of dilute, cold hydrochloric acid and extracted with ether. Concentration of the ether solution and recrystallization from methanol gave 2.9 g. (22%) of recovered crude 4-carbomethoxy-2-nitrochlorobenzene. On standing for 24 hr. the aqueous solution deposited the product and an amorphous material. Filtration, washing with water and recrystallization from cyclohexane gave 7.0 g. (42% yield), m.p. 88–89°.

(27) E. I. Montagne, *Rec. trav. chim.*, **19**, 55 (1900).

Anal. Calcd. for $C_{14}H_{15}NO_5$: C, 60.64; H, 5.45; N, 5.05. Found: C, 60.28; H, 5.41; N, 5.09.

Extraction of the aqueous acid filtrates with methylene chloride and concentration gave 9.0 g. of a yellow, amorphous solid which was soluble in methanol, ethanol, benzene or water (weakly acidic solution), gave a positive ferric chloride reaction and had infrared absorption at 3300–3400, 1710–1720, 1630 cm.$^{-1}$.

From a reaction refluxed for 4 hr. in dioxane, the initial ether extract of the aqueous acid solution contained a mixture of 4-carbomethoxy-2-nitrochlorobenzene and little 4-carbomethoxy-2-nitro-N-pyrrolidinobenzene, m.p. 68–69°, crystallized from cyclohexane.

Anal. Calcd. for $C_{12}H_{14}N_2O_4$: C, 57.59; H, 5.64; N, 11.20. Found: C, 57.63; H, 5.71; N, 11.02.

2-[5-Nitro-2-pyridyl]-cyclohexanone (XVa).—To a solution of 5.2 g. (0.033 mole) of 2-chloro-5-nitropyridine in 50 ml. of methylene chloride and 3.5 g. (0.035 mole) of triethylamine, under nitrogen, was added 5.0 g. (0.033 mole) of 1-pyrrolidinocyclohexene. After 3 days the solvent was removed under vacuum, an excess of iced, dilute hydrochloric acid added and the solution extracted well with ether. Concentration of the ether extract gave 3.0 g. of a mixture, m.p. 80–90°. Fractional recrystallization from methanol led to 2.4 g., m.p. 108–109° of recovered chloronitropyridine and 0.60 g. of the dark red product, m.p. 149–150°, with infrared absorption at 1630, 1610, 1570, 1530 and 1350 cm.$^{-1}$; 2,4-dinitrophenylhydrazone, m.p. 188–189°.

Anal. Calcd. for $C_{11}H_{12}N_2O_3$: C, 59.99; H, 5.49; N, 12.72. Found: C, 60.02; H, 5.54; N, 12.65. Calcd. for $C_{17}H_{16}N_6O_6$: C, 51.00; H, 4.03; N, 20.99. Found: C, 50.86; H, 4.20; N, 21.27.

After 24 hr. an additional 2.4 g. of the nitropyridyl ketone had crystallized from the aqueous acid (total yield 41%). The clear acid filtrate was made basic after further 24 hr. and extracted with methylene chloride. Concentration and crystallization from methanol gave 0.30 g. of 5-nitro-2-N-pyrrolidinopyridine, m.p. 136–137°.

Anal. Calcd. for $C_9H_{11}N_3O_2$: C, 55.95; H, 5.74; N, 21.75. Found: C, 56.22; H, 5.92; N, 21.67.

When the reaction was worked up after 24 hr., the same results were obtained. When the amount of triethylamine was increased to 10.5 g. (0.104 mole), 2.9 g. (56%) of chloronitropyridine was recovered and 1.7 g. (23% yield) of pyridyl ketone obtained. A reaction of 10.0 g. (0.066 mole) of enamine, 3.5 g. (0.035 mole) of triethylamine and 5.2 g. (0.033 mole) of chloronitropyridine gave 1.1 g. (21% recovery) of chloronitropyridine and 3.5 g. (48% yield) of product. Purification of the recovered chloronitropyridine was best achieved by chromatography over alumina (Woelm, basic, activity II) with 2:1 petroleum ether–benzene.

4-Chloro-3-nitropyridine.—A mixture of 15.0 g. of 4-pyridone, 44 g. of fuming nitric acid and 65 g. of fuming sulfuric acid (30% SO_3) was maintained at gentle reflux (110°) for 7 hr. The cooled solution was poured into 100 ml. of water and 19.1 g. of material filtered off. Recrystallization from water gave 0.9 g. of 3,5-dinitro-4-hydroxypyridine, m.p. 325°, and 15.4 g. of 3-nitro-4-hydroxypyridine, m.p. 278°.[28,29] The mononitro compound was ground with 24 g. of phosphorus pentachloride, a few drops of phosphorus oxychloride added and the mixture heated over a flame for 15 min., when a clear solution was obtained, and then on a steam-bath for 1 hr. With cooling, ethanol was added to the cold reaction mixture until the vigorous reaction subsided. Addition of a small amount of ether and filtration gave 15.0 g. of a salt, m.p. 145–150° dec. Digestion with several portions of methylene chloride, filtration, evaporation and crystallization from heptane gave 7.8 g. of 4-chloro-3-nitropyridine, m.p. about 25.°[29a]

Anal. Calcd. for $C_5H_3ClN_2O_2$: C, 37.89; H, 1.90; N, 17.67. Found: C, 37.36; H, 2.04; N, 17.62.

2-[3-Nitro-4-pyridyl]-cyclohexanone (XVb) and 6-[3-Nitro-4-pyridy]-hexanoic Acid (XVI).—To a solution of 7.9 g. (0.050 mole) of 4-chloro-3-nitropyridine in 100 ml. of

(28) E. Koenigs and K. Freter, *Chem. Ber.*, **57**, 1187 (1924).

