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STUDIES ON FUSED SYSTEMS CONTAINING THE 1,4-DIAZEPINE NUCLEUS

BY

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Synopsis

The benzo[*b*]1,4-diazepines formed when β-diketones condense with *o*-phenylenediamine have been studied.

A spectrophotometric method for determination of the basic strength of the diazepines has been elaborated.

The structure of a substituted ethyl pyruvate formed by Claisen-condensation of diethyl oxalate with 5-methyl-7-phenylbenzo[*b*]1,4-diazepine has been established.

Some derivatives of partially hydrogenated 4,8-diazaazulenes have been prepared. The dehydrogenation of these compounds to 4,8-diazaazulenes was not possible.

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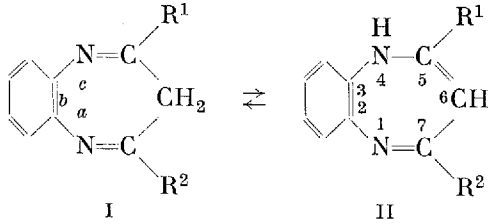
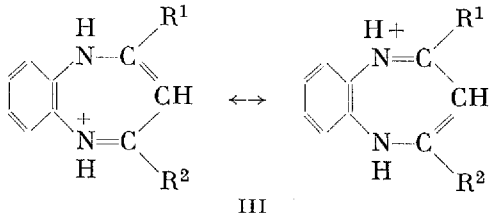
I. Structure of 5,7-disubstituted benzo[*b*]1,4-diazepines

THIELE and coworkers[1, 2] found that *o*-phenylenediamine is able to condense with β-dicarbonyl compounds, basic substances showing marked halochromism being formed in the reaction. For the structure of the condensation products two possibilities exist, a symmetrical (I) and an unsymmetrical (II):



I ⇄ II



III

Different authors[1–6] have studied the reaction and it is generally accepted that the coloured salts are derived from II, the cation III being stabilised by resonance between several structures, two of which are shown. For the colourless bases the symmetrical structure I is assumed.

According to this assumption the presence of at least one hydrogen atom at C^6 is a condition for obtaining coloured salts of the benzo[*b*]1,4-diazepines.

Several attempts[3, 7] have been made to condense *o*-phenylenediamine with 3,3-dimethylpentane-2,4-dione (3,3-dimethylacetylacetone) but without

success. One reason may be that the presence of at least one hydrogen atom at C^3 in the substituted acetylacetone is necessary for the condensation. This is the opinion of CROMWELL[8], who considers the enolised form of the diketone as the one able to condense with the diamine. Another reason for the inactivity of 3,3-dimethylacetylacetone may be the steric conditions. Thus HALFORD and FITCH[7] point out that if the 5,6,6,7-tetramethylbenzo[*b*]1,4-diazepine were formed, one of the methyl groups on C^6 would have to interfere with the π-orbital of the benzene nucleus, thereby causing such a strain in the diazepine nucleus that the gain in energy obtained by the condensation would not be sufficient to counterbalance the strain established.

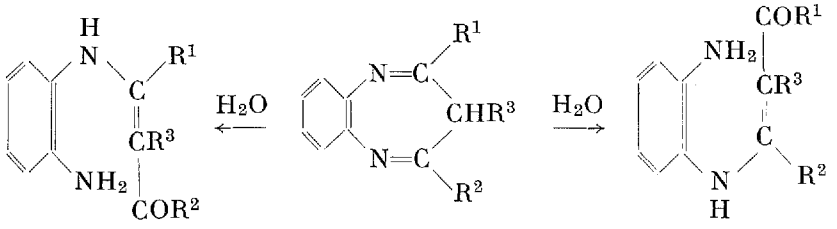
BARLTHROP *et al.*[6] claim to have obtained the introduction of a substituent for both of the hydrogen atoms at C^6 in 5,7-dimethylbenzo[*b*]1,4-diazepine by base-catalysed condensation of this substance with one (formula IX below) or two molecules of piperonal. It had been found previously that all benzo[*b*]1,4-diazepines with at least one hydrogen atom at C^6 in acid solution show a lowintensity absorption in the region of 5000 Å. The UV-spectra of the condensation products obtained by BARLTHROP *et al.* showed no such absorption and therefore the English authors are of the opinion that the first molecule of piperonal will condense on the methylene group, the next molecule of piperonal then attacking one of the methyl groups at C^5 and C^7. In both condensation products the C^6-atom should thus be sp^2-hybridized and the substances should, as the 6,6-disubstituted substance, be without the hydrogen atom necessary for the formation of the unsymmetrical structure.

We have repeated BARLTHROPS experiments but we cannot confirm that the condensation takes place on the methylene group. On the contrary, by examining the IR-spectra we have found that the aldehyde reacts only with the methyl group(s), thereby forming 5-mono- or 5,7-di-(3,4-methylenedioxystyryl)benzo[*b*]1,4-diazepines, the first one corresponding to formula IV below ($R^1 = CH_2O_2C_6H_3CH{=}CH-$). The evidence for this formulation is:

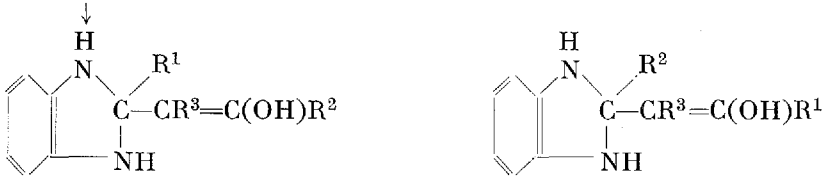
The substance containing one piperonylidene residue shows absorption at 1427 cm^{-1} and at 1364 cm^{-1}, corresponding to the absorption of a methyl group, but these absorptions are not found in the substance containing two piperonylidene residues. Otherwise the spectra of the two compounds are very much alike. They have an absorption at 960 cm^{-1} which we ascribe to the $-CH{=}CH-$ (trans) out-of-plane vibration. If the methylene group had reacted a $>C{=}CH-$ out-of-plane vibration should be expected to appear near 800 cm^{-1}.

Our formulation explains better than BARLTHROP's the products which he found by hydrolysis of the substance formulated by him as 5,7-dimethyl-3-piperonylidene-benzo[*b*]1,4-diazepine.

By hydrolysis of benzo[*b*]1,4-diazepines a (substituted) benzimidazole and a ketone are formed. With different substituents at C^5, C^6 and C^7 two different benzimidazoles and two different ketones may be formed (see formulas IV–VIII). According to generally accepted views the first step in

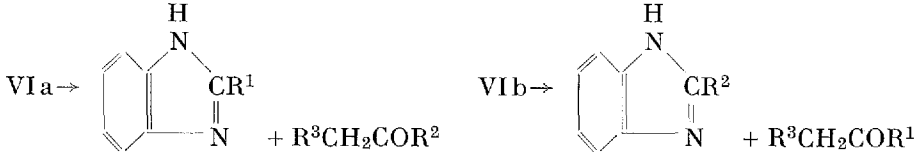


Va IV Vb



VIa VIb

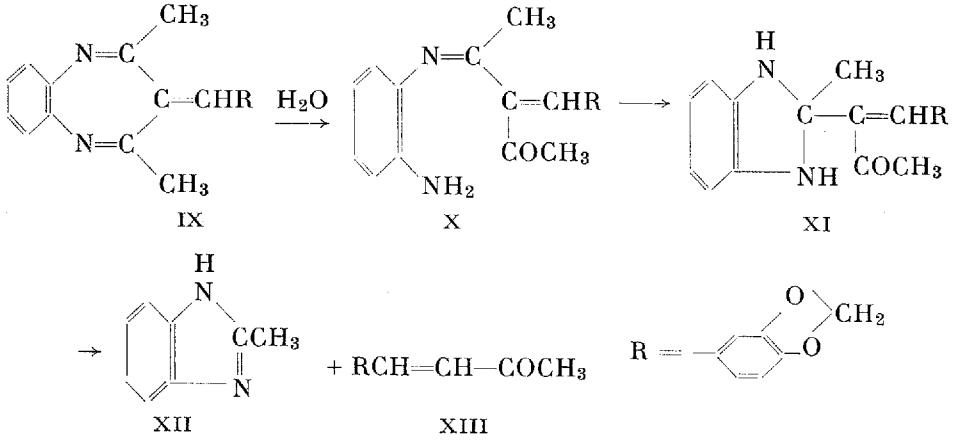
the hydrolysis is the formation of an anil which tautomerises to an α,β-unsaturated ketone (IV → Va or Vb). The next step is a 1,4-addition of the free amino group to the system of conjugated double bonds, and finally a stabilisation is obtained by the formation of benzimidazole and ketone (VIa → VII or VIb → VIII):



