[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUQUESNE UNIVERSITY]

Absorption Spectra of Azines[1a]

BY H. HARRY SZMANT AND HENRY J. PLANINSEK

Continuing our interest in the spectra of *p*-substituted acetophenone derivatives[1b] we have examined the spectra of a series of azines. In this paper we report the results of a study of the absorption spectra of the azines and discuss them in the light of the results obtained with the analogous 2,4-dinitrophenylhydrazone series.[1]

TABLE I

KETAZINES $R(CH_3)C{=}N{-}N{=}C(CH_3)R$

No.	R	Yield, %	Crystallization solvent	M. p., °C.[a]	Analyses,[b] % Carbon Calcd.	 Carbon Found	 Hydrogen Calcd.	 Hydrogen Found
1	C_6H_5	84	EtOH	123[c]	...	...	..	..
2	*p*-$C_6H_5C_6H_4$	60	Dioxane	278	85.66	85.55	6.23	6.03
3	*p*-$C_6H_5CH_2C_6H_4$	85	EtOH–C_6H_6	135	86.44	86.24	6.77	7.04
4	*p*-$C_6H_5OC_6H_4$	66	Pet. ether	166	79.48	79.24	5.75	6.11
5	*p*-$C_6H_5SC_6H_4$[d]	84	*i*-PrOH	172	74.43	74.32	5.35	5.26
6	*p*-$C_6H_5SOC_6H_4$[d]	85	EtOH–C_6H_6	214	69.40	69.55	4.99	5.03
7	*p*-$C_6H_5SO_2C_6H_4$[d]	59	EtOH–C_6H_6	211	65.10	65.10	4.65	4.45
8	2-Thienyl	65	EtOH	93	58.03	58.23	4.87	4.62

[a] All melting points are uncorrected. [b] Micro-Analytical Laboratory, University of Pittsburgh. [c] M. p. reported to the 121° (ref. 5.) [d] The ketones were prepared according to Szmant and Palopoli, THIS JOURNAL, 72, 1756 (1950).

TABLE II

ABSORPTION DATA OF AZINES AND 2,4-DINITROPHENYLHYDRAZONES

Ketone, $RCOCH_3$ R =	Azines $\lambda_{max.}$,[b] mμ	 $\epsilon \times 10^{-2}$, max.	 $\Delta\lambda_{max.}$,[c] mμ	 $\Delta\epsilon \times 10^{-2}$, max.	2,4-Dinitrophenylhydrazones[a] $\lambda_{max.}$,[b] mμ	 $\epsilon \times 10^{-2}$, max.	 $\Delta\lambda_{max.}$,[c] mμ	 $\Delta\epsilon \times 10^{-2}$, max.
C_6H_5	265[e]	216[e]	...	..	376	238	...	...
p-$C_6H_5C_6H_4$	276[f]	119	11[f]	−97	382	127	6	−109
p-$C_6H_5CH_2C_6H_4$	276	255	11	39	381	367	5	129
p-$C_6H_5OC_6H_4$	292	264	27	48	383	266	7	28
p-$C_6H_5SC_6H_4$	320 258 241	299	55	83	384	301	8	63
p-$C_6H_5SOC_6H_4$	291	345	26	129	372	294	−4	56
p-$C_6H_5SO_2C_6H_4$	289	372	24	156	373	281	−3	43
2-Thienyl	335 265	159 134	70	−57	392	255	16	17

[a] Ref. 1. [b] Absorption spectra in 95% ethanol. [c] $\Delta\lambda_{max.}$ = ($\lambda_{max.}$ of compound $-\lambda_{max.}$ of acetophenone derivative). [d] $\Delta\epsilon_{max.}$ = ($\epsilon_{max.}$ of compound $-$ $\epsilon_{max.}$ of acetophenone derivative). [e] Reported absorption data: $\lambda_{max.}$ 267.5 mμ, $\epsilon_{max.}$ 22500 (ref. 6); $\lambda_{max.}$ 265 mμ, $\epsilon_{max.}$ 20500 (ref. 4); $\lambda_{max.}$ 267 mμ, long ϵ 4.39 (ref. 5). [f] These values may be misleading since the absorption band appears as an almost flat shoulder stretching over 35 mμ (265–300 mμ).

