weighed 2.26 g. (13%) and its identification as 6-methyl-2-propenylpyridine is discussed later. The second fraction, b.p. 82–83° at 4 mm., was a yellow oil weighing 5.15 g. (30%). Its infrared spectrum was in good agreement with the spectrum of 5-methylpyrrocoline obtained by hydrolysis of II. Also, its ultraviolet absorption spectrum showed maxima, in mμ (log ε) at 344 (3.42), 294 (3.74), 288 (3.46), 281 (3.59) and 232 (4.53) as would be expected for 5-methylpyrrocoline.[8]

Anal. Calcd. for C_9H_9N:: C, 82.40; H, 6.92; N, 10.88. Found: C, 82.00; H, 7.15; N, 10.93.

Acetylation of this sample of 5-methylpyrrocoline by the procedure described earlier gave yellow crystals, m.p. 56.5–57°, undepressed by admixture of a sample of 3-acetyl-5-methylpyrrocoline (IV) from the previous preparation. Also, the infrared spectra of the two samples were superimposable.

That the oil obtained as the first fraction in the above distillation was **6-methyl-2-propenylpyridine** was shown both by its ultraviolet absorption spectrum (max. 286 (log ε 3.88) and 240 (log ε 4.07)) which was quite similar to that of 2-vinylpyridine and its composition.

Anal. Calcd. for $C_9H_{11}N$: C, 81.14; H, 8.34. Found: C, 81.10; H, 8.52.

The picrate of 6-Methyl-2-propenylpyridine formed readily in ethanol and was obtained after recrystallization from the same solvent as yellow needles, m.p. 146.5–147.5°.

Anal. Calcd. for $C_{15}H_{14}N_4O_7$: C, 49.73; H, 3.90. Found: C, 50.23; H, 4.23.

As final proof of structure of the 6-methyl-2-propenylpyridine, it was prepared by an independent synthesis. When 2,6-lutidyllithium in ether was treated with acetaldehyde and the lithium salt of the adduct, obtained after removal of the ether, was dry-distilled, a colorless oil, b.p. 105–107° at 39 mm., resulted. The infrared spectrum of this oil was superimposable with that of the sample of 6-methyl-2-propenylpyridine obtained before. Also, the picrate of this oil melted at 146–147°, undepressed by admixture of the picrate from the former sample.

Preparation of Pyrrocoline (XII) from 3-(2-Pyridyl)-1-propanol (XI).—Into a 25-ml. flask were introduced 12.0 g. of redistilled 3-(2-pyridyl)-1-propanol, 0.5 g. of a 10% palladium-on-charcoal catalyst and a small porcelain boiling stone. A fine capillary was inserted into the liquid, and nitrogen was passed though the capillary at the rate of 3 l. per hr. After the system had been flushed with nitrogen, the mixture was boiled vigorously under reflux by heating it at 280° for 12 hr. In the initial period of heating, the water which formed was removed. At the end of the period of heating, the contents of the flask were steam distilled. The solid which separated from the distillate, was collected and recrystallized from a minimum amount of methanol to give 5.5 g. (50%) of white crystals, m.p. 73–74°. These were identical in all respects with an authentic sample of pyrrocoline.[8]

3-(6-Methyl-2-pyridyl)-2-phenyl-1-propanol (XIII).—To a cold solution of phenyllithium, prepared by dissolving 2.31 g. of lithium in a mixture of 25.7 g. of bromobenzene and 130 ml. of ether, was added 17.8 g. of 2.6-lutidine. After this solution had been allowed to stand for 0.5 hr., it was stirred and cooled in an ice-bath while 20.0 g. of styrene oxide was added. Stirring was continued for 0.5 hr. after the addition was complete. The ether solution was then washed with water, dried and concentrated *in vacuo*. Distillation of the residue gave 21.0 g. (55%) of a colorless oil, b.p. 157–160° at 0.3 mm. The distillate slowly solidified and recrystallization from methylcyclohexane gave white plates, m.p. 74–75°.

Anal. Calcd. for $C_{15}H_{17}NO$: C, 79.31; H, 7.56. Found: C, 79.08; H, 7.95.

Conversion of 3-(6-Methyl-2-pyridyl)-2-phenyl-1-propanol (XIII) to 2-Phenyl-5-methylpyrrocoline (XIV).—A mixture of 5.0 g. of 3-(6-methyl-2-pyridyl)-2-phenyl-1-propanol and 0.5 g. of a 10% palladium-on-charcoal catalyst was heated at 290° for 6 hr. A stream of nitrogen was passed into the mixture to stir it and to carry off hydrogen evolved. The residue was then taken up in benzene and chromatographed on alumina. From the eluate there was isolated a fluorescent solid. This, on recrystallization from methanol, gave 1.3 g. (28%) of white needles, m.p. 80–81°. These were shown both by infrared spectral comparison and by a mixed melting point determination to be identical with an authentic sample of 2-phenyl-5-methyl-pyrrocoline.[3]

ROCHESTER, N. Y.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF ROCHESTER]

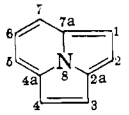
Cyclazines. A New Class of Aromatic Heterocycles[1]

BY R. J. WINDGASSEN, JR.,[2] W. H. SAUNDERS, JR., AND V. BOEKELHEIDE

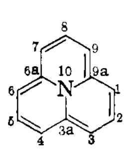
RECEIVED SEPTEMBER 2, 1958

The synthesis of cycl[3,2,2]azine (I), its properties, and some of its substitution reactions are described. Molecular orbital calculations for systems of this type are presented and their correlation with the experimental findings is discussed.

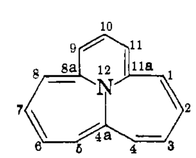
We have for some time been interested in the requirements for aromaticity, particularly in large rings and in polycycles.[3,4] One synthetic goal to which we have devoted our attention is the synthesis of a large conjugated carbocycle which would be held planar by bonding to an internal atom. With nitrogen as the internal atom, the type of molecules under consideration are exemplified by structures I, II and III. For ease of discussion and naming we propose that this new class of heterocycles be given the trivial name cyclazines.[5] It is the purpose of the present communication to report the synthesis of cycl[3,2,2]azine (I) as well as to discuss the implications from molecular orbital theory for all three of these aromatic systems.