(29) S. H. Crowe, *J. Chem. Soc.*, **127**, 2028 (1925).

(29) An unanalyzed substance, presumably the hydrochloride, with different properties, has been described as this compound in ref. 27.

methylene chloride and 3.5 g. (0.035 mole) of triethylamine, under nitrogen, was added 22.5 g. (0.150 mole) of 1-pyrrolidinocyclohexene. After 4 days the solvent was removed in vacuum, an excess of iced, dilute hydrochloric acid added and the solution extracted with ether. Concentration and recrystallization from ether gave 1.8 g. of crude product, m.p. 62–67°. Re-extraction after 24 hr. produced an additional 4.6 g., m.p. 68–69°, (total yield 58%), and 0.65 g. of impure product. A sample recrystallized repeatedly from ether had m.p. 70–71°.

Anal. Calcd. for $C_{11}H_{12}N_2O_3$: C, 59.99; H, 5.49; N, 12.72. Found: C, 60.12; H, 5.50; N, 12.66.

Heating of the clear acid solution for 2 hr. on a steam-bath, cooling, extraction with ether, concentration and recrystallization from ethyl acetate gave 0.65 g. of a water-insoluble, sodium bicarbonate-soluble, light-sensitive compound, m.p. 112–114°; infrared absorption at 1700 (CO_2H), 1600 (pyr.), 1530 and 1350 (NO_2), 3000 to 3400 cm.$^{-1}$ (bonded OH). This compound was also found as a slight contaminant of the initial pyridyl ketone.

Anal. Calcd. for $C_{11}H_{14}N_2O_4$: C, 55.44; H, 5.92; N, 11.76. Found: C, 55.20; H, 6.07; N, 11.55.

The arylation with one equivalent of triethylamine and one equivalent of enamine, carried out as with 2-chloro-5-nitropyridine, gave a 41% yield.

2-Chloro-4,5-dicarbethoxypyrimidine.—A solution of 30.0 g. (0.125 mole) of 2-hydroxy-4,5-dicarbethoxypyrimidine[30] in 250 ml. of phosphorus oxychloride was refluxed for 1 hr., concentrated in vacuum, the residue poured into 1 l. of ice-water and the product extracted with methylene chloride. Concentration and distillation gave 26 g. (81% yield), b.p. 140–145° (0.005 mm.), recrystallized from petroleum ether, m.p. 31–32°.[31]

2-[4,5-Dicarbethoxy-2-pyrimidyl]-cyclohexanone (XVc).—A mixture of 6.5 g. (0.025 mole) of 2-chloro-4,5-dicarbethoxypyrimidine and 7.5 g. (0.050 mole) of 1-pyrrolidinocyclohexene, under nitrogen, was heated briefly on a steam-bath to start the exothermic reaction and for an additional 15 min. when the reaction began to subside. The cooled mixture was then stirred into an excess of dilute hydrochloric acid and extracted with methylene chloride. Distillation of the concentrate gave 4.4 g., b.p. 200–210° (0.1 mm.), which was recrystallized from ethanol to 2.7 g. (34% yield), m.p. 59–60°.

Anal. Calcd. for $C_{16}H_{20}N_2O_5$: C, 59.99; H, 6.29; N, 8.75. Found: C, 59.92; H, 6.30; N, 8.72.

2-[2,4-Dinitrophenyl]-6-methylcyclohexanone (XIVd).—To a solution of 10.1 g. (0.050 mole) of 1-chloro-2,4-dinitrobenzene and 5.5 g. (0.055 mole) of triethylamine in 100 ml. of methylene chloride, under nitrogen, was added 8.2 g. (9.1 ml., 0.050 mole) of 6-methyl-1-pyrrolidinocyclohexene.[5] After 3 days the solvent was removed under vacuum, the residue stirred into an excess of dilute hydrochloric acid and the product filtered off, giving after 24 hr., 6.1 g.; after 48 hr., 0.75 g.; and after 60 hr., 0.20 g., m.p. 115–117°. Recrystallization from methylene chloride and methanol or carbon tetrachloride furnished 6.65 g. (48% yield) of product, m.p. 120–121°.

Anal. Calcd. for $C_{13}H_{14}N_2O_5$: C, 56.11; H, 5.07; N, 10.07. Found: C, 55.79; H, 5.33; N, 10.24.

7-Amino-1,2,3,4-tetrahydrocarbazole (XVIIa). a.—A solution of 2.64 g. (0.010 mole) of 2-[2,4-dinitrophenyl]-cyclohexanone in 20 ml. of dioxane was reduced with a 5% Pd–C catalyst. When hydrogen uptake stopped at 1.52 l. (0.063 mole at 21°), the solution was filtered, concentrated in vacuum and the residue recrystallized from hexane, giving 1.55 g. (83% yield), m.p. 103–104° (reported[32] m.p. 101°); ultraviolet absorption mμ (log ε) λ_{max} 235 (4.50), 270–276 (3.75), 307 (3.71); λ_{min} 256 (3.68), 288 (3.51) in methanol; and λ_{max}: 230 (4.47), shld. 275 (3.69), plat. 286 (3.76), plat. 291 (3.77), 293 (3.78), 314 (3.69), 325 (3.69), shld. 338 (3.54); λ_{min} 251 (3.56), 306 (3.68), 318 (3.68) in 2 *N* HCl.