Experimental Results

The azines were prepared by refluxing equimolar quantities of the ketone and 85% hydrazine hydrate with benzene in an apparatus equipped with a Dean–Stark trap. A few drops of acetic acid served to catalyze the reaction, and on recovering the crude product from the benzene solution, the azines were crystallized to constant melting point from a suitable solvent. The yields of the azines, the crystallization solvent, melting points and analytical data are summarized in Table I. The absorption spectra were examined by means of a Beckman DU spectrophotometer using solutions of concentrations in the range of 10 mg. of azine per liter of 95% ethanol. The absorption curves are reproduced in Figs. 1 and 2, and the spectral data obtained in this and the previous study are summarized in Table II.

Discussion

Before discussing the specific results of this study it seems appropriate to comment on the spectral behavior of azines in general.

The 300 mμ absorption band of benzalazine has been interpreted[2,3,4] in terms of resonance in which the oscillating electrons traverse the entire length of the molecule (I). The substitu-

---

[1] (a) Presented before the Organic Division of the American Chemical Society in Philadelphia, April, 1950. (b) Previous paper, Szmant and Planinsek, THIS JOURNAL, 72, 4042 (1950). Preliminary report presented before the Organic Division of the American Chemical Society in San Francisco, April, 1949.

[2] Ferguson and Branch, THIS JOURNAL, 66, 1467 (1944).

[3] Blout and Gofstein, *ibid.*, 67, 13 (1945).

[4] Barany, Braude and Pianka, *J. Chem. Soc.*, 1898 (1949).

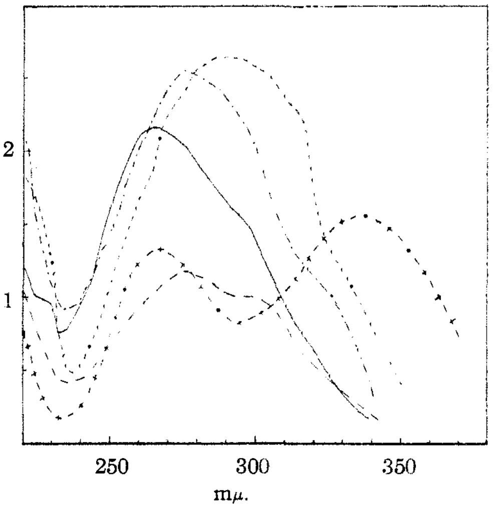


Fig. 1.—Absorption spectra of azines of: —, acetophenone; — —, *p*-phenylacetophenone; —·—·, *p*-benzylacetophenone; - - - -, *p*-phenoxyacetophenone; -x-x-x, 2-thienyl methyl ketone.

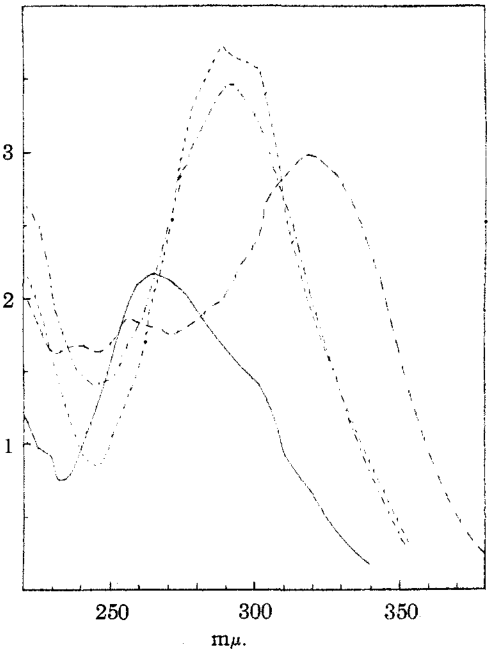
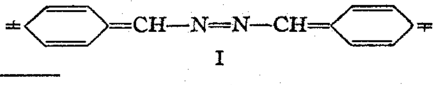


Fig. 2.—Absorption spectra of azines of: —, acetophenone; – –, *p*-phenylmercaptoacetophenone; —·—·, *p*-phenylthionylacetophenone; - - - -, *p*-phenylsulfonylacetophenone.

tion of alkyl groups in the alpha positions causes a hypsochromic shift of some 40 mμ and since the origin of this phenomenon has been the subject of some debate,[4,5,6] it appears advisable to summarize the facts which support the interpretation of the 304 mμ band in terms of structures I.