I



II



III

Of the possible routes to a synthesis of cycl[3,2,2]azine, the most obvious utilize pyrrocoline deriv-

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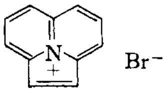
(1) Supported in part by the Office of Ordnance Research, Army Ordnance Contract No. DA-30-115-O. R. D.-723.

(2) National Science Foundation Predoctoral Fellow, 1956–1958.

(3) V. Boekelheide and W. G. Gall, *J. Org. Chem.*, **19**, 499 (1954).

(4) V. Boekelheide and G. K. Vick, THIS JOURNAL, **78**, 653 (1956).

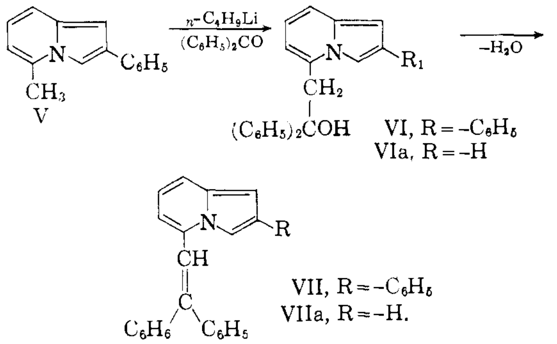
(5) In this proposal of nomenclature, the word cyclazine would refer to the general case of a conjugate, unsaturated cycle held planar by three covalent bonds to an internal nitrogen atom. The individual members would be distinguished by placing in brackets numerals corresponding to the number of atoms on the peripheral cycle between points of bonding to the internal nitrogen. Thus, in this scheme structure I would be cycl-[3,2,2]-azine, II would be cycl-[3,3,3]-azine and III would be cycl-[4,4,3]-azine. This system would also accommodate ionic structures such as IV, which would be named cycl-[3,3,2]-azinium bromide. The numbering has been designed to conform with the lowest possible numbers for simple substitution products.



IV

atives as a starting point. In the past the only generally useful pyrrocoline synthesis has been that of Chichibabin,[6] which has the drawback of being truly useful only for 2-substituted pyrrocolines. Therefore, our initial studies dealt with the synthesis of 2-substituted cycl[3,2,2]azines. In order to prepare the parent substance it was necessary to devise new syntheses which would yield pyrrocolines unsubstituted in the five-membered ring and these are dealt within an accompanying paper.[7]

For the proposed synthesis the first requirement was a knowledge of the activity of a methyl group at the 5-position in pyrrocoline. Presumably, such a methyl group should be comparable in activity to that in α-picoline, but apparently this has never been tested. When 2-phenyl-5-methylpyrrocoline (V) was treated with *n*-butyllithium, it gave a deep red color as expected for the 5-pyrrocolylmethyl anion and this color was discharged by addition of benzophenone. The resulting product had the correct composition for the desired carbinol VI and, furthermore, it readily underwent dehydration to give a product having the spectral properties to be anticipated for the styrylpyrrocoline VII. When 5-methylpyrrocoline[7] became available, it was carried through the same sequence to produce the corresponding carbinol VIa and the styrylpyrrocoline VIIa. Thus, it was clearly established that the methyl group in 5-methylpyrrocolines is sufficiently active to allow the convenient introduction of functional groups.

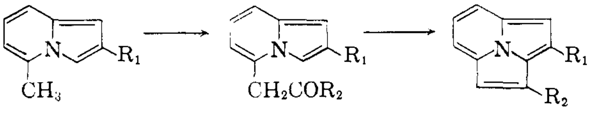


V

VI, R = $-C_6H_5$
VIa, R = $-H$

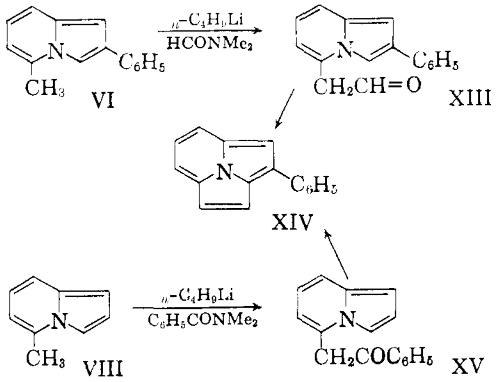
VII, R = $-C_6H_5$
VIIa, R = $-H$.

In a similar manner, 2-phenyl-5-methylpyrrocoline was treated with *n*-butyllithium followed by N,N-dimethylbenzamide to give, after hydrolysis, the corresponding phenacyl derivative IX. Although there was no precedent for the next step—the fusion of two unsaturated five-membered rings to an aromatic six-membered ring—it seemed likely that, if the resulting cyclazine had a high resonance energy, standard methods for building up aromatic carbocycles might be successful here. The method chosen was the elegant aromatic cyclodehydration procedure devised by Bradsher.[8] Surprisingly, the conditions necessary for aromatic cyclodehydration proved to be exceptionally mild. Simply heating IX in glacial acetic acid for a short period of time converted it smoothly in 91% yield to the desired 2,3-diphenylcycl[3,2,2]azine (XI). Actually, more severe conditions, such as the use of hydrogen fluoride, were ineffectual, presumably due to protonation of the pyrrocoline nucleus.



VI, R = $-C_6H_5$ IX, $R_1 = R_2 = -C_6H_5$ XI, $R_1 = R_2 = -C_6H_5$
VIII, R = $-H$ X, $R_1 = R_2 = -H$ I, $R_1 = R_2 = -H$

Although the method of synthesis was straightforward and the product had the correct composition and molecular weight required by XI, it seemed desirable to gain supporting evidence for the presence of the cyclazine ring. This was done in the following way. The previous reaction was repeated substituting dimethylformamide for N,N-dimethylbenzamide. This gave the corresponding aldehyde XIII which, on cyclization in acetic acid, yielded 2-phenylcycl[3,2,2]azine (XIV). On the other hand, treatment of 5-methylpyrrocoline (VIII) with *n*-butyllithium followed by N,N-dimethylbenzamide led to 5-(ω-phenacyl)-pyrrocoline (XV) which, on cyclization, again yielded 2-phenylcycl[3,2,2]azine (XIV). The fact that the same product is obtained by these two different routes establishes that the ring closure must occur at the 3- rather than the 6- position of the pyrrocoline ring and also the two five-membered rings, so formed, must be equivalent. The cyclazine structure is the only logical one which meets these requirements.