Anal. Calcd. for $C_{12}H_{14}N_2$: C, 77.38; H, 7.58; N, 15.04. Found: C, 77.16; H, 7.47; N, 15.27.

b.—To a warm solution of 2.6 g. (0.010 mole) of the dinitrophenyl ketone in 25 ml. of acetic acid was added 5.6 g. (0.047 g. atom) of granulated tin, followed by 13 ml. of concd. hydrochloric acid, added over 90 min., with heating on a steam-bath. A small amount of unreacted tin was filtered off, 50 ml. of water added and the solution made strongly basic with concd. sodium hydroxide. Recrystallization of the filtered precipitate from hexane gave 1.1 g. (59% yield), m.p. 101–103°.

c.—Similar reduction of 1.34 g. (0.0036 mole) of the enol benzoate with 2.0 g. (0.017 g. atom) of tin produced 0.35 g. (52% yield) of product, m.p. 103–104°.

7-Carbomethoxy-1,2,3,4-tetrahydrocarbazole (XVIIc). Reduction of 2.70 g. (0.00975 mole) of 2-[4-carbomethoxy-2-nitrophenyl]-cyclohexanone in 30 ml. of dioxane, with 5% Pd–C, stopped at consumption of 0.82 l. of hydrogen (0.034 mole at 22°). Filtration, concentration and recrystallization from methanol, then from benzene and petroleum ether, gave 1.35 g. (61% yield) of product, m.p. 156–158°; ultraviolet absorption in methanol mμ (log ε) λ_{max}: 225 (4.25), 251 (4.39), 299 (4.11), 331 (4.023); λ_{min} 237 (4.17), 267 (3.43), 313 (3.95).

Anal. Calcd. for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59; N, 6.11. Found: C, 73.55; H, 6.64; N, 6.26.

From the mother liquors 0.35 g. of a partially reduced compound, m.p. 145–146°, was obtained; ultraviolet absorption in methanol mμ (log $\epsilon^{1\%}$) λ_{max}: 225 (3.027), shld. 245–252 (2.52), 318 (2.034); λ_{min} 277 (1.51); infrared peaks at 3320, 3260, 1700, 1590 and 1310 cm.$^{-1}$.

Anal. Calcd. for $C_{28}H_{36}N_2O_7$: C, 65.60; H, 7.08; N, 5.46. Found: C, 64.99; H, 7.36; N, 5.27.

7-Amino-1-methyl-1,2,3,4-tetrahydrocarbazole (XVIIb). Hydrogenation of 2.78 g. (0.010 mole) of 2-[2,4-dinitrophenyl]-6-methylcyclohexanone on 10% Pd–C, in 20 ml. of dioxane, stopped at 1.26 l. (0.057 mole at 21°). Filtration, concentration and recrystallization from hexane gave 1.2 g. (60% yield) of product, m.p. 113–114°; ultraviolet absorption mμ (log ε) λ_{max} 234 (4.49), 271–277 (3.75), 307 (3.73), shld. 321 (3.50); λ_{min} 257 (3.64), 289 (3.52) in methanol; and λ_{max} 232 (4.56), 284 (3.81), shld. 290 (3.79), 296–305 (3.58); λ_{min}; 250 (3.25) in 2 *N* HCl.

Anal. Calcd. for $C_{13}H_{16}N_2$: C, 77.99; H, 8.05; N, 14.00. Found: C, 77.99; H. 8.14; N, 14.24.

Reduction of 2-[2,4-Dinitrophenyl]-cyclopentanone to XX.—A solution of 3.0 g. (0.012 mole) of the compound in 25 ml. of dioxane and 1.0 g. of 5% Pd–C absorbed 2.20 l. (0.091 mole at 21°) of hydrogen. Filtration, concentration and recrystallization from hexane gave 1.0 g. of the dihydroindole, m.p. 60–62°; ultraviolet absorption mμ (log ε) λ_{max} strong end abs., shld. 242–254 (3.75), 307–310 (3.62), shld. 320 (3.43); λ_{min} 278 (3.03) in methanol; and λ_{max} shld. 217 (3.76), 257 (2.87), 261 (2.95), 264 (2.96), 270 (2.97), 309 (3.54); λ_{min} 236 (2.54), 262 (2.95), 267 (2.84), 284 (2.40) in 2 *N* HCl.

Anal. Calcd. for $C_{11}H_{14}N_2$: C, 75.92; H, 8.10; N, 16.08. Found: C, 75.99; H, 8.16; N, 16.44.

7-Amino-3-aza-3-methyl-1,2,3,4-tetrahydrocarbazole (XVIId).—Reduction of 1.3 g. (0.0047 mole) of 3-[2,4-dinitrophenyl]-1-methyl-4-piperidone in 25 ml. of dioxane with 0.50 g. of 10% Pd–C led to absorption of 690 ml. (0.028 mole) of hydrogen. Filtration, concentration and crystallization from 20 ml. of benzene gave 0.60 g. of product (64% yield), m.p. 166–170°. For analysis the hydrobromide was prepared and recrystallized from methanol and ether, m.p. 265–266°; ultraviolet absorption mμ (log ε) λ_{max} 230–234 (4.51), shld. 258–263 (3.69), 269–276 (3.77), 305 (3.69), shld. 321–325 (3.31); λ_{min} 215 (4.48), 255 (3.67), 286 (3.47) in methanolic sodium hydroxide; and λ_{max} 223 (4.65), shld. 262 (3.66), shld. 272 (3.79), 278 (3.83), 282 (3.81), 288 (3.76); λ_{min} 240 (3.01), 287 (3.75) in 2 *N* HCl.

Anal. Calcd. for $C_{12}H_{15}N_3 \cdot 2HBr$: C, 39.70; H, 4.72; N, 11.58. Found: C, 39.33; H, 5.08; N, 11.35.

Reduction of 2-[3-Nitro-4-pyridyl]-cyclohexanone to XVIIIa or b and XIX a or b. a.—Hydrogenation of 2.85 g. (0.013 mole) of the compound in 20 ml. of dioxane with 1.0 g. of 5% Pd–C stopped after 0.74 l. (0.031 mole at 21°) had been absorbed. Filtration, digestion of the catalyst with hot methanol and concentration gave 1.5 g. (62% yield) of a polar compound, m.p. 192–195°; recrystallized from di-

(30) R. G. Jones and C. W. Whitehead, *J. Org. Chem.*, **20**, 1342 (1955).