I

The absorption maximum of 1,4-diphenylbutadiene, a structure electronically analogous to that of benzalazine, is located at 328 mμ.[7] The difference in the maxima of these two compounds namely, 24 mμ, is consistent with similar differences observed[4] when the carbon–carbon group of a conjugated system is replaced by the azine group. The hypsochromic effect caused by the azine group is interpreted as a result of the constraint exerted on the flow of electrons through the two electronegative nitrogen atoms. In simple polyenes, the maxima resulting from conjugated systems containing four and six double bonds are located at 296 and 360 mμ, respectively,[8,9] and by averaging these values one would expect a system containing five conjugated double bonds to show a maximum at about 328 mμ. This value is in excellent agreement with the experimentally determined maxima in compounds such as 1,4-diphenylbutadiene or cinnamalacetone[10] in which the resonating structure contains approximately five double bonds.[11] The benzalazine structure also contains approximately five double bonds, and when the correction resulting from the constrained electronic flow is made one finds the expected and observed positions of the maximum to be in excellent agreement: $328 - 24 = 304$ mμ. A further confirmation of the thesis that the 304 mμ band of benzalazine arises from resonance of almost five double bonds is obtained when one averages the maxima of polyene azines containing four and six double bonds[4,9]: $^1/_2(277 + 338) = 304$ mμ.

It is also of interest to compare the absorption maxima of the azines and the parent aldehydes. Thus, in the case of benzaldehyde, *p*-hydroxy-, *p*-methoxy- and *p*-dimethylaminobenzaldehyde (λ_{max} 243,[12] 283.5,[13] 277,[12] and 342[14] mμ, respectively) the corresponding azines (λ_{max} 300,[4] 335,[4] 331[4] and 400 mμ,[4] respectively) absorb 52–58 mμ farther toward the visible range. Since the resonating path of the benzaldehyde (equivalent to approximately 2.5 double bonds) is lengthened in the benzalazine by approximately 2.5 double bonds, the expected difference in the maxima of these two series of compounds is: $2.5 \times 32 - 24 = 56$ mμ. This calculation assumes that the addition of a double bond to the electronic path causes a bathochromic shift of

---

(5) Blout, Eager and Gofstein, This Journal, **68**, 1983 (1946).

(6) Ferguson and Goodwin, *ibid.*, **71**, 633 (1949).

(7) Hauser, Kuhn and Smakula, *Z. physik. Chem.*, **29**, 384 (1935).

(8) Kuhn and Grundmann, *Ber.*, **71**, 442 (1938).

(9) Blout and Fields, This Journal, **70**, 189 (1948).

(10) Wilds, *et al.*, *ibid.*, **69**, 1985 (1947).

(11) A phenyl group, when it functions as a path for oscillating electrons, is estimated to be equivalent to 1.3–1.4 double bonds (ref. 10).

(12) Morton and Stubbs, *J. Chem. Soc.*, 1347 (1940).

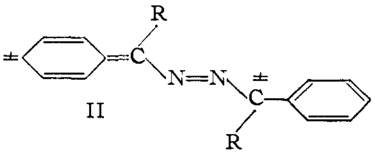
(13) Doub and Vandenbelt, This Journal, **69**, 2714 (1947).

(14) Kumler, *ibid.*, **68**, 1184 (1946).

32 $m\mu$,[15] and it includes the correction for the constrained electronic flow across the azine group.

The 300 $m\mu$ band of benzalazine, can be, in the light of the above mentioned arguments, safely assumed to result from the contribution of resonance structures represented by I. It is also seen that conclusions as to the length of a resonating path (in relatively simple molecules) can be subjected to critical comparisons and that, generally speaking, the conclusions must be able to withstand these critical tests.