VI XIII XIV VIII XV

Finally, to prepare the parent substance I itself, the reaction sequence was repeated starting with 5-methylpyrrocoline. Treating VIII with *n*-butyllithium followed by dimethylformamide gave the corresponding aldehyde X which underwent cyclodehydration to yield the desired cycl[3,2,2]azine (I).

All three cyclazines, I, XIV and XI, are nicely crystalline, fluorescent, yellow compounds which are remarkably stable toward light, heat and air. This is in sharp contrast to the general behavior of pyrrocolines and accentuates the fact that these molecules cannot be considered simply as vinylpyrrocolines. Cycl[3,2,2]azine has an odor indistinguishable from that of naphthalene and its behavior in many respects, including ease of sublimation, is reminiscent of that of naphthalene. Its infrared spectrum is given in Fig. 1 and its ultraviolet absorption spectrum in Fig. 2. Again, in contrast to

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(6) A. E. Chichibabin, *Ber.*, **60**, 1607 (1927).

(7) V. Boekelheide and R. J. Windgassen, Jr., This Journal, **81**, 1456 (1959).

(8) *Cf.* C. K. Bradsher, F. C. Brown and P. H. Leake, *ibid.*, **79**, 1471 (1957), and C. K. Bradsher, *Chem. Revs.*, **38**, 447 (1946), for leading references to their numerous publications on this procedure.

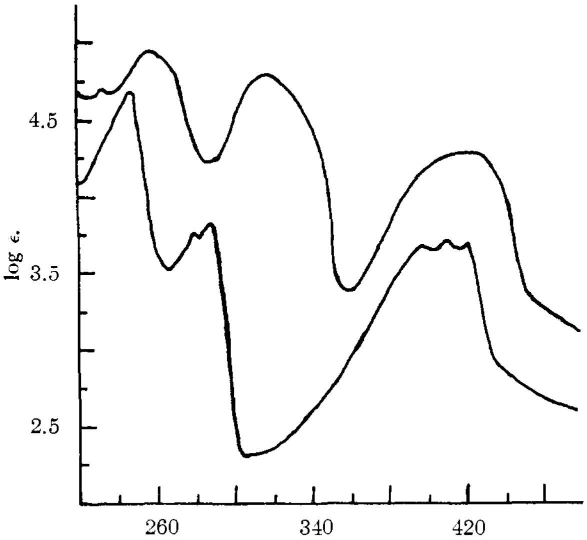
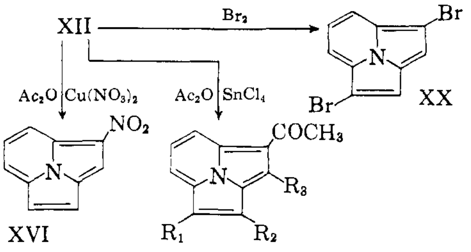


Fig. 1.—Ultraviolet absorption spectra of cycl[3,2,2]-azine (I, lower curve) and 2-phenylcycl[3,2,2]azine (XIV, upper curve) in ethanol as recorded by a Cary spectrophotometer, model 11 MS; log values for XIV have all been raised by 0.5 unit to separate the curves.

pyrrocolines, the cyclazines are not soluble in aqueous acid and their ultraviolet absorption spectra are unaffected by added acid. By these criteria the cyclazines are non-basic.

In terms of chemical reactivity, cycl[3,2,2]azine shows the normal behavior of a stable aromatic system undergoing substitution reactions smoothly and in good yield. Thus, treatment of I with cupric nitrate in acetic anhydride gave a mononitro derivative in 83% yield. The position of substitution has not yet been established but, as will be discussed later, the product is presumed from theoretical considerations to be 1-nitrocycl[3,2,2]azine (XVI).



XVII, $R_1 = R_2 = R_3 = -H$
XVIII, $R_1 = -COCH_3$; $R_2 = R_3 = -H$
XIX, $R_1 = -COCH_3$; $R_2 = R_3 = -C_6H_5$

Although pyrrocolines readily are acylated merely by heating in acetic anhydride, cycl[3,2,2]azine was unaffected by boiling acetic anhydride. In the presence of the usual Friedel–Crafts catalysts, it was attacked to give a mixture of mono- and diacetyl derivatives, presumably XVII and XVIII. Diacetylation occurred even though unchanged cycl-[3,2,2]azine was recovered. This would suggest that the rate of introduction of the second acetyl group is not appreciably decreased by the presence of the first. Similarly, bromination of cycl[3,2,2]azine led directly to a dibromo derivative (XX) and, as yet, we have been unable to isolate the monobromo compound which presumably is the intermediate.

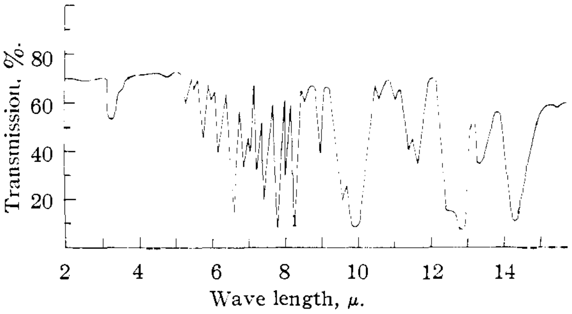


Fig. 2.—Infrared absorption spectrum of cycl[3,2,2]azine (I) recorded as a liquid film using a Perkin–Elmer spectrophotometer, model 21.

The acylation of 2,3-diphenylcycl[3,2,2]azine (XI) was also studied. Again, the compound was unaffected by heating with acetic anhydride, even at 230° for 24 hr. However, with acetyl chloride and aluminum chloride a smooth reaction occurred to give a diacetyl derivative, presumably XIX. That the acetyl groups were introduced into the cyclazine nucleus rather than the side-chain phenyls was established by subjecting the diacetyl derivative to strong oxidation with hydrogen peroxide. This gave benzoic acid in 58% yield and there was no evidence for the presence of an acetylbenzoic acid.