(31) This compound was first made by this method by Dr. W. Benzoe of these laboratories. The author gratefully acknowledges the helpful suggestions and permission to report these results.

(32) S. G. P. Plant, *J. Chem. Soc.*, 899 (1936).

methylformamide, m.p. 194–196°. The compound was insoluble in water but soluble in dilute hydrochloric acid or dilute sodium hydroxide. An acetate, m.p. 140–141°, crystallized from acetic acid and ether, decomposed to the initial compound at 110° under vacuum; ultraviolet absorption mμ λ_{max} 240, 270, 320; λ_{min} 260, 290 in methylene chloride; and λ_{max} 232, 265, 315; λ_{min} 249, 285 in ethanol; and λ_{max} 249, 278; λ_{min} 225, 270 in ethanolic sodium hydroxide; and λ_{max} 243, 273 and λ_{min} 220, 225 in ethanolic HCl.

Anal. Calcd. for $C_{11}H_{12}N_2O$: C, 70.18; H, 6.43; N, 14.88; active H, 0.53. Found: C, 69.91; H, 6.54; N, 14.87; active H, 0.22, 0.25 at room temp. in anisole and 0.48, 0.52 in hot anisole.

b.—To a solution of 1.1 g. (0.0050 mole) of the nitropyridyl ketone in 15 ml. of acetic acid, heated on a steam-bath, was added 1.4 g. (0.012 g. atom) of granulated tin and dropwise, over 30 min., 3.0 ml. of concd. hydrochloric acid. After heating for an additional 1 hr., cooling, filtration, concentration and crystallization from methanol and ether gave 1.3 g. (42% yield) of chlorostannate, m.p. 157–159°, recrystallized from methanol. From a solution of 0.20 g. in water, addition of sodium bicarbonate and filtration, 0.15 g. of the imine oxide or hydroxylamine compound, m.p. 194–196°, was obtained.

Anal. Calcd. for $C_{22}H_{24}SnCl_4N_4O_2$: C, 41.74; H, 3.82; N, 8.87. Found: C, 42.00; H, 4.21; N, 8.73.

N-[4-Nitrophenyl]-pyrrolidine (XXVa, n = 1).—A mixture of 5.2 g. (0.033 mole) of 4-chloronitrobenzene, 5.0 g. (0.033 mole) of 1-pyrrolidinocyclohexene and 3.5 g. (0.035 mole) of triethylamine was refluxed (120–130°) for 20 hr. under nitrogen. The cooled mixture was poured into an excess of dilute hydrochloric acid and extracted with ether. Combination of the ether concentrate with some insoluble material and crystallization from methanol gave 4.4 g. (71% crude yield) of dark material, m.p. 160–165°. Recrystallization from methylene chloride and methanol furnished 3.50 g. (55% yield), m.p. 167–168° (reported[33] 167–168°).

Variations of Conditions.—**a:** Repeating the sequence with 10.4 g. (0.066 mole) of 4-chloronitrobenzene produced identical amounts of crude and pure product as well as 2.35 g. (45% of excess) of recovered halide. **b:** Repeating the reaction in nitrobenzene at 125–130° for 20 hr. gave 3.50 g. (55% yield), m.p. 167–168°. **c:** Repeating the reaction in 40 ml. of refluxing dimethylformamide for 18 hr. gave 3.3 g. of crude and 2.1 g. (33% yield) of pure product. **d:** Refluxing in 40 ml. of dioxane for 18 hr. led to recovery of 3.8 g. (73%) of 4-chloronitrobenzene and no isolatable N-arylpyrrolidine. **e:** Substituting 4-fluoronitrobenzene in the same reaction and refluxing in 40 ml. of dioxane for 18 hr. gave 0.70 g. (11% yield) of product, m.p. 167–168°. **f:** With 4-fluoronitrobenzene in 20 ml. of refluxing dimethylformamide for 5 hr., 2.9 g. (46% yield) was obtained. **g:** N-[4-Nitrophenyl]-pyrrolidine, 2.3 g. (92% yield), m.p. 167–168°, was also formed by refluxing 2.3 g. (0.035 mole) of pyrrolidine and 2.0 g. (0.013 mole) of 4-chloronitrobenzene in 20 ml. of dioxane for 15 hr.

N-[4-Nitrophenyl]-hexamethyleneimine (XXVa, n = 3).—A mixture of 3.9 g. (0.025 mole) of 4-chloronitrobenzene, 4.5 g. (0.025 mole) of 1-hexamethyleneiminocyclohexene and 2.5 g. (0.025 mole) of triethylamine was heated under nitrogen at 130° for 24 hr. Addition of an excess of dilute hydrochloric acid, filtration and crystallization from methanol gave 2.1 g. (38% yield) of product, m.p. 74–76° (reported[34] m.p. 74–76°), identical with a sample obtained by refluxing 4-chloronitrobenzene in hexamethyleneimine.

N-[2-Benzoyl-4-nitrophenyl]-pyrrolidine (XXVb, n = 1).—A solution of 6.5 g. (0.025 mole) of 2-benzoyl-4-nitrochlorobenzene,[35] m.p. 83–84°, 3.75 g. (0.025 mole) of 1-pyrrolidinocyclohexene and 2.5 g. (0.025 mole) of triethylamine in 50 ml. of dimethylformamide was refluxed under nitrogen for 20 hr., poured into an excess of dilute hydrochloric acid and filtered. Recrystallization from ethanol gave 3.7 g. (50% yield), m.p. 136–137°, of arylpyrrolidine.