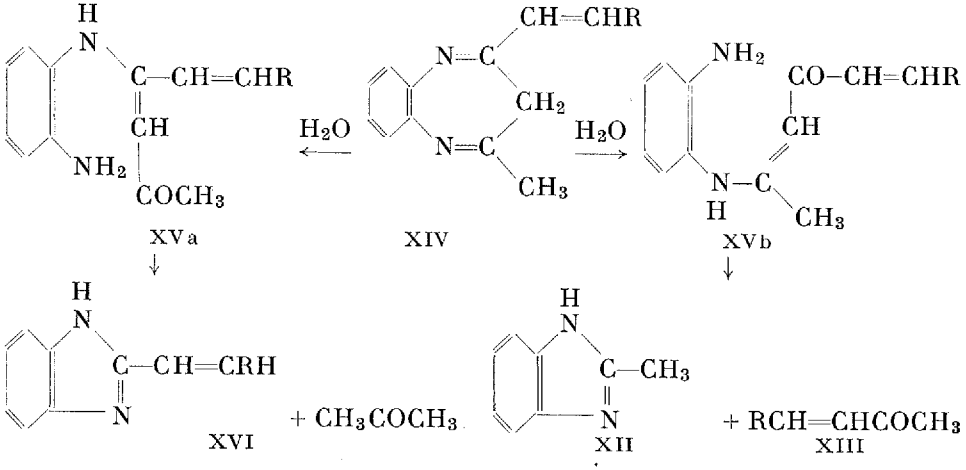
VII VIII

If, however, R^1 and R^2 are both CH_3 and R^3 is linked to C^6 by a double bond the first product of hydrolysis becomes the real anil, no hydrogen atom being present at C^6 to allow the formation of an α,β-unsaturated ketone able to be the precursor of benzimidazole-formation. Instead, an addition of the amino group over the –N=C-double bond might take place, fol-

lowed by a stabilisation to 2-methylbenzimidazole and piperonylideneacetone (IX–XIII; R = $CH_2O_2C_6H_3-$):



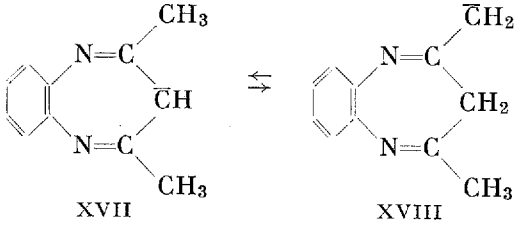
Barlthrop found these two products of hydrolysis and besides 2-(3,4-methylenedioxystyryl)benzimidazole (XVI) which cannot possibly be formed by simple hydrolysis of the 6-piperonylidene-substituted benzo-diazepine, whereas all 3 products of hydrolysis can be explained if the piperonal has reacted with one of the methyl groups instead of with the methylene group (XIV–XVI):



Of these products of hydrolysis only acetone, which may easily have escaped during the hydrolysis, has not been isolated, and we therefore

regard the condensation of the aldehyde on the methyl group more likely than the condensation on the methylene group.

The reaction of aromatic aldehydes with 5,7-disubstituted benzo[*b*]-1,4-diazepines is a base-catalysed reaction, and as shown is the methyl groups at C^5 and C^7 more reactive than the C^6-methylene group. Simple base-catalysed alkylation (*e.g.* with methyl iodide), on the other hand, leads to alkylation at C^6. In both instances it is the C=N-double bonds in the symmetrical structure I which activate a hydrogen atom in the methyl- or the methylene group, the anion left after elimination of a proton from the diazepine existing in tautomeric structures XVII and XVIII:

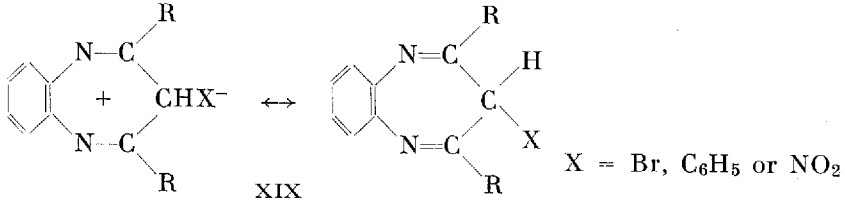


XVII XVIII

N-Methylsubstituted benzo[*b*]1,4-diazepines have been prepared from *N*-methyl-*o*-phenylenediamine and *β*-diketones[9]. They form, as the 6-unsubstituted or monosubstituted, *N*-unsubstituted benzo[*b*]1,4-diazepines, intensely coloured salts with acids, corresponding to the structure III.

Contrary to the base-catalysed substitution acid-catalysed electrophilic attack will take place at N^1 or at C^6.

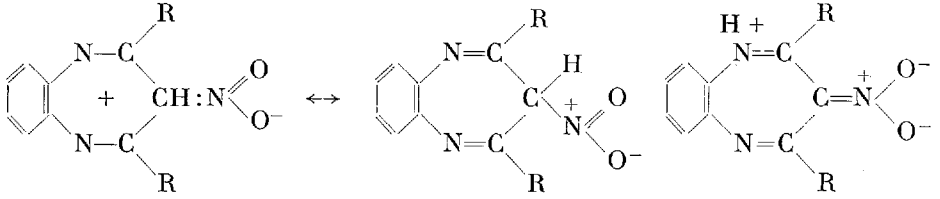
Substances for which the symmetrical structure I for the benzo[*b*]1,4-diazepine system is assumed are colourless with the exception of the 6-bromo-, 6-phenyl- and the 6-nitroderivatives, all of which are red coloured substances with high melting points (184°, 268° and 361°, respectively). The colour is, however, according to RUSKE and HÜFNER[10], not due to an unsymmetrical structure of the ring-system, but to a "cryptoionic" arrangement XIX:



XIX X = Br, C_6H_5 or NO_2

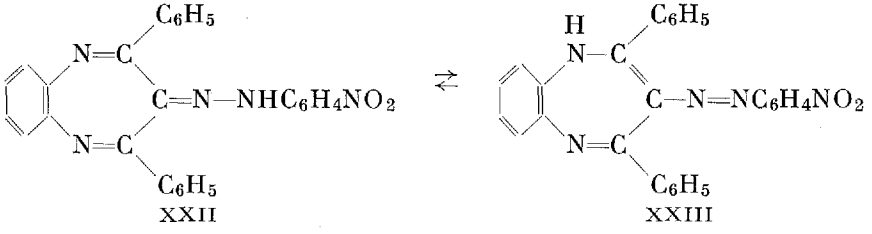
For the two first mentioned substances RUSKE and HÜFNER have shown the absence of NH-groups by IR-spectroscopy. For the third a "cryptoionic"

formulation would be XX. STAFFORD, REID and BARKER[11] are, on the other hand, of the opinion that the properties of this substance are better explained by the formulation XXI:



XX XXI

p-Nitrobenzenediazonium ions couple with 5,7-diphenylbenzo[*b*]1,4-diazepine at C^6 (BARLTHROP *et al.*[6]), forming a yellow *p*-nitrophenylhydrazone XXII or XXIII. By IR-spectroscopy the presence of an NH-group was established. The colour could therefore be due to the unsymmetrical diazepine ring, but as no colour shift takes place when the substance is dissolved in acid, the phenylhydrazone-structure is more likely than the azocompound-structure.



XXII XXIII

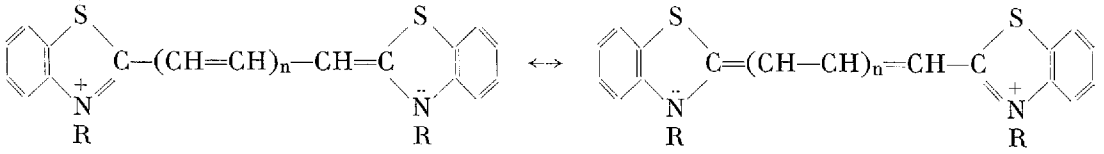
Basic strength of the benzo[*b*]1,4-diazepines

When the free benzo[*b*]1,4-diazepines are liberated from solutions of their salts by addition of a base the solution remains dark coloured for some seconds, but then colourless, crystalline substances spontaneously precipitate. When the coloured salts are treated with concentrated hydrochloric acid colourless salts with two equivalents of acid are formed. These salts are unstable in an atmosphere not saturated with hydrogen chloride, the coloured mono-salts being formed spontaneously by splitting off one molecule of hydrogen chloride from the colourless salt[2, 12].

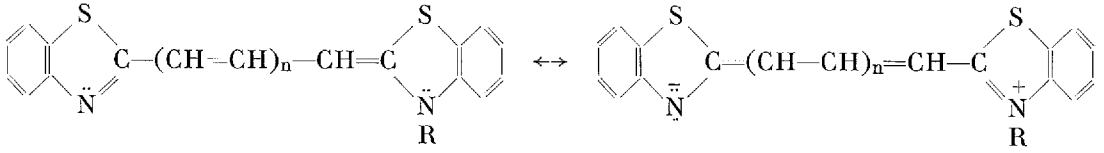
STEIMMIG[2] and with him all later investigators (latest LLOYD *et al.*[12]) assume for the colourless substances structure I, for the coloured structure

II. I remains symmetrical and thus colourless when two protons are taken up, whereas II by addition of one proton is transformed to the resonance-stabilised, coloured cation III (see *e.g.* VAISMAN[3]).