Molecular Orbital Calculations.—The application of molecular orbital theory[9a,b,c] to simple cyclic systems has been highly successful in predicting resonance energies and certain other properties. The generalization from these calculations known as the Hückel rule[10] is widely used as a criterion for aromatic character. Unfortunately, this generalization does not apply to polycyclic systems such as the cyclazines and to predict aromaticity a separate calculation must be made for each individual structure. However, the difficulties in applying M. O. theory to these more complex molecules have been eased in part by the more general availability of high-speed computers. In the present instance, the secular determinants were solved on an I.B.M. 650 digital computer, using a standard matrix-diagonalization program.[11]

In the first approximation, the model adopted was the carbanion isoelectronic to the corresponding cyclazine. Thus all coulomb integrals were assumed to be equal and, likewise, all resonance integrals between adjacent atoms were assumed to be equal. In this manner the resonance energies for structures I, II and III were computed and are given in Table I. In the same table are recorded the resonance energies of the corresponding peripheral systems.[12] In each case, isolation of the cen-

(9) (a) E. Hückel, *Z. Physik*, **70**, 240 (1931); (b) C. A. Coulson "Valence," Oxford University Press, London, England, 1952, Chap. IX; (c) H. Eyring, J. Walter and G. E. Kimball, "Quantum Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1944, Chap. XIII.

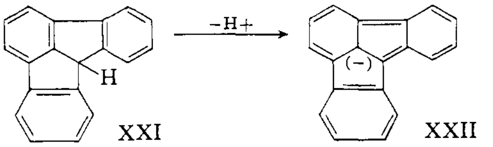
(10) E. Hückel, *Z. Elektrochem.*, **43**, 752 (1937).

(11) We would like to thank the University of Rochester Computing Center for donating the time on the computer, and Dr. P. L. Goodfriend, Dr. Thomas Keenan and Miss Betty Lee for advice and assistance.

(12) "Peripheral system" means the planar, monocyclic, conjugated system left when the central nitrogen with its electron pair is isolated from the rest of the system. For example, the peripheral system for cycl[3,2,2]azine (I) is cyclodecapentaene.

tral atom results in a substantial loss of resonance energy and the observed lack of basicity in cycl[3,2,2]azine (I) is therefore not surprising, since quaternization of the nitrogen would require isolation of the central atom.

In this connection the recent discovery of Rapoport and Smolinsky that fluoradene (XXI) is an unusually acidic hydrocarbon[13] is of interest. The carbanion XXII contains the same polycyclic nucleus used as a model for the calculations of cycl[3,2,2]azine and the high acidity of fluoradene more probably is related to the stability of the anion of this portion of the molecule than it is to the fact that the molecule is a triphenylmethane derivative.



XXI XXII

From the coefficients of the atomic orbitals may be calculated charge densities, bond orders and free valences.[9b] These quantities are summarized for structures I, II and III in Tables II–IV. If the charge density is taken as a measure of reactivity in electrophilic substitution, compound I should react at position 1 (position 2a, of higher charge density, has no replaceable hydrogen), II at position 1, and III at positions 1 or 3. If the free valence is taken as a measure of reactivity in radical substitution, the same pattern would be expected except that III should react mainly or entirely at position 1. In III there is a markedly greater tendency for alternation in the bond order values. This is perhaps suggestive of more unsaturated character in III than in II or I. In this connection, the advantage in resonance energy over its peripheral system is also least for III.

A few interesting side issues present themselves. In analogy to cyclopentadienyl, the hydrocarbon corresponding to I shows the order of resonance stabilization of anion > radical > cation. The reverse order (in analogy to cycloheptatrienyl) is predicted for the hydrocarbon corresponding to III. Perinaphthenyl, the hydrocarbon residue corresponding to II, is an alternant hydrocarbon and its molecular orbital of highest energy which is occupied in the ground state has a coefficient of zero. Therefore, in this approximation, it is predicted that the anion, cation and radical derived from perinaphthene should be of equal stability. The experimental evidence presently available[14a,b,c] is in qualitative agreement with this prediction. Thus, it is apparent that for these polycyclic systems the order of stability of anion, radical and cation can only be predicted after the results of molecular orbital calculations are known and there is no magic number of π-electrons which can be used to predict the order of stability as is true in the simple monocyclic cases where the Hückel rule applies.

In order to improve the values for cycl[3,2,2]azine (I), further calculations were made in which the greater electronegativity of nitrogen than carbon was taken into account. In one such calculation the coulomb integral for nitrogen was altered by $+2.00\beta$ and the coulomb integral for the carbons adjacent to nitrogen by $+0.25\beta$, the values used in published calculations on some nitrogen heterocycles[15a]; another calculation was performed using the more recently suggested value[9b] of $\alpha_N = \alpha_0 + 0.50\beta$, and the coulomb integrals of the adjacent carbons were altered by $+0.17\beta$, after a suggestion by Dewar.[15b]

The resulting resonance energies provide evidence that the value $\alpha_N = a_0 + 2.00\beta$ is unrealistic, since the low resonance energy so obtained is inconsistent with the known stability and non-basicity of I. The value $\alpha_N = \alpha_0 + 0.50\beta$ gives a much more reasonable result. Electrophilic attack at position 5 is still expected for both sets of parameters. The prediction of the position of radical attack becomes ambiguous, however, since the position of maximum free valence changes.

There is general agreement that molecular orbital calculations are more reliable with alternant than with non-alternant hydrocarbons.[16] In particular, free valence as a prediction of radical reactivity appears to be unreliable with non-alternants.[17] Since I and III are non-alternants, predictions of electrophilic and radical reactivity were made by the localization approximation.[18] In this method the attacking reagent is assumed to be attached to the aromatic system in the transition state, so that the position attacked is effectively removed from conjugation. One thus computes the energy required to isolate this position. Such calculations were carried out on I, using the parameters $\alpha_N = \alpha_0 + 0.50\beta$ and, for the adjacent carbons, $\alpha_C = \alpha_0 + 0.17\beta$. The results are summarized in Table V.

Attack will be at the atom requiring the least localization energy. Electrophiles therefore should attack at position 1, in agreement with predictions from the charge densities. Similarly, for radical attack positions 2 and 5 are about equally favored. Free valences (for this set of parameters) are about equal for positions 1, 2 and 5. Predictions on radical attack therefore remain ambiguous. Finally, nucleophilic attack is expected to occur at position 5, which is also the position of lowest charge density.

Certainly the calculations provide a number of interesting predictions which need to be tested experimentally. Work in progress is directed toward establishing the position of attack for various types of substitution reactions in the case of cycl[3,2,2]azine. Also, syntheses of II and III are being attempted. Probably the most interesting prediction with regard to the corresponding hydrocarbons is the high resonance energy (6.31β) accorded the carbonium ion corresponding to III, particularly when this is compared to the value of 2.99β as-

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(13) H. Rapoport and G. Smolinsky, This Journal, **80**, 2910 (1958).