The principal contribution to the explanation of the origin of the hypsochromic shift in the absorption spectrum of acetophenone azine (when compared to benzal azine) was made by Blout and co-workers.[5] These investigators attribute the 270 $m\mu$ band of α-substituted benzalazines to resonance structures represented by II in which one of the benzene rings is not coplanar with the conjugated portion of the structure. The non-planarity of the benzene ring was thought to be brought about by the steric effects of α-alkyl groups. The same authors also observed that most of the α-substituted benzalazines retained an absorption band in the 300 $m\mu$ range which appeared at least as an inflection point or in some cases as a secondary maximum.

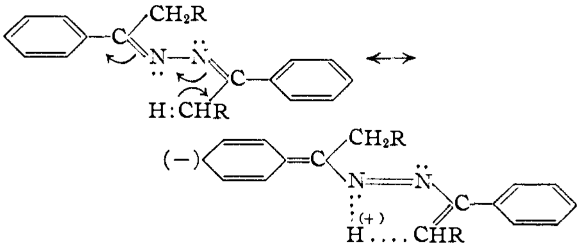


II

Some of the results obtained by Blout[5] with mixed azines are rather unexpected when viewed in the light of the above-mentioned interpretation of the origin of the 270 $m\mu$ band. Thus, it is indeed surprising that benzaldehyde–acetophenone azine, with one strong maximum at 278 $m\mu$, should exhibit the steric phenomenon to such a great extent as to exclude a prominent absorption at 300 $m\mu$. On the other hand, the maximum of benzaldehyde–benzophenone is restored into the 300 $m\mu$ range (307 $m\mu$), from which fact one would have to conclude that the steric effect of the phenyl group is smaller than that of the methyl group. The spectrum of benzophenone azine, from the viewpoint of steric interference of phenyl groups, should be limited to absorption in the 270 $m\mu$ range, but that compound (in addition to the principal maximum at 278 $m\mu$ shows an unquestionably prominent absorption in the 310 $m\mu$ range. Finally, propiophenone azine exhibits an absorption curve almost identical to that of acetophenone azine, and it stands to reason that the α-ethyl groups should have caused an increase in the non-planarity of the phenyl groups and thus should have enriched the 270 $m\mu$ band at the cost of the absorption in the 300 $m\mu$ range.

These incongruous results were presumably responsible for the conclusion of Blout and coworkers[5] that the steric effect of alpha substituents is a "contributing...but not the only operative effect." Also Barany, Braude and Pianka,[4] who recently discussed the hypsochromic shifts caused by alkyl groups in the benzalazine (and glyoxime) system, concluded that this effect is "unlikely to be a steric one...but is presumably conditioned by the electronic properties of the azomethine group."

Our results obtained with acetophenone azines containing electron withdrawing substituents in the para position (phenylsulfonyl and phenylthionyl) are unexpected in view of the observed bathochromic displacements of the 270 $m\mu$ acetophenazine maximum. In order to explain these experimental results we wish to propose an interpretation of the 270 $m\mu$ maximum of acetophenazines alternate to that of Blout and coworkers which involves the electronic interaction of the alpha substituent with one of the nitrogen atoms of the azine group. This proposed hyperconjugation phenomenon amounts to a weak hydrogen bond formation in the excited state of the molecule and may be represented by III. The hyperconjugation is probably facilitated by the proximity of the electron donating nitrogen atom of the azine, and it may also be aided by the repulsion between the phenyl and alkyl groups. The latter phenomenon would shorten the distance between the interacting nitrogen and hydrogen atoms. The difference of 3 $m\mu$ between the principal absorption bands of aceto- and propiophenone azines[5] may be significant in this connection since it could represent the lowering of the energy requirement for the hyperconjugation involving a secondary hydrogen atom, or else it may be caused by the greater proximity of the interacting atoms in the bulkier ethyl group.



III

The characteristic feature of the resonance represented by III is the increase in the electron density of one of the aromatic rings without the simultaneous deprivation of the other aromatic ring of electrons. Consequently, the presence of electron withdrawing substituents on the aromatic rings should favor the postulated hyperconjuga-

---

[15] This value was chosen by plotting the reported maxima of over twenty compounds reported in refs. 7, 8, 9 *vs.* the number of double bonds (assuming the phenyl and α-furyl groups to be equivalent to 1.5 and 2.5 double bonds, respectively) and computing the slope of the best straight line.

tion, and the electronic oscillations in the azines should have a lower energy requirement than those in the parent ketones. This is expected to be true since the electron withdrawing groups in the ketones are opposed to the equally electron withdrawing carbonyl group. That this prediction is fulfilled can be seen from the inspection of Table III in which are tabulated the maxima of a number of substituted acetophenones and of the corresponding azines, as well as the difference in the positions of the maxima of each ketone-azine pair.