Anal. Calcd. for $C_{17}H_{16}N_2O_3$: C, 68.91; H, 5.78; N, 9.45. Found: C, 68.91; H, 5.53; N, 9.56.

From a reaction in refluxing dioxane or in methylene chloride at room temperature, for 30 days, 2-benzoyl-4-nitrochlorobenzene was recovered unchanged.

N-[5-Cyano-2-pyridyl]-pyrrolidine (XXVc, n = 1).—A mixture of 7.5 g. (0.050 mole) of 1-pyrrolidinocyclohexene and 3.5 g. (0.025 mole) of 2-chloro-5-cyanopyridine[36] was heated at 200° for 2 hr. under nitrogen. The reaction mixture was poured into an excess of dilute hydrochloric acid, extracted with methylene chloride, the aqueous portion made basic and re-extracted with methylene chloride. Distillation of both concentrates at 150–180° (0.001 mm.) and crystallization from hexane gave the aminopyridine, m.p. 76–77°; combined product 2.2 g. (51% yield).

Anal. Calcd. for $C_{10}H_{11}N_3$: C, 69.34; H, 6.40; N, 24.26. Found: C, 69.35; H, 6.46; N, 24.13.

The same compound was formed by refluxing 2.0 g. (0.014 mole) of 2-chloro-5-cyanopyridine and 3.0 g. (0.042 mole) of pyrrolidine in 25 ml. of dioxane for 1 hr. On concentration and recrystallization 1.9 g. (77% yield) was obtained.

N-[2-Quinolinyl]-pyrrolidine (XXVd, n = 1).—A mixture of 16.4 g. (0.10 mole) of 2-chloroquinoline and 15.1 g. (0.10 mole) of 1-pyrrolidinocyclohexene was heated under nitrogen at 250° for 3 hr. The cooled reaction was poured into water and extracted with ether. Concentration and distillation gave 8.4 g., b.p. 120–130° (5 mm.), of recovered 2-chloroquinoline and 6.0 g., b.p. 158–160° (1 mm.), of crude pyrrolidinoquinoline. Recrystallization of the product from hexane gave 5.1 g. (25% yield), m.p. 86–87°.

Anal. Calcd. for $C_{13}H_{14}N_2$: C, 78.75; H, 7.12; N, 14.13. Found: C, 78.24; H, 7.15; N, 13.94.

2-Phenylcyclohexanone from Diphenyliodonium Salts (X).—A suspension of 20.2 g. (0.063 mole) of diphenyliodonium chloride[37] in 150 ml. of dimethylformamide and 9.7 g. (0.064 mole) of 1-pyrrolidinocyclohexene was stirred under nitrogen for 6 days and then 4.4 g. of recovered iodonium salt was filtered off. Addition of 1.5 l. of water to the filtrate, acidification, extraction with methylene chloride, concentration and distillation gave, after removal of low boiling material, a fraction with b.p. 120–160° (0.3 mm.). Recrystallization from hexane produced 0.90 g. (8% yield), m.p. 53–55°, identical with an authentic sample.[38]

Other Conditions.—The reaction gave: In dimethyl sulfoxide with diphenyliodonium chloride a 4% yield; from diphenyliodonium tosylate[37] in dimethylformamide, a 6% yield; from the morpholinoenamine in dimethyl sulfoxide with diphenyliodonium chloride, a 6% yield. From the diphenyliodonium fluoroborate[8] in *t*-butyl alcohol at 210° for 10 min. with two equivalents of enamine a 7% yield; from diphenyliodonium fluoroborate and two equivalents of enamine in methylene chloride at room temperature for 5 hr., a 7% yield; from a mixture of diphenyliodonium fluoroborate and two equivalents of enamine, combined and maintained at 200° for 20 min. without solvent, no phenylcyclohexanone was obtained, but purification of a basic fraction produced N-[3-cyclohexenyl]-pyrrolidine, b.p. 78–80° (5 mm.), with no significant ultraviolet absorption and no infrared absorption at 1500 to 1800 cm.$^{-1}$. A picrate, m.p. 165–167°, was formed in 18% over-all yield.

Anal. Calcd. for $C_{16}H_{20}N_4O_7$: C, 50.52; H, 5.30; N, 14.73. Found: C, 50.37; H, 5.67; N, 14.73.

Reaction of 4,4′-Dichlorodiphenyliodonium Chloride.—A mixture of 5.0 g. (0.033 mole) of 1-pyrrolidinocyclohexene and 12.8 g. (0.033 mole) of the iodonium salt in 100 ml. of dimethylformamide was stirred under nitrogen for 3 days. Addition of excess aqueous hydrochloric acid, methylene chloride extraction, concentration and distillation gave 4.0 g. (50% yield) of 4-chloroiodobenzene, b.p. 78–82° (5 mm.), m.p. 56–57° (reported[39] 56–57°). From the concentrate 1.2 g. (9% recovery) of iodonium salt was obtained.

2-[3-Nitrophenyl]-cyclohexanone (XXVII).—A solution of 2.9 g. (0.017 mole) of 1-piperidinocyclohexene in 50 ml. of dimethylformamide was stirred for 6 days, under nitrogen, with 7.45 g. (0.016 mole) of 3,3′-dinitrodiphenyliodonium bromide. Addition of 800 ml. of water, acidification, extraction with methylene chloride and re-extraction after 20

(33) J. E. LuValle, D. B. Glass and A. Weissberger, *J. Am. Chem. Soc.*, **70**, 2223 (1948).

(34) M. S. Raasch, U. S. Patent 2,612,500 (1952) [*C. A.*, **47**, 3736c (1953)].

(35) A. Fries, *Ann.*, **454**, 287 (1927).