(14) (a) V. Boekelheide and C. E. Larrabee, *ibid.*, **73**, 1245 (1950); (b) R. Pettit, *Chemistry & Industry*, 1306 (1956); (c) D. H. Reid, *ibid.*, 1504 (1956).

(15) (a) H. C. Longuet-Higgins and C. A. Coulson, *Trans. Faraday Soc.*, **43**, 87 (1947); (b) M. J. S. Dewar, *J. Chem. Soc.*, 463 (1949).

(16) See, for example, H. C. Longuet-Higgins, *Proc. Chem. Soc.*, 157 (1957).

(17) F. H. Burkett, C. A. Coulson and H. C. Longuet-Higgins, *Trans. Far. Soc.*, **47**, 553 (1951).

(18) G. W. Wheland, This Journal, **64**, 900 (1942). R. D. Brown, *Quarterly Revs.*, **6**, 63 (1952).

signed to the cycloheptatrienyl carbonium ion.[19] Its synthesis is obviously a prime objective.

TABLE I

CALCULATED RESONANCE ENERGIES OF THE CYCLAZINES

Structure	R.E.[a]	R.E. of periphery[a,b]
I	5.256[c]	2.944[c]
	4.923[d]	....
	0.181[e]	....
II	5.827[c,f]	2.928[c]
III	5.694[c]	3.976[c]

[a] In units of the resonance integral, β. [b] Periphery refers to the monocyclic conjugated system obtained by isolating the central nitrogen from the rest of the system. [c] Assumes all coulomb integrals equal, all resonance integrals between adjacent atoms equal, all other resonance integrals zero. [d] Same as (*c*), except the coulomb integral of nitrogen, $\alpha_N = \alpha_0 + 0.50\beta$ and the coulomb integral of carbons adjacent to nitrogen, $\alpha_{C(N)} = \alpha_0 + 0.17\beta$. [e] Same as (*d*), except $\alpha_N = \alpha_0 + 2.00\beta$, $\alpha_{C(N)} = \alpha_0 + 0.25\beta$. [f] R. Pettit (ref. 14b) and V. Gold and F. Tye (*J. Chem. Soc.*, 2184 (1952)) report 5.828 for the corresponding cation, which to this approximation has the same R.E. as our value for the anion.

TABLE II

CALCULATED PROPERTIES OF CYCL[3,2,2]AZINE

Atom[a]	Charge density[b]	Free valence[c]	Bond[a]	Bond order
1	1.168[d]	0.482	1–2	1.747
	1.132[e]	.462		1.746
	1.070[f]	.432		1.722
2	1.062[d]	.336	2–2a	1.649
	1.048[e]	.458		1.528
	1.026[f]	.442		1.568
2a	1.188[d]	.061	2a–8	1.373
	1.192[e]	.154		1.522
	1.128[f]	.184		1.412
4a	1.058[d]	.124	4a–5	1.609
	1.086[e]	.130		1.606
	1.066[f]	.178		1.614
5	0.997[d]	.462	4a–8	1.496
	.966[e]	.458		1.472
	.948[f]	.454		1.362
6	1.043[d]	.410	5–6	1.661
	1.030[e]	.396		1.668
	1.002[f]	.404		1.664
8	1.196[d]	.367	7a–1	1.503
	1.318[e]	.266		1.524
	1.654[f]	.596		1.578

[a] See formula I for numbering. [b] Relative to 1.000 for a carbon atom in benzene. Since nitrogen has a nuclear charge one greater than carbon, the charge density at the nitrogen atom (8) should be reduced by 1.000 before comparing it with the other charge densities. [c] Assuming *N* (max.) = 4.732, see C. A. Coulson, "Valence," Oxford University Press, London, England, 1952, p. 253. [d] All data in this line obtained with the assumptions of footnote *c*, Table I. [e] All data in this line obtained with the assumptions of footnote *d*, Table I. [f] All data in this line obtained with the assumptions of footnote *e*, Table I.

TABLE III

CALCULATED PROPERTIES OF CYCL[3,3,3]AZINE

Atom[a]	Charge density[b]	Free valence[c]	Bond[a]	Bond order
2	1.000[d]	0.392	2–3	1.670
3	1.167[d]	.510	3–3a	1.552
3a	1.000[d]	.101	3a–10	1.527
10	1.000[d]	.151		

[a] See formula II for numbering. [b,c,d] See corresponding footnotes of Table II.

TABLE IV

CALCULATED PROPERTIES OF CYCL[4,4,3]AZINE

Atom[a]	Charge density[b]	Free valence[c]	Bond[a]	Bond order
1	1.212[d]	0.601	1–2	1.735
2	0.954[d]	.437	2–3	1.560
3	1.218[d]	.549	3–4	1.623
4	0.985[d]	.493	4–4a	1.616
4a	1.151[d]	.239	4a–12	1.261
8a	0.998[d]	.520	8–8a	1.396
9	1.002[d]	.522	8a–9	1.604
10	1.007[d]	.134	8a–12	1.598
12	1.101[d]	.275	9–10	1.606

[a] See formula III for numbering. [b,c,d] See corresponding footnotes of Table II.

TABLE V

LOCALIZATION ENERGIES FOR CYCL[3,2,2]AZINE

Atom[a]	Nucleophilic loc.E.[b]	Radical loc.E.[c]	Electrophilic loc.E.[d]
1	2.610	2.326	2.042
2	2.348	2.282	2.216
5	2.217	2.285	2.352
6	2.650	2.543	2.436

[a] See formula I for numbering. [b] Energy (in units of the resonance integral, β) to isolate the atom without any electrons. [c] Energy to isolate the atom with one electron. [d] Energy to isolate the atom with two electrons.

Experimental[20]

2-Phenyl-5-methylpyrrocoline (V) was prepared according to the general procedure of Chichibabin.[6] A mixture of 95.5 g. of ω-phenacyl bromide and 62.7 ml. of 2,6-lutidine was heated at 50° for two days. The resulting, hard crystalline mass was treated with 50 ml. of boiling chloroform and then allowed to cool, whereupon 95.1 g. (62%) of yellow crystals, m.p. 220° dec.,.separated from solution. Then, a solution of the 95 g. of phenacyl-2,6-lutidinium bromide so obtained and 95 g. of sodium bicarbonate in 900 ml. of water was heated at 100° for 2 hr. When the mixture was allowed to cool, the oily organic layer, that had separated, solidified. Recrystallization of this solid from methanol gave 54.5 g. (86%) of slightly yellow crystals, m.p. 79.5–81°. A second recrystallization from methanol gave white crystals, m.p. 81–81.5°, ultraviolet absorption maximum at 257 mμ (log ε 4.69).