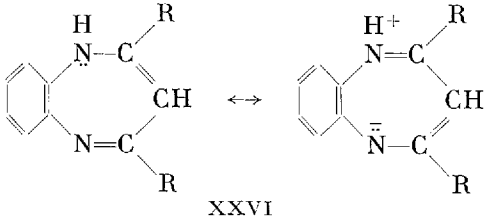
No explanation has been given for the colour of the unsymmetrical free base II. An explanation may possibly be found, for the free base as well as for the mono-cation, when comparing their structure with the structures of the cyanine dyes XXIV and XXV[13]: For II resonance structures with separate charges as in the unsymmetrical cyanines may be written (XXVI):



XXIV. Symmetrical cyanines, absorption for n = 0 at 4300 Å.



XXV. Unsymmetrical cyanines, absorption for n = 0 at 3700 Å.

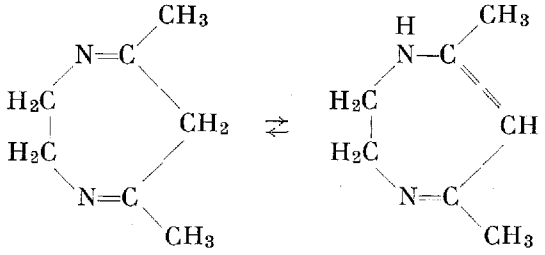


XXVI

In all three cases a double vinyl-shift of electrons will transfer one canonical structure into the other.

Of the two structures I and II the unstable, unsymmetrical structure II, according to SCHWARTZENBACH and LUTZ[4] and to LLOYD *et al.*[12], is the strongest base with a pK_a-value of 9.0 in aqueous solution, whereas pK_a for the equilibrium mixture was found to be 4.5.

The symmetrical structure I is stabilised by the two C=N double bonds in conjugation to the aromatic benzene system. For other 1,4-diazepines without annellation to an aromatic system the unsymmetrical form is the most stable, as shown *e.g.* for 2,3-dihydro-5,7-dimethyl-1,4-diazepine, XXVII and XXVIII (SCHWARTZENBACH and LUTZ[4]).



XXVII XXVIII

It is seen that XXVIII is stabilised by the $-NH-C(R)=CH-C(R)=N-$ conjugation. XXVII is a diketimine, XXVIII a monoketimine-monoenamine, and as in open-chain compounds the equilibrium diketimine $\rightleftarrows$ monoketimine-enamine is displaced still more towards monoketimine-enamine than is the displacement towards the ketone-enol structure in β-diketones, it is reasonable to assume that the unsymmetrical structure is the most stable.

This assumption has recently been confirmed by STAAB and VÖGTLE[14], using NMR-spectroscopy. The following signals were found:

$\delta = 7.76$ Integrated to one proton.
$\delta = 4.40$ Integrated to one proton.
$\delta = 3.42$ Integrated to 4 protons, corresponding to 2 methylene groups, placed nearly identically.
$\delta = 1.88$ Integrated to 6 protons, corresponding to 2 methyl groups.

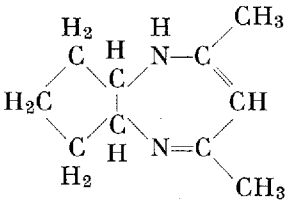
Of the two signals given by single protons that at $\delta = 7.76$ corresponds to the NH-group (N^1), that at $\delta = 4.40$ to the $\rangle\!\!=$CH-group (C^6).

For the benzo[*b*]1,4-diazepines STAAB and VÖGTLE found the symmetrical structure confirmed by the NMR-spectrum. No signals corresponding to NH-groups or a $\rangle\!\!=$CH-group were found. A signal at $\delta = 2.70$ was integrated to two protons, corresponding to a methylene group (at C^6). As the seven-membered ring is not plane the methylene group should give rise to a doublet. At 39° a singlet is found, but at −50° the singlet is broadened, showing a slight difference between the two protons.

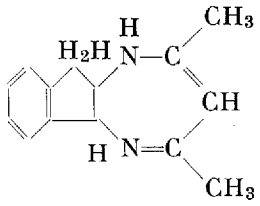
The monocation of this substance is of course unsymmetrical, but dissolved in concentrated sulphuric acid a symmetrical structure is again formed, the two NH^+-groups giving rise to a signal at $\delta = +13.4$. This signal disappears when an exchange of D^+ for H^+ has taken place.

We have prepared 5,7-dimethyl-2,3-dihydro-1,4-diazepines by condensation of acetylacetone with cyclopentylene-1,2-diamine and indanylene-

1,2-diamine, respectively. A study of the infrared spectrum of 5,7-dimetyl-cyclopenta[*b*]1,4-diazepine (XXIX) and 5,7-dimethylindano[1,2-*b*]1,4-diazepine (XXX) and the IR-spectra of a series of benzo[*b*]1,4-diazepines has confirmed that in the benzo[*b*]diazepines no absorption corresponding to a NH-stretching is found, whereas in the two "non-aromatic" diazepines an absorption at 3240–3210 cm^{-1} indicates the presence of an NH-group.



XXIX



XXX

The "non-aromatic" diazepines are, therefore, considerably stronger bases than the benzo[*b*]1,4-diazepines. Schwartzenbach and Lutz[4] have determined the pK_a-value of XXVIII to 13.8, and Lloyd *et al.*[12] indicate for this substance $pK_a = 13.4$.

The existence of two tautomeric forms of 6-mono- or unsubstituted benzo[*b*]1,4-diazepines with very different basic strengths makes it difficult to determine the real pK_a-value of one of the two forms without knowledge of the equilibrium constant of the tautomeric system. Schwartzenbach and Lutz[4] have, for the above mentioned estimation of pK_a-values, used a complicated system of potentiometric measurement of pK_a immediately after the liberation of the base from its salt, *i.e.* before the establishment of the equilibrium I $\rightleftarrows$ II. They found an initial value of $pK_a = 9.0$, which dropped to $pK_a = 4.5$ when the equilibrium had been established. This means that the equilibrium in aqueous solution is nearly quantitatively displaced towards I, a result which as mentioned above has been corroborated by spectroscopic studies, both UV, IR and NMR-spectra.

We found it possible to determine the apparent pK_a-value of the equilibrium system I $\rightleftarrows$ II, using UV-spectroscopy. As mentioned above Barlthrop *et al.*[6] found that the violet benzodiazepinium ion shows a lowintensity absorption at about 5000 Å, an absorption which the neutral molecule does not show. The absorption at a given pH will therefore be dependent on the fraction of the benzodiazepine present as benzodiazepinium ion. By measuring the absorption at different pH-values and considering the benzodiazepinium ion as an acid, the free benzodiazepine molecule as the corresponding base a plot of $D = \log I_0/I = \varepsilon \cdot c \cdot l$ against pH will allow the determination

of pK_a of the system I $\rightleftarrows$ II $\underset{OH^-}{\overset{H^+}{\rightleftarrows}}$ III (D = optical density, I_0 and I = intensity of the incident and the transmitted light, c = total concentration of (protonised and unprotonised) benzodiazepine and l the path lenth of light through the solution, in cm.

In the first approximation we disregard the equilibrium I $\rightleftarrows$ II and consider only the equilibrium between III and (I + II), *i.e.* the benzo[*b*]-diazepinium ion and the "benzo[*b*]diazepine base". We then have:

(1) $pH = pK_a + \log c_b/c_a$
where c_b is the concentration of the free benzodiazepine, c_a the concentration of the benzodiazepinium ion.

(2) $c = c_b + c_a$
c being the total concentration of benzodiazepine, calculated from the amount of benzodiazepinium salt weighed out.

(3) $pH = pK_a + \log [(c - c_a)/c_a]$
which by multiplication of the logarithmic expression with ε/c gives

(4) $$pH = pK_a + \log \frac{\varepsilon - \frac{\varepsilon \cdot c_a}{c}}{\frac{\varepsilon \cdot c_a}{c}}.$$

As c_a is the concentration of the absorbing molecules we have

(5) $D = \varepsilon \cdot c_a \cdot l$ or $\varepsilon \cdot c_a/c = D/l \cdot c = \varepsilon'$,

ε' thus being the apparent molar extinction coefficient, disregarding that only a fraction of the substance present will absorb at the wavelenth considered.

By introducing (5) in (4) we get

(6) $pH = pK_a + \log [(\varepsilon - \varepsilon')/\varepsilon']$.

By measuring D at a series of known pH-values (buffer solutions) ε' can be calculated for the pH-values considered, l and c being known. The only unknown quantities in (6) are thus pK_a and ε, the molar extinction coefficient of the benzodiazepinium ion. In determining two not interdependent sets of values of pH and ε' and introducing these values in (6) 2 equations with 2 unknown quantities will allow the calculation of pK_a and ε.

The following procedure was used:

Phosphate-buffers were prepared according to BJERRUM[15]. It was planned to dissolve the benzodiazepines in these buffer-solutions to a concentration of $10^{-4} - 10^{-5}$ *M*, but some of the benzodiazepines were not sufficiently soluble in aqueous buffers with pH above 4. We therefore used an ethanol/water buffer system with 50 % (by volume) of ethanol which allowed the preparation of solutions of all the benzodiazepines investigated up to pH about 14. The pH-values in the ethanol/water system are different from those indicated by BJERRUM for aqueous solutions and had to be determined potentiometrically, using a pH-meter calibrated by means of the aqueous buffer solutions.

a. pK_a of 5-methyl-7-phenylbenzo[b]1,4-diazepinium ion.