TABLE III

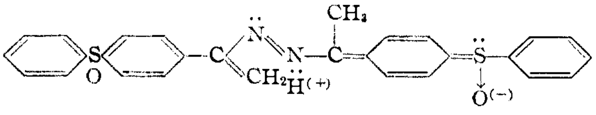
ABSORPTION MAXIMA OF ACETOPHENONES AND AZINES

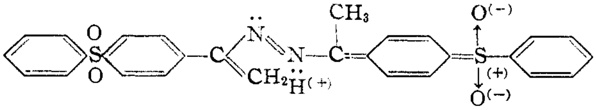
$RC_6H_4COCH_3$	λ_{max} ketone, mμ	λ_{max} azine, mμ	$\Delta\lambda^a_{max}$, mμ
H	$246^{b,d}$	267^c	20
p-C_6H_5S	305^d	320	15
p-H_2N	317^g	333^c	16
p-C_6H_5	283.5^d	300^e	16.5
p-$C_6H_5CH_2$	$255^{d,e}$	276	21
p-C_6H_5O	270^d	292	22
p-CH_3O	276.5^f	303^h	26.5
p-HO	275^f	303^c	28
m-O_2N	230^d	266^i	36
p-$C_6H_5SO_2$	252^d	289	37
p-C_6H_5SO	252^d	291	39

[a] $\Delta\lambda_{max}$ = (λ_{max} azine) − (λ_{max} ketone). [b] Doub and Vandenbelt, THIS JOURNAL, 62, 2906 (1940). [c] Ref. 5. [d] Szmant and Planinsek, manuscript in preparation. [e] The longest wave length of an almost flat shoulder. [f] Ref. 13. [g] Ref. 14. [h] Ref. 4. [i] Ref. 6.

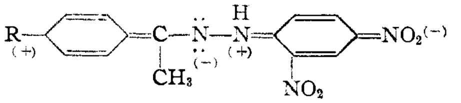
The inspection of the last column of Table III reveals that greatest gain in the bathochromic displacement of the maximum is made by the azines in which the substituents are electron withdrawing, and the smallest gain by those azines in which a readily electron donating substituent is present.[16]

The bathochromic displacement in the case of compounds 6 and 7 is almost twice as large as that of the other substituted acetophenones. This difference is interpreted by the large contribution of resonance structures IV and V, respectively.[17]

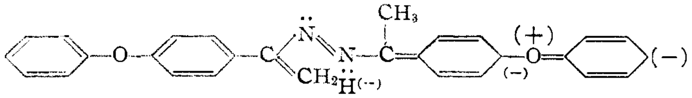

IV


V

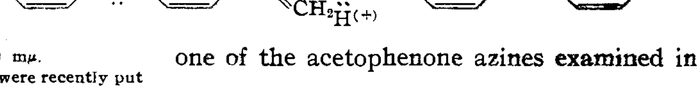
The postulated hyperconjugation effect in the acetophenone azines receives further support when one compares the relative effects of the substituents in the azine and the 2,4-dinitrophenylhydrazone .(DNPH) series (Table II). Using the unsubstituted acetophenone derivative as a standard for comparison, it is noticed that, in general, the bathochromic displacements are relatively small in the DNPH series and the sulfoxide and sulfone groups cause hypsochromic displacements. This is understandable in view of the fact that none of the substituents is particularly electron donating in character and therefore they do not aid appreciably in the stabilization of the polarized form of the DNPH (VI).


VI

On the other hand, these same substituents in the azine series, because of their poor electron donating qualities and because the electron flow represented by III is directed *toward* the substituents, give large bathochromic displacement of the acetophenone azine maximum. The p-phenoxyacetophenone derivatives are of interest in this connection. In the DNPH the bathochromic effect of the p-phenoxy group is relatively small because of the competitive electron flow from the oxygen atom into the terminal phenyl group,[18] but in the azine the electron flow toward the phenoxy group is thus aided by the electron withdrawing effect of the terminal phenyl group (VII).