Anal. Calcd. for $C_{15}H_{13}N$: C, 86.91; H, 6.32. Found: C, 87.16; H, 6.65.

2-Phenyl-5-(2′,2′-diphenyl-2′-hydroxyethyl)-pyrrocoline (VI).—To a solution of *n*-butyllithium prepared from 0.18 g. of lithium and 1.45 ml. of *n*-butyl bromide in 20 ml. of ether maintained at −15° there was added 2.0 g. of 2-phenyl-5-methylpyrrocoline. After the solution had stood at room temperature for 18 hr. under a nitrogen atmosphere, formation of the 2-phenyl-5-pyrrocolylmethyl anion appeared complete as judged from the deep red color that developed. There was then added dropwise with stirring a solution of 2.0 g. of benzophenone in 10 ml. of ether. As the last of the benzophenone was added, the red color of the anion was discharged. The resulting solution was then washed with water, dried and concentrated to give a viscous oil. When this oil was triturated with benzene, a solid separated which was collected and washed with petroleum ether to give 2.6 g. (53%) of a white powder. This powder did not have a definite melting point and recrystallization from benzene did not improve its melting point behavior. Its general properties, spectra, loss of weight on heating at 100° and its composition, suggest that the powder is the desired carbinol VI containing benzene of crystallization; ultraviolet absorption maximum at 258 mμ, (log ε 4.67).

Anal. Calcd. for $C_{28}H_{23}NO \cdot C_6H_6$: C, 87.33; H, 6.25. Found: C, 87.36; H, 6.36.

2,2-Diphenyl-1-(2′-phenyl-5′-pyrrocolyl)-ethylene (VII).—A mixture of 100 mg. of VI in 2 ml. of benzene and 6 drops of

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[19] J. D. Roberts, A. Streitwieser, Jr., and C. M. Regan, THIS JOURNAL, **74**, 4579 (1952).

[20] All melting points are corrected. Analyses by Miss A. Smith and the Micro-Tech Laboratories, Skokie, Ill.

concd. hydrochloric acid was boiled under reflux for 1 hr. After the acid was neutralized with aqueous ammonia, the benzene layer was separated, washed with water and concentrated. The yellow residue, after recrystallization from ethanol–ethyl acetate, gave 46 mg. (70%) of yellow needles, m.p. 187.5–188.5°. The ultraviolet absorption spectrum showed maxima at 385 mμ (log ε 3.62) and 257 (log ε, 4.62).

Anal. Calcd. for $C_{28}H_{21}N$: C, 90.53; H, 5.70. Found: C, 90.50; H, 6.01.

2-Phenyl-5-(ω-phenacyl)-pyrrocoline (IX).—To an ether solution of 2-phenyl-5-pyrrocolylmethyllithium, prepared as before by adding 5.0 g. of 2-phenyl-5-methylpyrrocoline to 50 ml. of an ether solution containing an equimolar amount of *n*-butyllithium, there was added dropwise with stirring a solution of 3.65 g. of N,N-dimethylbenzamide in 20 ml. of ether, the whole mixture being maintained at −10° under nitrogen. After the solution had been stirred for 15 min., it was acidified with glacial acetic acid. The ether solution was then washed with water, dried and concentrated. The resulting solid was taken up in benzene, passed over a short column of alumina and concentrated. After recrystallization from benzene–cyclohexane, the residual solid gave 5.1 g. (66%) of slightly tan crystals, m.p. 125–126°.

Anal. Calcd. for $C_{22}H_{17}NO$: C, 84.86; H, 5.50. Found: C, 84.92; H, 5.83.

The oxime of IX was obtained by heating a mixture of 250 mg. of IX, 100 mg. of hydroxylamine hydrochloride and 5 ml. of pyridine at 100° for 1.5 hr. After dilution with water, the mixture was extracted with methylene chloride. Concentration of the methylene chloride extract followed by crystallization of the residue from 1-propanol gave white needles, m.p. 168–169° dec.

Anal. Calcd. for $C_{22}H_{18}N_2O$: C, 80.95; H, 5.56. Found: C, 80.09; H, 5.83.

2,3-Diphenylcycl[3,2,2]azine (XI).—A solution of 2.5 g. of 2-phenyl-5-(ω-phenacyl)-pyrrocoline (IX) in 20 ml. of glacial acetic acid was boiled under reflux for 1.5 hr. After the cold solution had been diluted with water, it was extracted with methylene chloride and the methylene chloride extract was washed with aqueous base, dried and concentrated. Recrystallization of the solid residue from benzene–cyclohexane gave 2.14 g. (91%) of yellow crystals, m.p. 141–141.5°; ultraviolet absorption maxima (log ε): 420 (3.79), 321 (4.40), 260 (4.57) and 231 mμ (4.42). The fact that the ultraviolet absorption spectrum is essentially the same as that for 2-phenylcycl[3,2,2]-azine is probably due to the steric hindrance of the phenyl groups which prevents their both being coplanar with the cyclazine nucleus.

Anal. Calcd. for $C_{22}H_{15}N$: C, 90.07; H, 5.15; N, 4.78; mol. wt., 293. Found: C, 90.09; H, 5.22; N, 4.79; mol. wt. (isothermal distillation, benzene), 293.

A trinitrobenzene derivative of XI formed readily in 1-propanol and, after recrystallization from the same solvent, was obtained as orange needles, m.p. 144–145°.

Anal. Calcd. for $C_{28}H_{28}N_4O_6$: C, 66.40; H, 3.58. Found: C, 66.35; H, 3.69.

Peroxide Oxidation of 2,3-Diphenylcycl[3,2,2]-azine.—To a boiling solution of 200 mg. of XI in 10 ml. of glacial acetic acid there was added dropwise 5 ml. of a 30% hydrogen peroxide solution. Initially, the solution became dark and turbid but after 10 min. it turned to a clear yellow. After this solution had been boiled an additional 2 hr., it was concentrated to a volume of 4 ml. and then diluted to 40 ml. with water. When the aqueous solution was extracted with benzene and the benzene extract was concentrated, a solid resulted which, on sublimation, gave 110 mg. (67%) of white crystals, m.p. 122°, that were identified as benzoic acid.