(36) H. S. Forest and J. Walker, *J. Chem. Soc.*, 1939 (1948).

(37) F. M. Beringer, R. A. Falk, M. Karniol, I. Lillien, G. Masullo, M. Mausner and E. Sommer, *J. Am. Chem. Soc.*, **81**, 342 (1959).

(38) C. C. Price and J. V. Karabinos, *ibid.*, **62**, 1159 (1940).

(39) F. Keppler, *Chem. Ber.*, **31**, 1136 (1898).

hr. and concentration gave a thick oil which was extracted with hot cyclohexane. Concentration, distillation at 180–240°, bath temp. (0.001 mm.) and crystallization from heptane gave 0.7 g. (20% yield) of product, m.p. 78–79°; 2,4-dinitrophenylhydrazone m.p. 185–187°.

Anal. Calcd. for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.69; H, 6.12; N, 6.34.

The same results were obtained with dimethyl sulfoxide as solvent or with the pyrrolidine enamine.

Reaction of 1-Pyrrolidinocyclohexene with Phenyldiazonium Fluoroborate (XXXIV and XXXV).—To a solution of 7.5 g. (0.050 mole) of 1-pyrrolidinocyclohexene in 250 ml. of methylene chloride, at −75°, under nitrogen, was added 4.8 g. (0.025 mole) of phenyldiazonium fluoroborate.[40] The solution was warmed to room temperature over 2 hr. and then shaken for 10 min. with an excess of dilute hydrochloric acid. Extraction of the acid with methylene chloride, concentration of the combined organic solutions, evaporation and trituration with ethanol gave 6.5 g. of a red solid, m.p. 160–162°, recrystallized from ethanol to 2.7 g. (32% yield) of the fluoroborate, m.p. 194–195°.

Anal. Calcd. for $C_{16}H_{21}N_3 \cdot HBF_4$: C, 55.99; H, 6.47; N, 12.24. Found: C, 56.27; H, 6.48; N, 12.41.

More vigorous nitrogen evolution was seen at room temperature and only 1.5 g. (18% yield) of recrystallized boron tetrafluoride salt was obtained. Vapor phase chromatography of the mother liquor material at 160° on a Dow Corning Hi-Vac grease column showed the presence of 2-phenylcyclohexanone, but distillation and attempted crystallization did not yield the pure compound.

Digestion of 0.50 g. of the boron tetrafluoride salt in 25 ml. of 5% sodium hydroxide and 5 ml. of methanol for 10 min., filtration and recrystallization from methylene chloride and ethanol gave 0.29 g. (100% yield) of 1,2-cyclohexanedione monophenylhydrazone, m.p. 183–184° (reported[41] m.p. 183–185°).

6-Amino-N,N′-dibenzenesulfonyl-1,2,3,4-tetrahydrocarbazole (XXXII).—An exothermic reaction was found on addition of 1.50 g. (0.010 mole) of 1-pyrrolidinocyclohexene to a solution of 3.5 g. (0.0091 mole) of *p*-quinonedibenzenesulfonimide.[42] After 2 days the solvent was removed in vacuum, the residue taken up in methanol and 10% hydrochloric acid added to *p*H 4, causing 0.90 g. of crude product to crystallize. Recrystallization from methylene chloride and methanol gave 0.70 g. (17% yield), m.p. 260–261°; infrared absorption at 3260 (NH), 1610 (arom.), 1370, 1330, 1180, 1150 cm.$^{-1}$ (SO_2).

Anal. Calcd. for $C_{24}H_{22}N_2O_4S_2$: C, 61.79; H, 4.75; N, 6.00. Found: C, 61.30; H, 4.68; N, 6.00.

The same yield was obtained with 3.0 g. (2 equivalents) of pyrrolidine enamine. A reaction of 1.80 g. (0.010 mole) of the hexamethyleneimino enamine gave 0.46 g. (10% yield) of product and 1.65 g. (41% yield) of *p*-dibenzenesulfonamidobenzene, m.p. 248–251°, identical with an authentic sample.

Reaction of 1-Pyrrolidinocyclohexene with Benzyne. a (From Piperidyllithium).—To a refluxing solution of 10.0 g. (0.066 mole) of 1-pyrrolidinocyclohexene and 6.35 g. (0.063 mole) of fluorobenzene in 200 ml. of ether, under nitrogen, was added a solution of 5.80 g. (0.063 mole) of piperidyllithium in 200 ml. of ether, over 90 min. After refluxing for 20 hr. water and excess dilute hydrochloric acid were added, the layers separated and the aqueous portion extracted with ether. Concentration and distillation gave 1.2 g. of oil, b.p. about 170° (15 mm.), after removal of low boiling material. Crystallization from petroleum ether produced 0.50 g. (4% yield) of 2-phenylcyclohexanone, identical with an authentic sample. Addition of excess sodium hydroxide to the aqueous portion, extraction with ether, concentration and distillation gave 4.1 g., b.p. 110–150° (5 mm.), in four fractions and 3.2 g., b.p. about 130° (0.001 mm.). Picrate formation from the four lower fractions and recrystallization from ethanol yielded in each case the picrate of N-phenylpiperidine, m.p. 147–148° (reported[43] 147–148°), with a strong mixed m.p. depression with the picrate of XXXIX. Picrate formation from the high boiling fraction gave a sample with m.p. 220–222°. (The pyrrolidine enamine of 2-phenylcyclohexanone formed an amorphous picrate which would not crystallize when seeded with the above compounds.)