The absorption of $10^{-4} - 10^{-5}$ *M* solutions of this compound was measured at 5060 Å at 6 different pH-values, ε' calculated for each pH (equation (5)) and plotted against pH, see table I and fig. 1.

TABLE I. Determination of ε' for the 5-methyl-7-phenyl-benzo[*b*]-1,4-diazepinium ion.

	1	2	3	4	5	6	7
pH	−0.7	0.43	1.57	3.45	4.34	5.83	6.20
ε'	1.43	1.367	1.343	1.226	0.905	0.110	0.0594

From equation (6) it is seen that this plot is a titration curve for the diazepinium ion, and pK_a is thus pH at the point of veering, 4.7.

This graphical method is, however, not sufficiently accurate. More reliable results are obtained by inserting in (6) a series of corresponding values of pH and ε', calculating the corresponding pK_a-values and ascribing each pK_a-value a weight from 1 to 6 according to how the two points are situated on the curve drawn through all the experimental points (fig. 1). The results of this calculation are given in Table II.

TABLE II. Weighted determination of pK_a for the 5-methyl-7-phenylbenzo[*b*]1,4-diazepinium ion.

Combination ...	2–5	2–6	3–5	4–5	4–6	4–7	5–6
ε	1.368	1.366	1.348	1.290	1.232	1.271	1.191
pKa	4.63	4.77	4.65	4.84	4.82	4.89	4.85
Weight.....	1	3	3	4	5	5	6

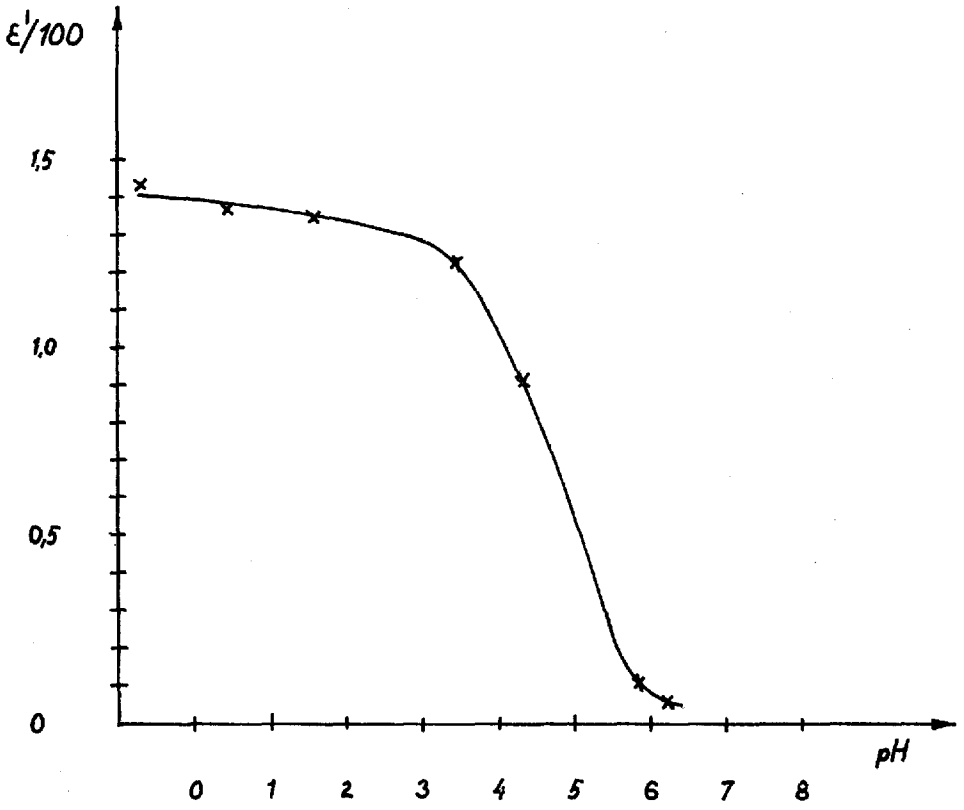


Fig. 1. Variation of ε' with pH.

The average weighted value of pK_a is 4.81, of pK_b thus 9.19.

The same procedure was followed for determining the pK_a for the 5,7-dimethylbenzo[*b*]1,4-diazepinium ion. Graphically pK_a was determined to 5.55; the weighted values were $pK_a = 5.76$, $pK_b = 8.24$.

The pK_a-value for the equilibrium mixture of 5,7-dimethylbenzo[*b*]1,4-diazepine was determined by SCHWARTZENBACH and LUTZ[4] to 4.5; for the unsymmetrical structure II the value was found to be 9.0. As it seems reasonable to locate the protolytic activity to the unsymmetrical structure, at all events in the first approximation, this means than the equilibrium constant for the equilibrium I $\rightleftarrows$ II is $10^{-4.5}/10^{-9.0} = 10^{4.5}$.

From the value 5.76 for pK_a in 50 % ethanolic solution it is seen that the equilibrium in this solvent is displaced somewhat, but not much, towards I as the equilibrium constant here is $10^{-5.8}/10^{-9.0} = 10^{3.2}$.

The spectroscopic method for determining the basic strength of the benzodiazepines is more complicated than the potentiometric titration usually applied for such determinations. The potentiometric method implies a linear dependence between the half neutralisation potentials and pK_a, which is usually found within certain limits, determined mainly by the protolytic activity of the solvent used. In order to use this linear dependence it is necessary to know the pK_a-values of at least two bases of the type considered. By plotting the half neutralisation potentials of these two bases against their pK_a-values the straight line drawn through these two points may be used for determining the basic strength of other bases of the same type, their pK_a-values being the abscissae corresponding to the half neutralisation potentials found when titrating the bases.

We have applied this method for the determination of approximative pK_a-values of the substituted benzo[*b*]1,4-diazepines listed in Table III, using the half-neutralisation potentials of the substances 3 and 6 and their pK_a-values found by the spectroscopical method for drawing the line illustrating the dependence between half neutralisation potentials and pK_a. The diazepines were dissolved in acetonitrile (0.1 millimole in 50 ml) and titrated with 0.1 *N* perchloric acid in dioxan. Table III and fig. 2 give the results.

TABLE III. Half neutralisation potentials and pK_a-values of some substituted benzo[*b*]1,4-diazepines.

Substance	Half neutralisation potential (mV)	pKa
1. 5-Methyl-7-(3,4-methylenedioxystyryl)benzo[*b*]1,4-diazepine	−134	5.2
2. 5,7-bis(3,4-methylenedioxystyryl)-benzo[*b*]1,4-diazepine ...	−230	4.4
3. 5,7-Dimethylbenzo[*b*]1,4-diazepine	− 76*	5.76*
4. 5,6,7-Trimethylbenzo[*b*]1,4-diazepine	−178	4.8
5. 5,7-Diphenylbenzo[*b*]1,4-diazepine.....	−295	3.8
6. 5.-Methyl-7-phenylbenzo[*b*]1,4-diazepine	−180*	4.81*

The points marked with an asterisk used for drawing the line.

These results are only approximate values for at least two reasons:

1). The points used for drawing the line have been fixed by using the pK_a-values found in 50 % ethanol, but the titrations were carried out in acetonitrile/dioxan where the equilibrium constant I $\rightleftarrows$ II is not known, and as shown above the equilibrium is dependent on the solvent.

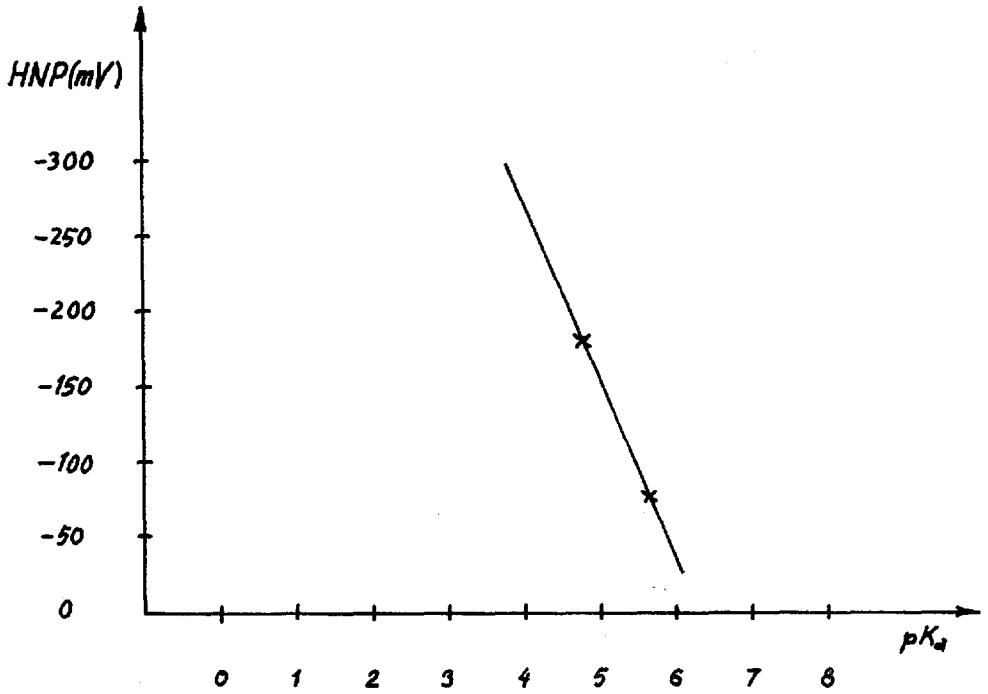


Fig. 2. Potentiometric determination of pK_a for substituted benzo[*b*]1,4-diazepines.