VII

Compound 5 shows the greatest displacement of the acetophenone azine band, and the 320 mμ maximum is interpreted as a result of resonance contributions shown in VIII. This is the only


VIII

one of the acetophenone azines examined in this

---

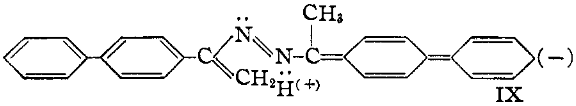
[16] The exceptions to this statement are the p-hydroxy- and p-methoxyacetophenone azines. However, on inspection of the reported absorption curves for the p-hydroxy- and p-ethoxyacetophenone azines in ref. 5 (the curve for the p-methoxy compound is not reproduced in ref. 4) one notices an unusually broad maximum with no fine structure apparent over a range of some 100 mμ; this probably indicates that there occurs a fusion of the absorption peaks corresponding to structures I and III. Strongly electron donating substituents would be expected to favor the resonance of the benzalazine type. The absorption curve of p-aminoacetophenone azine (ref. 5), while also possessing a rather broad peak, shows the presence of resonance of the benzalazine type by an inflection point near 360 mμ.

[17] Similar interpretations of the sulfone group were recently put forward by Fehnel and Carmack (THIS JOURNAL, 71, 231 (1949)) and by Koch (*J. Chem. Soc.*, 408 (1949)).

[18] This effect can also be noticed on comparing the maxima of p-methoxy and p-phenoxyacetophenones(Table III).

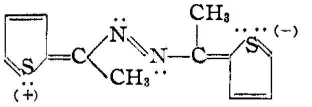
study which has a maximum beyond that of the benzalazine peak, but the postulated resonance contributions (VIII) are justified on the ground that the parent ketone possesses its maximum absorption at 305 mμ (Table II). The secondary absorption bands of compound 5 are typical of the reported 250 mμ bands in phenyl sulfide,[19,20] and originate from the independent absorption of the phenyl sulfide unit present in VIII.

The absorption curve of compound 2 presents an almost flat shoulder stretching from 265 to 300 mμ. Since the absorption maximum of biphenyl lies at 250 mμ[21] and that of *p*-phenylacetophenone at 283.5 mμ (Table III), the flat peak probably results from the overlapping absorption bands of the absorption units in resonance structures IX.

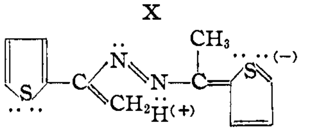


IX

The 2-thienyl methyl ketazine exhibits two absorption peaks, the major one at 325 mμ, and a minor (but only slightly weaker) one at 265 mμ. Since 2-thienyl ketones possess a characteristic absorption peak in the neighborhood of 260 mμ,[22] we interpret the 335 mμ band of the azine arising from contributions of structures X or XI.



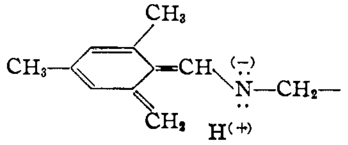
X



XI

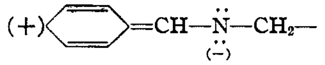
The thiophene absorption unit in structure XI accounts for the strong 265 mμ peak observed in the spectrum. Since the location and intensity of the maximum in 2-thienyl phenyl ketone[22] are almost identical with the characteristics of the secondary peak in compound 8, it is possible that the 265 mμ absorption arises from a resonance phenomenon which would amount to transitions between structures X and XI.[23]

In conclusion, the authors would like to call attention to the unexplained anomaly in the spectral characteristics of dibenzal- and dimesitylalethylenediamines which were reported recently.[24] A hyperconjugation phenomenon very similar to that proposed in structure III may be the explanation for the observed differences between the above-mentioned ethylenediamines, while the oximes and *p*-nitrophenylhydrazones of the two aldehydes show insignificant absorption differences. In the dimesitylalethylenediamine there is possible the contribution of structures represented by XIII in which the electronic