Anal. Calcd. for $C_{22}H_{24}N_4O_7$: C, 57.89; H, 5.30; N, 12.28. Found: C, 57.58; H, 5.37; N, 12.61 (m.p. 220–222° sample).

b (From Butyllithium).—The reaction a was repeated with substitution of 4.1 g. (0.063 mole) of butyllithium for the piperidyllithium. No 2-phenylcyclohexanone could be isolated from a neutral fraction of 0.6 g., b.p. about 110° (5 mm.), and 1.3 g., b.p. 140–160° (0.1 mm.). A basic fraction of 3.7 g., b.p. 140–165° (5 mm.), formed 3.2 g. of ethanol recrystallized picrate (of XXXIX), m.p. 138–145° (of practical purity, see d). Repeated recrystallization gave a sample, m.p. 146–147°.

Anal. Calcd. for $C_{22}H_{24}N_4O_7$: C, 57.89; H, 5.30; N, 12.28. Found: C, 57.93; H, 5.47; N, 12.14.

c (From *o*-Bromofluorobenzene and Lithium Amalgam). A solution of 15.0 g. (0.10 mole) of 1-pyrrolidinocyclohexene and 17.5 g. (0.10 mole) of *o*-bromofluorobenzene was refluxed for 2 days, under nitrogen, over lithium amalgam, formed from 0.69 g. (0.10 g. atom, 0.5 equiv.) of lithium and 200 g. of mercury at 210°. Decantation and shaking with an excess of hydrochloric acid for 30 min., evaporation and distillation produced 11.1 g., b.p. 157–160°, of a mixture of cyclohexanone and recovered *o*-fluorobromobenzene, 1.2 g. of material, b.p. to 210° (0.05 mm.), from which no 2-phenylcyclohexanone could be isolated and 1.0 g. of resinous residue. Addition of excess base to the aqueous portion, extraction with ether, concentration and distillation gave 2.5 g., b.p. 130–150° (3 mm.), in four fractions which formed the practical picrate of XXXIX, m.p. 138–146°. A sample recrystallized from ethanol had m.p. 151–153°, undepressed on mixture with that in b (identical infrared spectra).

Anal. Calcd. for $C_{22}H_{24}N_4O_7$: C, 57.89; H, 5.30; N, 12.28. Found: C, 57.74; H, 5.44; N, 12.08.

d (From *o*-Bromofluorobenzene and Magnesium).—A suspension of 1.62 g. (0.067 g. atom) of magnesium in 200 ml. of tetrahydrofuran and 11.6 g. (0.067 mole) of *o*-bromofluorobenzene was warmed gently, under nitrogen, until a reaction started and 10.0 g. (0.066 mole) of 1-pyrrolidinocyclohexene was then added. After 6 hr. at reflux and 20 hr. at room temperature an excess of dilute hydrochloric acid and water were added, the aqueous layer extracted well with ether and the extracts washed with dilute hydrochloric acid. Concentration of the solvent, distillation at b.p. 60–95° (0.02 mm.) and crystallization from petroleum ether gave 2.0 g. (17% yield) of 2-phenylcyclohexanone, m.p. 54–56°. Addition of excess sodium hydroxide to the aqueous portion, extraction with ether, concentration and distillation at b.p. 110–112° (0.02 mm.) gave 3.0 g. (20% yield) of the crude pyrrolidinobenzocyclobutene. Picrate formation and recrystallization from ethanol gave 4.5 g., m.p. 130–135°, undried, which was chromatographed in methylene chloride on 200 g. of alumina (Woelm, neutral, activity II). From the concentrated eluates 2.0 g. (13% yield), b.p. 112° (0.02 mm.), of analytically pure XXXIX was obtained; ultraviolet absorption mμ (log ε) λ_{max} 253–256 (3.00), 260 (3.20), 266 (3.35), 273 (3.32), shld. 289–295 (1.26); λ_{min} 243 (2.76), 262 (3.16), 270 (3.07) in ethanol.

Anal. Calcd. for $C_{16}H_{21}N$: C, 84.54; H, 9.31; N, 6.16. Found: C, 84.13; H, 9.25; N, 6.58.

The compound did not absorb hydrogen when stirred 8 hr. in ethanol with 10% Pd–C. Formation of an N-oxide from 0.43 g. of compound in 10 ml. of methanol, by addition of 880 mg. of 30% hydrogen peroxide in four equal portions over 24 hr. and decomposition of the excess peroxide with platinum black over 24 hr. gave 0.55 g. of a hydrate, m.p. 60–61°, recrystallized from ethyl acetate and petroleum ether.

Anal. Calcd. for $C_{16}H_{21}NO \cdot 3.5H_2O$: C, 62.73; H, 9.21; N, 4.57. Found: C, 62.84; H, 9.69; N, 4.49.

The same sample, dried at 25° (0.01 mm.), gave a very hygroscopic, clear gum which formed the crystalline polyhydrate after exposure to the atmosphere for 15 min.

Anal. Calcd. for $C_{16}H_{21}NO \cdot 0.5\ H_2O$: C, 76.15; H, 8.79; N, 5.55. Found: C, 75.42; H, 9.02; N, 5.57.

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(43) R. Huisgen and J. Sauer, *Chem. Ber.*, **91**, 1453 (1958).

The reaction of *o*-bromofluorobenzene, magnesium and 1-pyrrolidinocyclohexene in refluxing ether for 2 days led to recovery of much *o*-bromofluorobenzene and magnesium and 0.40 g. of 2-phenylcyclohexanone but only a few mg. of pure picrate of XXXIX, from the basic fraction, together with a mixture of picrates, m.p. 105-166°.

Control.—Addition of 10.0 g. (0.066 mole) of 1-pyrrolidinocyclohexene to phenylmagnesium bromide, prepared from 17.0 g. (0.11 mole) of bromobenzene and 2.4 g. (0.10 g. atom) of magnesium, in 300 ml. of ether, gave 0.15 g. (1.3% yield) of 1-phenylcyclohexanol (derived from contaminating cyclohexanone), m.p. 61–62° (reported[44] 61°), in the neutral fraction and in the basic fraction 0.15 g. (1% yield) of crude 1-pyrrolidino-1-phenylcyclohexane, which formed 0.15 g. of picrate, m.p. 183–185°, after recrystallization from ethanol.