2). Possibly for this reason, possibly for other reasons too, the slope of the line $pK_a = f(HNP)$ is 100 mV per pK_a-unity, whereas it according to HALL[16] should be only 59 mV.

Nevertheless, we are confident that they represent the relative basic strengths of the benzodiazepines studied. The values found reflect in fact the influence expected of the electronegativity of the substituents in the seven-membered ring on the basic strength of the substances.

III. Structure of ethyl 7-phenylbenzo[*b*]1,4-diazepinyl-5-pyruvate, formed by condensation of diethyloxalate on 5-methyl-7-phenylbenzo[*b*]-1,4-diazepine

STEIMMIG[2] prepared a pyruvic ester by Claisen-condensation of diethyl oxalate on 5-methyl-7-phenylbenzo[*b*]1,4-diazepine, using sodium ethanolate as catalyst, whereas VEIBEL and HROMADKO[17] thought they obtained a substituted 5,8-diaza-benzo[*g*]azulene when potassium ethanolate was used as catalyst for the Claisen-condensation (cf. VEIBEL and ILUM NIELSEN[18]).

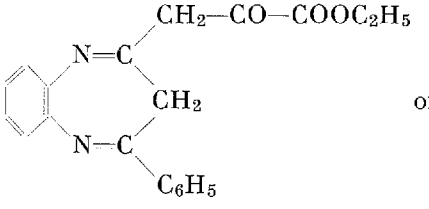
We have confirmed both types of condensation and have discussed the results when potassium ethanolate is used as catalyst. Here we discuss the results obtained when carrying out the condensation *ad modum* STEIMMIG, the main difference between the two *modi* being (1) that *ad modum* STEIMMIG the reaction mixture remains basic and the product obtained precipitates from the basic solution, whereas *ad modum* VEIBEL and HROMADKO the reaction mixture is acidified before isolating the precipitate. Besides, there are differences in (2) the amount of catalyst used and (3) the temperature, STEIMMIG using 1 mole of sodium ethanolate per mole of diethyl oxalate and operating at the reflux temperature of an ether/ethanol mixture 6:1 (by volume), VEIBEL and HROMADKO using 2 moles of potassium ethanolate per mole of diethyl oxalate and operating at the temperature of the ice-box (0–2°).

Operating *ad modum* STEIMMIG we obtained as he did a yellow precipitate with m.p. 150.5–151.5° in 50 % yield. This substance is the pyruvic ester. When the filtrate from this precipitate was acidified with acetic acid a red precipitate, identical with the substance isolated by VEIBEL and HROMADKO, is obtained. This red precipitate had not been described by STEIMMIG.

When water is added to the reaction mixture before filtering off the precipitate (the potassium salt of the end form of the pyruvic ester) the salt will dissolve. When the alkaline solution is left to stand for some time another substance precipitates. It was found to be the potassium salt of 3-(7-phenylbenzo[*b*]1,4-diazepinyl-5)-pyruvic acid, from which the free acid could be liberated by addition of acetic acid to an aqueous solution of the salt.

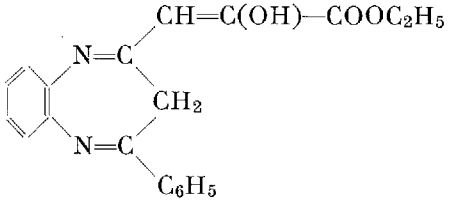
Repeating an experiment of STEIMMIG, who refluxed a methanolic solution of the yellow ester for 1 hour, we obtained, as he did, a mixture of yellow and violet crystals which could be separated by extraction with boiling ligroin, in which the yellow crystals, but not the violet, dissolved. M.p. of the violet crystals is 167.5–168.5°.

STEIMMIG assumed for the yellow ester the structure XXXI or XXXII,



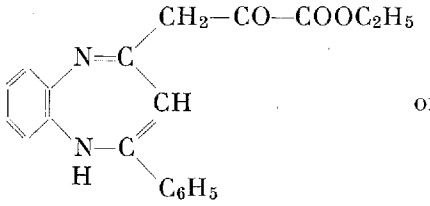
XXXI

or



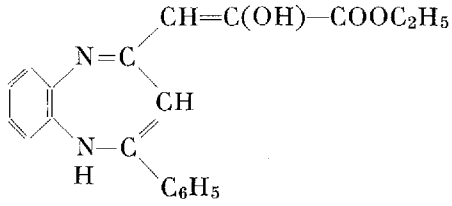
XXXII

for the violet ester the structure XXXIII or XXXIV,



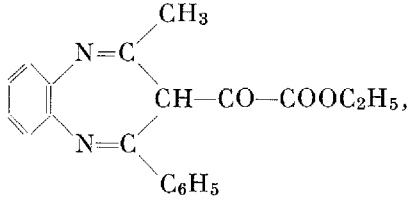
XXXIII

or

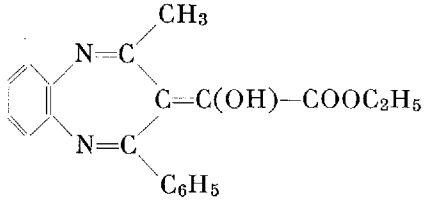


XXXIV

other possibilities, not discussed by STEIMMIG, being XXXV, XXXVI or XXXVII.

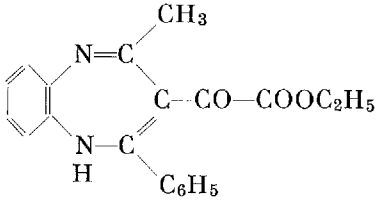


XXXV



XXXVI

or



XXXVII

IR-spectra obtained using potassium bromide technique indicated that the yellow ester in the solid state, showing neither OH- nor NH-absorption, must be either XXXI or XXXV, the violet ester, showing OH- or NH-absorption, one of the other structures.

We have tried to exclude some of these possibilities by studying the NMR-spectra of the yellow substance dissolved in deuterochloroform. The following signals were observed:

1. δ = 13.2, integrated to 1 proton, not split up.
2. δ = 8.0–7.25, fixed to 9 protons, characteristic for aromatic protons in *o*- or monosubstituted benzene nuclei.
3. δ = 6.15, integrated to 1 proton, not split up.
4. δ = 4.50–4.15, integrated to 2 protons (a quadriplet, 1331).
5. δ = 3.50, integrated to 2 protons, not split up.
6. δ = 1.50–1.25, integrated to 3 protons (a triplet, 121).

Signal 1 may be OH or NH.

Signal 2 corresponds to the aromatic protons. Their number is fixed to 9, forming the basis for the calculation of the number of protons corresponding to the other signals.

Signal 3 is a single proton at a $-C=C-$ double bond. The neighbouring carbon atoms can have no protons as the signal is not split up.

Signal 4 is in the methylene region. As it is split up to a quadruplet it must be located as neighbour to a carbon atom with 3 protons.

Signal 5 is at so low a δ-value that it might be an $-OCH_3$ group but its size shows that it must be a methylene group. The neighbouring carbon atoms have no protons as the signal is not split up.

Signal 6 corresponds to the methyl group in the ethyl radical as the triplet indicates a neighbouring group with two protons.

The signals 4 and 6 together correspond to the $-COOC_2H_5$ group.

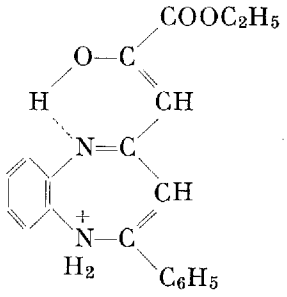
As one and only one methylene group beside the one in the ester is seen, the structures XXXI, XXXIV, XXXV, XXXVI and XXXVII must be eliminated. The structures XXXV, XXXVI and XXXVII are eliminated also because they claim the presence of a methyl group beside the one in the ester.

This leaves only the structures XXXII and XXXIII for the yellow ester dissolved in chloroform, which means that XXXI will tautomerise to XXXII or XXXIII when dissolved.

A peculiar observation was made in connection with the preparation of a perchlorate of STEIMMIGS ester (yellow form). The ethanolic-ethereal solution of the ester turned dark on addition of perchloric acid, but the perchlorate isolated was yellow. We therefore considered the possibility of the formation of a di-perchlorate, but elemental analysis showed the substance to be a mono-perchlorate.