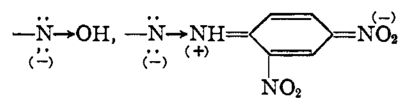
XIII

path is longer than that of dibenzalethylenediamine (XIV), but in which the *o*-quinoid



XIV

structure causes a decrease in the absorption intensity. The analogous hyperconjugation in the oxime and *p*-nitrophenylhydrazone of mesitylaldehyde is less probable because the donor qualities of the nitrogen atoms are decreased by the adjacent strong electron attracting groups



The absorption spectra of other acetophenazines are currently being investigated, and work with benzalazines containing substituents in the alpha positions other than methyl groups is also planned in order to evaluate the merit of the proposed hyperconjugation hypothesis.

Acknowledgment.—The authors gratefully acknowledge the financial aid of the Research

---

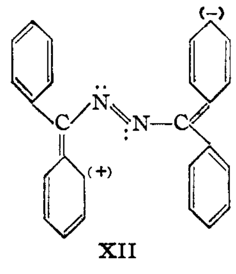
(19) Koch, *J. Chem. Soc.*, 887 (1949).

(20) Fehnel and Carmack, THIS JOURNAL, 71, 84 (1949).

(21) Friedel, Orchin and Reggel, *ibid.*, 70, 202 (1948).

(22) Szmant and Basso, manuscript in preparation.

(23) One of the possible objections to the postulated hyperconjugation phenomenon in alpha alkyl benzalazines is the fact that hypsochromic effects are known to be caused also by alpha phenyl groups. Thus, benzophenone azine[5] shows the most prominent peak at 278 mμ (log ε 4.29) but it also possesses a prominent inflection point at about 310 mμ (log ε 4.11). The 310 mμ band suggests a large contribution of the benzalazine type of resonance, while the 278 mμ peak may be visualized by a resonance phenomenon (XII) essentially analogous to III.



XII

Structure XII does not seem at all impossible when one considers the proximity of the electron donating nitrogen atom to the ortho position of one of the phenyl groups and the consequent electrostatic interaction. However, it may be expected that contribution of structures such as XII to the spectrum of benzophenone azine is less than the contribution of structures III to the spectrum of acetophenone azine, and it is noteworthy that while one alpha methyl group has the characteristic hypsochromic effect on the maximum of benzalazine, one alpha phenyl group is insufficient[5]. This difference in the effectiveness of the alpha alkyl and phenyl groups is in accord with the lower stability of structure XII. Work on various benzophenone azines is in progress in order to elucidate the possible contributions of these systems.

(24) Ferguson and Robinson, THIS JOURNAL, 71, 742 (1949).

Corporation in defraying a part of the cost of this study.

Summary

The absorption spectra of six *p*-substituted acetophenone azines and of 2-thienyl methyl ketazine were determined. The results of this study lead to the interpretation of the hypsochromic effects of alpha alkyl groups on the absorption spectrum of benzalazine in terms of a hyperconjugation phenomenon. The spectral behavior of sulfur containing azines strongly supports the belief in the expansion of the octet of the sulfur atom in the excited state.

PITTSBURGH, PENNA. RECEIVED FEBRUARY 9, 1950

[CONTRIBUTION FROM THE WARNER INSTITUTE FOR THERAPEUTIC RESEARCH]

3-(Alkoxyphenoxy)-1,2-propanediols

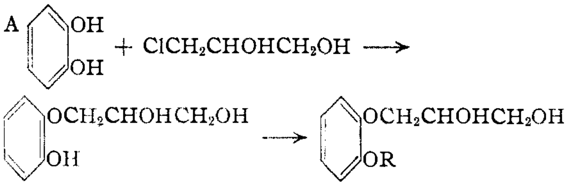
BY ROBERT I. MELTZER AND JOHN DOCZI

The search for improved muscle-relaxing drugs led to the preparation of a number of 3-(alkoxyphenoxy)-1,2-propanediols in these laboratories. Launoy[1] observed that 3-phenoxy-1,2-propanediol inhibited certain muscular contractions and Berger and Bradley[2] reported that many glyceryl ethers have such activity. The use of the best of these drugs, 3-(2′-methylphenoxy)-1,2-propanediol, is limited, however, by certain of its pharmacological properties as well as by low water solubility.