Anal. Calcd. for $C_{22}H_{26}N_4O_7$: C, 57.65; H, 5.74; N, 12.28. Found: C, 57.40; H, 5.98; N, 12.61.

(44) P. Sabatier and A. Mailhe, *Compt. rend.*, **138**, 1321 (1904).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, VANDERBILT UNIVERSITY, NASHVILLE, TENN.]

Organic Disulfides and Related Substances. VI. A One-step Synthesis of Aromatic Sulfinic Esters from Lead Tetraacetate and Aromatic Disulfides or Thiols[1,2]

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Alkyl esters of variously substituted aromatic sulfinic acids were prepared, as well as representative heterocyclic and polynuclear esters. The novel and convenient one-step synthesis used was an oxidation of aromatic disulfides of thiols with lead tetraacetate in a mixture of chloroform and the appropriate alcohol. Primary, secondary or tertiary alcohols could be used. Steric effects of ring substituents reduced the yield much less than electron-withdrawing power. A sequence of reactions is advanced to account for the synthesis, and a modified value is offered for the molecular refraction constant of the sulfinoxy group, S(O)O–.

Relatively little is known of the action of lead tetraacetate on divalent organic sulfur compounds. It oxidizes sulfides specifically to sulfoxides, apparently in an ionic reaction[3]; thioanisole gives acetoxymethyl phenyl sulfide (43%), however, in addition to methyl phenyl sulfoxide (40%).[4] Although the reaction does not appear to proceed ordinarily to the most highly oxidized form of sulfur, oxidation of a sulfide to a sulfone has been reported (ruthenium dioxide catalysis).[5] With dibenzyl mercaptals of sugars, cleavage occurs and the principal sulfur-containing product is benzyl disulfide.[6]

In earlier work, we found that thiols could be oxidized conveniently to disulfides using lead tetraacetate.[7] With benzene or acetic acid as solvents, oxygenated derivatives of disulfides were not found, and use of lead tetraacetate thus provided an effective conversion for a variety of thiols to the disulfides. Despite this specificity of oxidation, however, it seemed quite likely that disulfides could be oxidized further under other conditions. Preliminary results showed that further oxidation did indeed occur in chloroform mixed with alcohols and that the reaction afforded a useful one-step preparation of sulfinic esters,[2] which hitherto have been difficultly obtainable. This paper elaborates upon and extends the preliminary observations.[2]

(1) Presented in part at the Southeastern Regional Meeting of the American Chemical Society at Birmingham, Ala., Nov. 3–5, 1960. Abstracted from portions of the Ph.D. dissertations of C.B.H., January, 1960, and J.M.L., January, 1962. Paper V, L. Field, W. D. Stephens and E. L. Lippert, Jr., *J. Org. Chem.*, **26**, 4782 (1961). Research supported by the U. S. Army Research Office, Durham, N. C.

(2) Preliminary account published by L. Field, C. B. Hoelzel, J. M. Locke and J. E. Lawson, *J. Am. Chem. Soc.*, **83**, 1256 (1961).

(3) H. E. Barron, G. W. K. Cavill, E. R. Cole, P. T. Gilham and D. H. Solomon, *Chemistry & Industry*, 76 (1954).

(4) L. Horner and E. Jürgens, *Ann.*, **602**, 135 (1957).

(5) M. Neeman and A. Modiano, Abstracts of the National A.C.S. Meeting at Miami, Fla., April 7–12, p. 83-O (1957).

(6) E. J. Bourne, W. M. Corbett, M. Stacey and R. Stephens, *Chemistry & Industry*, 106 (1954).

(7) L. Field and J. E. Lawson, *J. Am. Chem. Soc.*, **80**, 838 (1958).

A reasonable equation for the over-all reaction seems to be

$$RSSR + 3Pb(OAc)_4 + 4R'OH \longrightarrow 2RS(O)OR' + 3Pb(OAc)_2 + 4AcOH + 2AcOR'$$

Thiols also can be used, owing to their facile oxidation to disulfides by lead tetraacetate.[7] In an attempt to substantiate the stoichiometry implicit in the equation, presumed lead diacetate and methyl acetate formed in one of the oxidations in chloroform–methanol (to compound VIII of Table I) were isolated. Based on the disulfide consumed, the product thought to be lead diacetate was found in three times the stoichiometry required by the above equation and the methyl acetate in more than four times the amount required. Evidently there is a substantial involvement of reactions other than that formulated, a result which is not really surprising in view of the excess amounts of both the tetraacetate and methanol which were used in this experiment.

The preparation of aromatic sulfinic esters from disulfides or thiols generally is superior to other known methods,[8,9] owing to the stability and ready availability of starting materials, the relatively attractive yields frequently obtained, the convenience of the process, and the fact that sulfonic esters (which usually are impurities in other routes) seem to be absent. Hopefully, the simplicity of this synthesis will lead to more extensive use and study of the interesting class of aromatic sulfinic esters.

Two general procedures were used in preparing the esters. In procedure A, lead tetraacetate (about four molar proportions) was added slowly to the disulfide in chloroform containing a large

(8) R. Connor in "Organic Chemistry. An Advanced Treatise," H. Gilman, Ed., Vol. I, 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1943, pp. 916–917.

(9) F. Muth in "Methoden der Organischen Chemie (Houben-Weyl)," E. Müller, Ed., Vol. 9, 4th ed., G. Thieme Verlag, Stuttgart, 1955, pp. 338–340.