The IR-spectrum showed differences from IR-spectra of the violet salts of other benzodiazepines. No absorption was found at 1460 cm^{-1} or at 1360 cm^{-1}, but an absorption due to the perchlorate ion (at about 1070 cm^{-1}) is visible. Besides, a broad absorption band is seen at about 3000 cm^{-1}.

The absorption at 1070 cm^{-1} means that the substance has taken up a proton. As this does not lead to a coloured cation the conditions for resonance must be different from those in the previously considered benzo[*b*]-1,4-diazepine cations. A structure like XXXVIII might explain both the absorption at 3000 cm^{-1} and the lack of resonance. A hydrogen bonding from the enolised carbonyl function to the N^4-nitrogen atom is sufficiently strong to prevent this atom from taking up the proton which, therefore, is



XXXVIII

taken up by the N^1-nitrogen atom, forming a grouping $-\overset{+}{N}H_2-C\lessgtr$. This grouping may be responsible for the absorption at 3000 cm^{-1}, which also may include an absorption caused by the $-O-H\cdots N\lessgtr$ hydrogen bond.

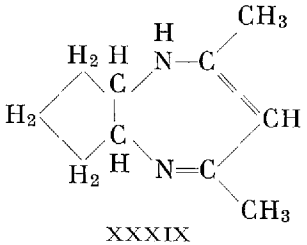
IV. Experiments aiming at the preparation of derivatives of 4,8-diazaazulenes

VEIBEL *et al.*[17, 18] having shown that derivatives of 4,9-diazabenzo[*f*]-azulene can be formed by a double Claisen-condensation of diethyl oxalate on a 5-methylsubstituted benzo[*b*]1,4-diazepine, we considered the possibility of preparing diazaazulenes not fused to a benzene nucleus by reacting a β-diketone with cyclopentylene-1,2-diamine.

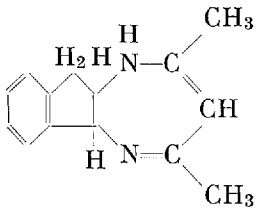
TREIBS and coworkers[19, 20], working on the preparation of azaazulenes with N in the 7-membered ring, arrived at the conclusion that owing to the greater electronegativity of nitrogen as compared with carbon a nitrogen in the 7-membered ring will cause a decrease in the aromaticity of the azulene system. PETERS[21] has expressed a similar opinion, based on calculation of the distribution of π-electrons, using HÜCKELS L.C.A.O. molecular orbital theory.

TREIBS *et al.*[19, 20, 22] succeeded in preparing benzo-monoazaazulenes with nitrogen in the 7-membered ring. The compounds showed, as expected, considerably less aromatic character than nitrogenfree azulenes. HAFNER and KREUDER[23] have prepared the unsubstituted 5-azaazulene which they describe as a substance stable dissolved in water or in organic solvents. As a solid (m.p. 35°), however, it is stable only in an inert atmosphere. It is to be expected, therefore, that 4,8-diazaazulenes will be still less aromatic and possibly not even stable.

We found it possible to prepare 5,7-dimethyl-1,2,3,3a,8,8a-hexahydro-4,8-diazaazulene or 5,7-dimethyl-2,3-dihydrocyclopenta[*b*]1,4-diazepine (XXXIX), but all attempts to dehydrogenate this compound failed.



XXXIX



XL

We then tried to increase the tendency to create an aromatic system by fusion of the cyclopentylenediamine with a benzene nucleus, using indylene-1,2-diamine instead of cyclopentylene-1,2-diamine. Here, too, we succeeded in preparing a hydrogenated diazaazulene-derivative (XL), although in a very poor yield, but as above all attempts to dehydrogenate the compound to the fully aromaticised system failed.

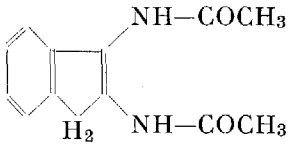
The preparation of the indanylene-1,2-diamine by reduction of indane-1,2-dione dioxime or its diacetate was extremely difficult. 6 atoms of hydrogen per molecule of the dioxime diacetate were easily taken up, but then the reduction came to a standstill. We were able to prove by NMR-spectroscopy that the substance obtained after uptake of 6 atoms of hydrogen is 1,2-diacetaminoindene (XLI). Experimental details are given below, but the evidence for the structure of the compound is given here.

A solution of the substance in dimethylsulfoxide gave the following signals:

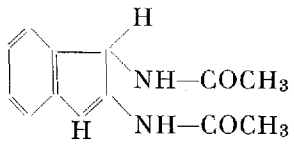
1. δ = 1.65 a double signal with 2 peaks of nearly the same size, corresponding together to 6 protons.
2. δ = 4.15 a single peak corresponding to 2 protons.
3. δ = 7.50 a single peak corresponding to 4 protons.
4. δ = 6.50 a single bond corresponding to 2 protons.

For a substance obtained from indane-1,2-dione dioxime diacetate by reduction with 6 equivalents of hydrogen the structures XLI–XLIV have to be considered.

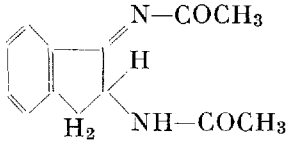
Signal 1 corresponds to two nearly identical methyl groups without hydrogen at the neighbouring carbon atoms, *i.e.* the two CH_3CO-groups.



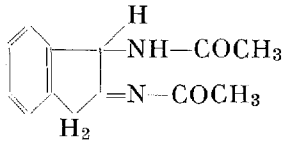
XLI



XLII



XLIII



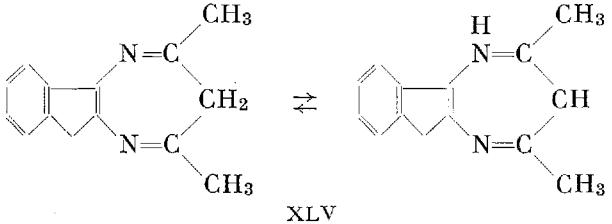
XLIV

Signal 2 corresponds in size and position to a methylene group. As it is not split up no hydrogen atom can be present at the neighbouring carbon atoms. This signal thus eliminates XLII, which contains no methylene group, and XLIII, which has a hydrogen atom at one carbon atom neighbouring the methylene group.

Signal 3 is easily interpreted as the 4 aromatic protons.

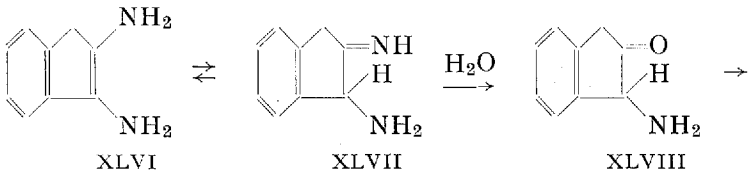
Finally, it must be concluded from signal 4, showing two nearly identical protons, that structure XLI is more likely than structure XLIV.

A substance with structure as XLI would be useful for the preparation of a diazaazulene-derivative if it could be deacetylated to the diamine. By condensation with a β-diketone this diamine should produce a 5,7-disubstituted 1,6- (or 1,4-) dihydro-benzo[*b*]-4,8-diazaazulene (XLV):

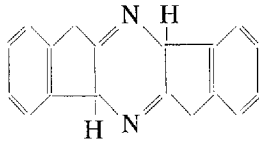


XLV

We did not succeed in isolating the indenediamine, presumably because it will immediately tautomerise to 1-iminoindane-2-amine which in acid solution easily is hydrolysed to 2-aminoindan-1-one[24]. As an α-aminoketone this substance will immediately form a pyrazine-derivative (XLVI–IL):



XLVI XLVII XLVIII



IL

Experimental part

5,7-Dimethylbenzo[*b*]1,4-diazepine, 5-methyl-7-phenylbenzo[*b*]1,4-diazepine, 5,7-diphenylbenzo[*b*]1,4-diazepine and the corresponding hydrochlorides were prepared according to STEIMMIG[2] with mp.'s as indicated by him. 5,6,7-Trimethylbenzo[*b*]1,4-diazepine was prepared both *ad modum* BARLTHROP[6] by methylation of 5,7-dimethylbenzo[*b*]1,4-diazepine with methyl iodide and *ad modum* VAISMAN[3] by condensation of *o*-phenylenediamine with 3-methylpentane-2,4-dione, the latter method being preferable to the former.

10 g of *o*-phenylenediamine (0.0925 mole) were dissolved in a mixture of 20 ml of ethanol and 10 ml of glacial acetic acid. The solution was cooled to 0° and 12 g (0.1 mole) of 3-methylpentane-2,4-dione were added dropwise. A slight rise of temperature occurred and the solution turned cherry-red. After 5–10 minutes 50 g of water and ice were added, followed by 30 ml of concentrated hydrochloric acid in several portions. Brick-red crystals separated and were collected by suction and washed with cold dilute hydrochloric acid.

To isolate the free base the salt was dispersed in 200 ml of water and the dispersion little by little added to 200 ml of 10 % aqueous sodium hydroxide. A yellow amorphous solid separated which rapidly changed to white glimmering crystals. The crystals were filtered off, washed with water and dried. Yield 12.6 g = 73 % with m.pm 77–80° which was raised to 85–86° as indicated by VAISMAN by dissolving the base in dilute hydrochloric acid and reprecipitating it by neutralisation with base.