5-(2′,2′-Diphenyl-2′-hydroxyethyl)-pyrrocoline (VIa).—To a solution of *n*-butyllithium (prepared by dissolving 0.18 g. of lithium in a solution of 1.45 ml. of *n*-butyl bromide in 20 ml. of ether) maintained at −15° under a nitrogen atmosphere there was added dropwise with stirring 1.26 g. of 5-methylpyrrocoline.[7] After the addition was complete, the mixture was allowed to come to room temperature and stand for 18 hr. Then a solution of 2.0 g. of benzophenone in 15 ml. of ether was added, the red color of the anion disappearing during the final addition. The resulting ether solution was washed with water, dried and passed over alumina. From the eluate there was isolated 1.0 g. (32%) of a solid which, after recrystallization from a chloroform–carbon tetrachloride mixture, gave white crystals, m.p. 104–105°.

Anal. Calcd. for $C_{22}H_{19}NO$: C, 84.31; H, 6.11. Found: C, 83.71; H, 6.16.

2,2-Diphenyl-1-(5′-pyrrocolyl)-ethylene (VIIa).—A solution of 200 mg. of VIa in 3 ml. of concd. hydrochloric acid was boiled under reflux for 45 min. It was then neutralized with sodium bicarbonate and extracted with benzene. After the benzene extract had been washed with water and dried, it was passed over a short column of alumina. Concentration of the eluate gave 140 mg. (74%) of a solid which, after recrystallization from benzene–cyclohexane, formed orange needles, m.p. 115–116°.

Anal. Calcd. for $C_{22}H_{17}N$: C, 89.46; H, 5.80. Found: C, 89.22; H, 5.61.

5-(ω-Phenacyl)-pyrrocoline (XV).—A solution of 5-pyrrocolylmethyllithium was prepared by treating 1.26 g. of 5-methyl-pyrrocoline with 20 ml. of an ethereal solution containing an equimolar quantity of *n*-butyllithium just as before. To this stirred solution held at −30° under an atmosphere of nitrogen there was added dropwise a solution of 1.46 g. of N,N-dimethylbenzamide in 15 ml. of ether. After the mixture had been allowed to warm to room temperature, it was stirred for one hour and then acidified by adding 1.1 g. of glacial acetic acid. The resulting ether solution was washed with water, dried and concentrated. Recrystallization of the residual solid from di-*i*-propyl ether gave 0.8 g. (36%) of light yellow plates, m.p. 109–110°.

Anal. Calcd. for $C_{16}H_{13}NO$: C, 81.68; H, 5.57. Found: C, 81.32; H, 5.51.

2-Phenylcycl[3,2,2]azine (XIV) (a) From 5-(ω-Phenacyl)-pyrrocoline.—A solution of 100 mg. of 5-(ω-phenacyl)-pyrrocoline in 3 ml. of glacial acetic acid was refluxed for 30 min. This solution was then neutralized with aqueous sodium bicarbonate. The solid which separated was collected; a sublimation of this solid gave 70 mg. (76%) of yellow crystals, m.p. 93.5–94.5°; ultraviolet absorption maxima (log ε): 417 (3.76), 321 (4.31), 258 (4.45) and 233 mμ (4.21).

Anal. Calcd. for $C_{16}H_{11}N$: C, 88.45; H, 5.10. Found: C, 88.12; H, 5.27.

The trinitrobenzene derivative of 2-phenylcycl[3,2,2]-azine formed readily in 1-propanol and, after recrystallization from this solvent, was obtained as orange needles, m.p. 152.5–153.5°

Anal. Calcd. for $C_{22}H_{14}N_4O_6$: C, 61.40; H, 3.28. Found: C, 61.58; H, 3.57.

(b) **From 2-Phenyl-5-methylpyrrocoline.**—To an ether solution of the lithium salt of 2.0 g. of 2-phenyl-5-methylpyrrocoline (VI) maintained at −30° was added a solution of 0.75 g. of dimethylformamide in 10 ml. of ether. The resulting solution was slowly warmed to room temperature, after which 15 ml. of glacial acetic acid was added. After the ether had been removed by distillation, the resulting acetic acid solution was refluxed for one hour. Subsequent neutralization of this acetic acid solution with aqueous sodium carbonate gave a black solid which was taken up in benzene and passed over an alumina column. Elution with low boiling petroleum ether gave a yellow solid. Sublimation of this solid, followed by recrystallization of the sublimate from ethyl acetate, gave 0.95 g. (45%) of yellow needles, m.p. 93.5–94.5°. The identity of this product with the one prepared in the previous experiment was shown by comparison of the infrared spectra. When the two samples of 2-phenylcycl[3,2,2]azine were mixed, there was no depression of melting point.

Cycl[3,2,2]azine (I).—A solution of 5-pyrrocolylmethyllithium was prepared as before by treating 11.34 g. of 5-methylpyrrocoline with 200 ml. of an ether solution containing an equimolar quantity of 1-butyllithium. This was cooled to −30° under an atmosphere of nitrogen and a solution of 6.75 g. of dimethylformamide in 50 ml. of ether was added dropwise with stirring. After the solution had been allowed to warm to room temperature, it was stirred an additional hour and then 10.0 g. of glacial acetic acid was added. The resulting solution was washed with water, placed in an addition funnel and slowly added to a 500-ml., three-necked flask containing 300 ml. of boiling acetic acid. A stream of nitrogen was passed through the gas by-pass of the addition funnel to prevent the hot acetic acid vapors from reaching the tip of the addition funnel. During the addition ether was continuously removed from the boiling acetic acid solution by distillation. After addition of the ether solution had been completed, the acetic acid solution was cooled and diluted with 300 ml. of benzene. The acetic acid was then neutralized by washing with aqueous sodium carbonate. The benzene solution was dried and passed over alumina to remove intractable tars. The benzene eluate was concentrated to a small volume leaving a dark residue. This was taken up in *n*-pentane and chromatographed over acid-washed alumina. Elution with *n*-pentane gave a yellow solid which, on sublimation, yielded 2.8 g. (23%) of cycl[3,2,2]azine. Recrystallization of a sample from methanol gave yellow needles, m.p. 63.5–64.5°; ultraviolet absorption maxima (log ϵ): 419 (3.65) 408 (3.66), 398 (3.56), 289 (3.86), 274 (3.74) and 244 mμ (4.57).

Anal. Calcd. for $C_{10}H_7N$: C,85.08; H, 5.00; N, 9.92. Found: C, 84.93; H, 5.30; N, 9.87.