Guaiamar, 3-(2′-methoxyphenoxy)-1,2-propanediol, has a lower but similar activity[3] to 3-(2′-methylphenoxy)-1,2-propanediol and is much more soluble. The investigation in these laboratories included the study of the effect of the introduction into 3-phenoxy-1,2-propanediol of more than one methoxyl group and also of an alkoxyl group higher than methoxyl. Accordingly, there were prepared the six isomeric 3-(dimethoxyphenoxy)-propanediols and the three isomeric 3-(ethoxyphenoxy)-propanediols.

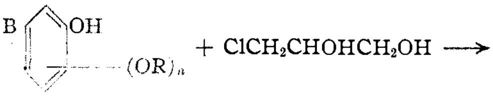
Compounds of desirable solubility were obtained among the dimethoxyl compounds. These compounds were unsatisfactory, however, as motor depressants.[3] Among the ethoxyl compounds, only the ortho-substituted compound had good solubility and appeared of interest pharmacologically.[3] This prompted the preparation of compounds in which the ethyl group of 3-(2′-ethoxyphenoxy)-1,2-propanediol was replaced by *n*-propyl, isopropyl, *n*-butyl and isobutyl. The solubilities of these compounds are low. The pharmacological investigation of all these compounds will be reported elsewhere.

All the phenoxypropanediols were prepared according to one of two general methods. In Method A, catechol was condensed with glycerol chlorohydrin to give 3-(2′-hydroxyphenoxy)-1,2-propanediol. The phenolic hydroxyl was then etherified by the appropriate alkyl bromide using sodium ethylate as condensing agent.

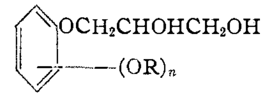


I, R = $CH_2CH_2CH_3$
II, R = $CH(CH_3)_2$
III, R = $CH_2CH_2CH_2CH_3$
IV, R = $CH_2CH(CH_3)_2$

According to Method B, the appropriate alkoxyphenol in the form of its sodium salt was condensed with glycerol chlorohydrin in absolute ethanol.



Va	$n = 1$	OR = 2-OC_2H_5
VIa	$n = 1$	OR = 3-OC_2H_5
VIIa	$n = 1$	OR = 4-OC_2H_5
VIIIa	$n = 2$	OR = 2,6-$(OCH_3)_2$
IXa	$n = 2$	OR = 3,5-$(OCH_3)_2$
Xa	$n = 2$	OR = 2,5-$(OCH_3)_2$
XIa	$n = 2$	OR = 3,4-$(OCH_3)_2$
XIIa	$n = 2$	OR = 2,4-$(OCH_3)_2$
XIIIa	$n = 2$	OR = 2,3-$(OCH_3)_2$



V	$n = 1$	OR = 2-OC_2H_5
VI	$n = 1$	OR = 3-OC_2H_5
VII	$n = 1$	OR = 4-OC_2H_5
VIII	$n = 2$	OR = 2,6-$(OCH_3)_2$
IX	$n = 2$	OR = 3,5-$(OCH_3)_2$
X	$n = 2$	OR = 2.5-$(OCH_3)_2$
XI	$n = 2$	OR = 3,4-$(OCH_3)_2$
XII	$n = 2$	OR = 2,4-$(OCH_3)_2$
XIII	$n = 2$	OR = 2,3-$(OCH_3)_2$

Three of the requisite phenols were prepared by peracetic acid oxidation of the corresponding benzaldehyde. These three phenols, the 2,3-, the 2,4- and the 3,4-dimethoxyphenols, were prepared by a modification of the Waeck and Bezard[4] oxidation of veratraldehyde to 3,4-dimethoxyphenol.

For the preparation of 2,6-dimethoxyphenol, gallic acid was completely methylated and then

---

(1) Launoy, *Compt. rend. soc. biol.*, **69**, 191 (1910).

(2) Berger and Bradley, *Brit. J. Pharmacol.*, **1**, 265 (1946).

(3) Communication from the Pharmacology Department of this Institute.

(4) Waeck and Bezard, *Ber.*, **74**, 845 (1941).