No doubt the yellow amorphous substance is the unsymmetrical sub-

stance corresponding to II (p. 3), the white crystals the symmetrical form corresponding to I.

Attempts to prepare 5,6,6,7-tetramethylbenzo[*b*]1,4-diazepine were all unsuccessful, 2-methylbenzimidazole being the only product isolated.

Condensation of piperonal with 5,7-dimethylbenzo[*b*]1,4-diazepine

Following the indications of BARLTHROP *et al.*[6] 5.0 g (0.029 mole) of 5,7-dimethylbenzo[*b*]1,4-diazepine and 4.35 g (0.029 mole) of piperonal were dissolved in 150 ml of anhydrous ethanol containing 0.66 g (0.029 atom) of sodium. The solution was refluxed for 40 minutes. 50 ml of ethanol were then distilled off, the residue filtered when still hot, yielding 0.95 g of a substance which after recrystallisation from benzene showed m.p. 261–262°. BARTLHROP *et al.* indicate m.p. 257–258° for a bis-piperonylidene derivative of 5,7-dimethylbenzo[*b*]1,4-diazepine.

The filtrate was left for 2 days at room temperature when 2 g of a substance with m.p. 189–192° were isolated, corresponding to the mono-piperonylidene-derivative described by BARLTHROP *et al.*

As indicated above (p. 4–7) we disagree with BARLTHROP in considering these derivatives as the 5-methyl-7-methylenedioxystyrene-6-piperonylidene-benzo[*b*]1,4-diazepine and the 5,7-dimethyl-6-piperonylidenebenzo[*b*]1,4-diazepine respectively, the structures 5,7-bis(methylenedioxystyrene)benzo[*b*]1,4-diazepine and 5-methyl-7-(methylenedioxystyrene)benzo[*b*]-1,4-diazepine explaining better than the first mentioned the products of hydrolysis of the substances in question.

Condensation of ethyl oxalate with 5-methyl-7-phenylbenzo[*b*]1,4-diazepine

Ethyl 5-(7-phenylbenzo[*b*]1,4-diazepinyl)-3-pyruvate was prepared according to STEIMMIG[2]. Yellow crystals with m.p. 150.5–151.5° as indicated by STEIMMIG.

From the acidified filtrate a red substance precipitated. It was by closer study found to be identical with the 10-phenyl-4,9-diazabenzo[*f*]azulene described by VEIBEL et al.[17, 18].

300 mg of the yellow ester were refluxed for 1 hour with 5 ml of methanol. The solution turned dark and on cooling a mixture of yellow and violet crystals separated. The yellow crystals dissolved in ligroin on boiling, leaving the violet crystals undissolved. The violet crystals had m.p. 167.5–168,5° STEIMMIG (*l.c.*) indicates m.p. 166–167°.

The structures of these compounds are discussed p. 17–19.

The perchlorate of the yellow ester was prepared by dissolving the ester in a mixture of ethanol and ether and then adding an excess of 60 % perchloric acid. The solution turned dark but deposited yellow crystals with m.p. 224–225° (dec.).

Due to the yellow colour the possibility of an uptake of 2 protons was considered, but the elemental analysis* showed the substance to be a monoperchlorate.

		C	H	N	Cl
$C_{20}H_{19}N_2O_7Cl$	calc.	55.25	4.40	6.44	8.15
434.8	found	54.72	4.56	6.75	8.05

The structure of the cation has been discussed above, p. 19–20. The formation of the chelate prevents the N^4-nitrogen atom from taking part in the resonance stabilisation usually leading to the violet coloured benzodiazepinium cation.

Potassium salt of 3-(7-phenylbenzo[*b*]1,4-diazepinyl)-pyruvic acid and the free acid

2.4 g (0.061 mole) of potassium were dissolved in a mixture of 12.5 ml of anhydrous ethanol and 8 ml of anhydrous ether. 6 g (0.026 mole) of 5-methyl-7-phenylbenzo[*b*]1,4-diazepine were dissolved in the mixture, 4.5 g (0.031 mole) of diethyl oxalate were added at room temperature and the mixture kept the night over in the ice box. After addition of water (100 ml) a clear solution was obtained from which after some time yellow crystals precipitated. They were filtered off, washed on the filter with ice-cold water (which redissolved part of the crystals), dried and then purified by extraction with boiling benzene. After renewed filtration and drying 0.7 g with m.p. 225° remained. Elemental analysis indicated a potassium salt of the above named substituted pyruvic acid, crystallising with 1 mole of water.

		C	H	N	K	H_2O
$C_{18}H_{15}N_2O_4K$	calc.	59.65	4.17	7.73	10.79	4.97 %
362.4	found	58.50	4.27	7.60	11.00	5.09 %

Dried over phosphorus pentoxide in vacuum at 80° 5.09 % of water were removed.

From the benzene-solution 0.39 g of the original benzo[*b*]1,4-diazepine could be isolated.

* Elemental analyses here and in the following by Mr. PREBEN HANSEN, Chemical Laboratory of the University, Copenhagen.

2 g of the potassium salt were dissolved in 200 ml of water on the steam bath. 1 ml of glacial acetic acid was added. On cooling the substituted pyruvic acid precipitated. It was isolated by filtration, washed with dilute acetic acid, then with water and dried. M.p. 205°.

		C	H	N	E
$C_{18}H_{14}N_2O_3$	calc.	70.58	4.61	9.14 %	306.3
306.3	found	70.45	4.81	9.02 %	307 (titration with 0.1 *N* NaOH)

5,7-Dimethyl-2,3-dihydrocyclopenta[*b*]1,4-diazepine

This substance was prepared mainly according to LLOYD and MARSHALL[25] from cyclopentylene-1,2-diamine and acetylacetone.

For the preparation of the *diamine* cyclopentane-1,2-dione dioxime was prepared according to COPE *et al.*[26] and the dioxime reduced with sodium and anhydrous ethanol according to JAEGER and BLUMENDAL[27].

4 g (0.03 mole) of cyclopentane-1,2-dione dioxime were heated to reflux with 200 ml of anhydrous ethanol, and then 30 g of sodium, cut into small pieces, were added as fast as possible, forming a large ball of molten sodium. The solution turned very dark and remained dark when all sodium had reacted, but after addition of further 200 ml of ethanol and 20 g of sodium a clear straw-yellow coloured solution was obtained.

The diamine was isolated by steam-distillation. First the ethanol and then 1 liter of water, containing the amine, was collected. The distillate was slightly acidified with dilute hydrochloric acid (indicator methyl red) and then evaporated to dryness on a rotating vacuum-evaporator. Yield 3.82 g (71 %) with m.p. 292°. COPE[26] indicates m.p. 287–290°.

For further identification a dipicrate was prepared and recrystallised from aqueous ethanol. M.p. 250° (COPE indicates 233–233.5°). Equivalent weight (titration with perchloric acid in glacial acetic acid) 276, calculated 279.

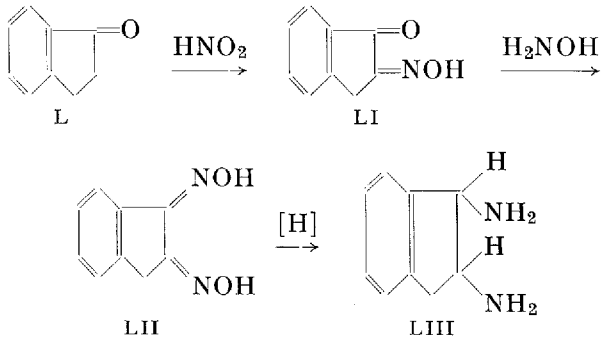
We tried to obtain the diamine by catalytic reduction of the acetylated dioxime according to VIGNEAU[28] but the result was that ammonia was liberated (compare below, indanylidene-1,2-diamine).

5,7-Dimethyl-2,3-dihydroindano[1,2-*b*]1,4-diazepine

For the synthesis of this compound a condensation of indanylene-1,2-diamine with acetylacetone presents itself as the obvious procedure. As, however, indanylene-1,2-diamine has not, to our knowledge, been described

we had to develope a method for its preparation, and here we encountered unforeseen difficulties.

As a natural way for the synthesis we tried the nitrosation of indan-1-one, oximation of the resulting indan-1,2-dione monoxime and reduction of the dioxime to the diamine (L–LIII).



The first two steps presented no serious difficulties, but for the final reduction most of the conventional methods failed.

Indan-1-one was prepared in two different ways from β-phenylpropionic acid, *viz.* either according to AMAGAT[29] via the acid chloride, which under the influence of aluminium chloride cyclises to indan-1-one, or according to KOO[30] by direct cyclisation of the acid by heating it to 70° for 85 minutes with polyphosphoric acid. The first method resulted in an overall yield of 47–48 %, the second in a yield of 72 %.

Indane-1,2-dione-2-oxime was prepared according to LEVIN *et al.*[31] by nitrosation of indan-1-one with butyl nitrite. Yield 68.5 % of a product with m.p. 206,5–207° (dec.). LEVIN *et al.* indicate darkening at 200°.