The trinitrobenzene derivative of cycl[3,2,2]azine was prepared in 1-propanol and, after recrystallization from the same solvent, was obtained as orange needles, m.p. 222–226° dec.

Anal. Calcd. for $C_{16}H_{10}N_4O_6$: C, 54.24; H, 2.85. Found: C, 53.92; H, 3.18.

1-Nitrocycl[3,2,2]azine (XVI).—To a solution of 160 mg. of powdered cupric nitrate trihydrate in 4 ml. of acetic anhydride was added 75 mg. of cycl[3,2,2]azine. After this solution had stood for 1.5 hr., it was neutralized with aqueous sodium carbonate and extracted with methylene chloride. Concentration of the methylene chloride extract left a solid residue which on sublimation gave 90 mg. (83%) of orange crystals, m.p. 175–185°. Recrystallization of the sublimate from chloroform–carbon tetrachloride gave orange needles, m.p. 193.5–195°; ultraviolet absorption maxima (log ϵ): 425 (4.18), 415 (4.14), 338 (3.82), 261 (4.12), and 227 mμ, (4.45).

Anal. Calcd. for $C_{10}H_6N_2O_2$: C, 64.52; H, 3.22. Found: C, 64.37; H, 3.15.

1-Acetylcycl[3,2,2]azine (XVIII) and 1,4-Diacetylcycl[3,2,2]azine (XVIII).—To a solution of 0.10 ml. of acetic anhydride and 75 mg. of cycl[3,2,2]azine in 10 ml. of *sym*-tetrachloroethane maintained at 0° was added 0.25 ml. of anhydrous stannic chloride. After this mixture had stood for 16 hr. at room temperature, it was diluted with 10 ml. of methylene chloride and stirred into a small amount of ice-water. After sufficient 5% hydrochloric acid had been added to effect solution of a tarry residue, the methylene chloride and *sym*-tetrachloroethane layer was separated, washed with aqueous base, dried and then chromatographed over acid-washed alumina. Elution with ether rapidly removed some fluorescent yellow material which was presumably cycl[3,2,2]azine, but this was not isolated. Further elution with ether gave 30 mg. (30%) of 1-acetylcycl[3,2,2]azine as a yellow oil. This oil was further purified by bulb-to-bulb distillation *in vacuo;* infrared absorption band (carbonyl) at 6.05μ.

Anal. Calcd. for $C_{12}H_9NO$: C, 78.67; H, 4.95. Found: C, 78.64; H, 5.16.

Further elution with ether containing 5% of methanol gave 35 mg. (33%) of 1,4-diacetylcycl[3,2,2]azine as a yellow solid. Sublimation of this solid, followed by recrystallization of the sublimate from ethanol, gave yellow needles, m.p. 183–184°, ultraviolet absorption maxima (log ϵ): 420 (4.42), 410 (4.21) and 283 mμ, (4.44); infrared absorption (carbonyl) at 6.08μ.

Anal. Calcd. for $C_{14}H_{11}NO_2$: C, 74.65; H, 4.92, Found: C, 74.93; H, 4.93.

1,4-Dibromocycl[3,2,2]azine (XX).—To a solution of 75 mg. of cycl[3,2,2]azine in 15 ml. of methylene chloride was added with vigorous swirling 17.1 ml. of a solution containing 10 mg. of bromine per ml. of methylene chloride. The residue obtained by concentration of the resulting solution *in vacuo* was then sublimed. Recrystallization of the sublimate from cyclohexane gave 120 mg. (78%) of yellow crystals, m.p. 121–122°; ultraviolet maxima (log ϵ): 430 (3.76), 342 (3.73), 254 (4.33) and 240 mμ (4.24).

Anal. Calcd. for $C_{10}H_5NBr_2$: C, 40.17; H, 1.68. Found: C, 40.07; H, 1.69.

1,4-Diacetyl-2,3-diphenylcycl[3,2,2]azine (XIX).—To a solution of 0.2 cc. of acetyl chloride and 300 mg. of 2,3-diphenylcycl[3,2,2]azine in 10 ml. of *sym*-tetrachloro-ethane was added 500 mg. of anhydrous aluminum chloride. After this mixture had been heated for one hour at 60° and allowed to stand for 24 hr., it was diluted with 30 ml. of methylene chloride and shaken with 30 ml. of 2 *N* hydrochloric acid to decompose the aluminum chloride. The methylene chloride solution was then washed with dilute base, dried, concentrated to 20 ml. and chromatographed over alumina. Elution with methylene chloride gave recovery of 100 mg. of starting material. Elution of the strongly-held yellow band remaining at the top of the column with methylene chloride containing 57% of methanol gave 220 mg. (59%) of 1,4-diacetyl-2,3-diphenylcycl[3,2,2]azine as a yellow solid, m.p. 187–188°. Recrystallization of this yellow solid from benzene–cyclohexane gave yellow needles, m.p. 189–190°. Carbonyl absorption in the infrared occurred at 6.13μ.

Anal. Calcd. for $C_{26}H_{19}NO_2$: C, 82.74; H, 5.07. Found: C, 82.47; H, 5.18.

In another experiment 0.5 cc. of anhydrous stannic chloride was added to a solution of 250 mg. of 2,3-diphenylcycl[3,2,2]azine and 0.2 ml. of acetic anhydride in 10 ml. of *sym*-tetrachloroethane. This mixture was allowed to stand for 24 hr. Work-up of this mixture by a procedure similar to the one employed in the previous experiment gave 40 mg. of starting material and 250 mg. (78%) of 1,4-diacetyl-2,3-diphenylcycl[3,2,2]azine (XIX).

Peroxide Oxidation of 1,4-Diacetyl-2,3-diphenylcycl[3,2,2]azine.—To a boiling solution of 150 mg. of 1,4-diacetyl-2,3-diphenylcycl[3,2,2]azine in 15 ml. of glacial acetic acid was added 5 ml. of 30% hydrogen peroxide. No darkening was observed, and the solution remained fluorescent for 15 min. after the peroxide had been added. After the solution had been refluxed for an additional 2 hr., it was concentrated to 3 ml. and then diluted with 20 ml. of water. Then the aqueous solution was extracted with methylene chloride. Concentration of the methylene chloride extract, followed by sublimation of the residue *in vacuo*, gave 56 mg. (58%) of white crystals, m.p. 122°, identified as benzoic acid.

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