Indane-1,2-dione dioxime. For the preparation of this compound the following procedure was worked out:

35 g (0.5 mole) of hydroxylammonium chloride were dissolved in 300 ml of ethanol. 41.3 g (0.5 mole) of anhydrous sodium acetate were added, precipitating sodium chloride. The resulting suspension was added to a solution prepared by heating 54 g (0.35 mole) of indane-1,2-dione-2-oxime with 500 ml of ethanol to 70–80° with mechanical stirring. The mixture was kept at 70–80° with mechanical stirring for 20 hours and then filtered hot. The filter-cake was washed with cold ethanol and with water, leaving 26.3 g. of a white, crystalline substance with m.p. 211.5–212° (dec.). From the filtrate crystallised on cooling 9.3 g with m.p. 204–205° (dec.); total yield

35.6 g = 61 %. After evaporation of the filtrate to 200 ml followed by addition of 500 ml of water 23.1 g of a substance with m.p. 190–191° (dec.) were obtained. It was shown by IR-spectroscopy that this compound mainly consisted of the dioxime, but it contained an impurity which was not the monoxime.

For purification of the dioxime it was treated with 2 *N* sodium carbonate which removes any monoxime present. The residue was then recrystallised from ethanol.

		C	H	N
(LII) $C_9H_8N_2O_2$	calc.	61.36	4.58	15.90 %
176.2	found	61.12	4.73	15.72 %

Indanylene-1,2-diamine. For the transformation of this dioxime to the diamine reduction with sodium and ethanol (see above, p. 26), with lithium aluminium hydride and with titanous chloride was tried unsuccessfully. With sodium and ethanol a small amount of a substance with m.p. about 132° (dec.) was obtained. This substance gave a picrate with m.p. 212–214° and is possibly the expected diamine (see below, p. 30).

Treated with titanous chloride an equivalent weight of, in 3 experiments, 29.9, 29.6, and 28.8, respectively, showed that only 6 equivalents of hydrogen had been taken up and not 8 as calculated for the reduction to the diamine. From the reduced solution a red coloured substance with m.p. 121–127° (dec.) not able to form a picrate, was isolated.

We then tried the method recommended by VIGNEAU[28], catalytic reduction of the diacetate of the dioxime.

In a hydrogenation apparatus for low-pressure hydrogenation 6 g (0.034 mole) of the dioxime were added little by little to 80 ml of acetic anhydride containing 2 g of anhydrous sodium acetate. The flask was heated to 50–60° for some minutes. After cooling to room temperature 2–5 g of W-2 Raney nickel were added and a hydrogen pressure of 35 cm mercury was established. After 110 minutes at room temperature 5.43 equivalents of hydrogen per mole of dioxime had been taken up, after 190 minutes 6.4 equivalents. The hydrogenation was then interrupted.

The acetic anhydride had assumed a red colour, and a colourless substance had precipitated. The colourless substance was filtered off together with the Raney-nickel, the adhering red colour removed by washing with cold ethanol and the colourless substance separated from the Raney-nickel by extraction with boiling absolute ethanol, from which 5.8 g of a substance with m.p. 233–236° separated on cooling.

The red colour was similar to the colour resulting from the reduction with titanous chloride where 6 equivalents of hydrogen were used up. If in the reduction of the acetylated dioxime the same reduction state has been reached, the reduction product has been isolated in a yield of 74 %.

		C	H	N
$C_{13}H_{14}N_2O_2$	calc.	67.81	6.13	12.16 %
230.3	found	67.60	6.07	12.07 %

We tried to remove the acetyl groups by acid hydrolysis. 0.5 g of the substance were refluxed for 20 minutes with 5 ml of concentrated hydrochloric acid. After cooling the acid mixture was extracted twice with 5 ml of chloroform to remove impurities, and then a slight excess of 50 % sodium hydroxide solution was added, producing precipitation of a red, crystalline substance which dissolved nearly colourless in chloroform but regained the red colour when the chloroform was removed by evaporation. Yield 210 mg with m.p. 122–131° (comp. p. 28, where a similar substance was isolated from the reduction of the dioxime with titanous chloride).

The IR-spectrum of the substance indicated the presence of an associated NH-group (3278 cm^{-1}), a C=O-group (1710 cm^{-1}) and a CH_2-group (1428 cm^{-1}). It might therefore be an aminoindanone, resulting from the hydrolysis of bis-acetylaminoindene, or a transformation product of the aminoindanone, comp. the discussion p. 22–23.

The red substance is insoluble in 2 *N* sodium hydroxide but dissolves without colour in 4 *N* hydrochloric acid.

We tried to purify the red substance chromatographically on an alumina column, but the compound was decomposed. From 150 mg of the substance 75 mg of a colourless substance with m.p. 151–155°, insoluble both in 2 *N* sodium hydroxide and in 4 *N* hydrochloric acid, were obtained. This compound may, too, be one of the products mentioned p. 22.

According to the discussion of the NMR-spectrum of the main product from the reduction this is considered to be the 1,2-diacetaminoindene.

Finally we tried to reduce the remaining double bond in the 5-membered ring by using a palladium/carbon catalyst as recommended by HARTUNG[32]. The catalyst was prepared as indicated in [33].

5 g (0.0217 mole) of 1,2-bis-acetaminoindene were dispersed and partially dissolved in 75 ml of anhydrous ethanol (magnetically stirred). 2 g of a 10 % palladium/carbon catalyst were added and the mixture hydrogenated at room temperature at an overpressure of hydrogen corresponding

to 50 cm of water. After 15 hours the theoretical amount of hydrogen had been taken up.

The catalyst was filtered off and washed with ethanol and water. Filtrate + washings were combined and evaporated in a rotating vacuum evaporator, leaving 4.5 g of a colourless substance with m.p. 196–201° which on recrystallisation from ethanol could be raised to 209–210°. Yield 2.75 g = 55 %.

According to the amount of hydrogen taken up the substance should be 1,2-bis-acetaminoindane, and elemental analysis was in agreement with this assumption.

		C	H	N
$C_{13}H_{16}O_2N_2$	calc.	67.21	6.94	12.06 %
232.3	found	67.05	7.06	12.23 %

Indanylene-1,2-diammonium dichloride, dipicrate and the free indanylene-1,2-diamine. 1.5 g of 1,2-bis-acetaminoindane were refluxed with concentrated hydrochloric acid for 3 hours. The solution was then evaporated to dryness in a rotating vacuum evaporator. The residue was dissolved by boiling it with 10 ml of anhydrous ethanol and precipitated after cooling by addition of ether. This procedure was repeated, but elemental analysis showed that it was not possible to isolate the pure dichloride in this way.

Hoping that it might be easier to obtain a pure dipicrate a solution of the dichloride was added to an aqueous solution of picric acid. A yellow picrate precipitated which after repeated recrystallisations from ethanol showed m.p. 215–216° (cf. the picrate mentioned p. 28). Elemental analysis could be interpreted as a not quite pure dipicrate crystallising with 3 moles of water.

		C	H	N
$C_{21}H_{24}N_8O_{17}$	calc.	38.19	3.66	16.97 %
660.5	found	39.25	3.93	16.60 %

The free diamine was liberated from an aqueous solution of 200 mg of the dichloride by adding an excess of 2 *N* sodium hydroxide, extracting the alkaline solution with ether, which removed a small quantity of a greenish substance, then with chloroform, from which after evaporation 75 mg of a nearly colourless substance were isolated, sintering at 139° and being completely molten at 153–154°.

5,7-Dimethyl-2,3-dihydro[1,2-*b*]indano-1,4-diazepinium perchlorate

We tried to prepare this compound by a method analogous to one indicated by SCHWARTZENBACH and LUTZ[34].

0.1 g of indylene-1,2-diamine (m.p. 153–154°) was heated in an oil-bath for 2 minutes with 5 drops of acetylacetone, after which, with 10 second intervals, 4 drops of glacial acetic acid were added. The heating was continued for 10 minutes.

After cooling the mixture was dissolved in 3 ml of water. On addition of 0.2 ml of 60 % aqueous perchloric acid a yellowish oil separated. The reaction mixture was shaken with 5 ml of ether which caused crystallisation of the oil. The crystals were filtered off, washed with a few ml of cold ether and dried. Yield 90 mg of a yellowish-white substance with m.p. 164–167° which after two recrystallisations from water was raised to 167–169°.

Its composition as the substance wanted was verified by elemental analysis.

		C	H	N	Cl
$C_{14}H_{17}N_2O_4Cl$	calc.	53.76	5.48	8.96	11.34 %
312.8	found	53.17	5.55	9.04	11.35 %

Aromatisation of the partially hydrogenated benzo-4,8-diazaazulene was tried, but without success. We examined all usually applied methods for dehydrogenation of partially hydrogenated azulenes or azaazulenes with *N* in the 5-membered, ring, *vic.* chloroanil[35, 36], sulphur[37], palladium (combined with cinnamic acid as hydrogen acceptor[38]), but without obtaining any indication of the formation of a 4,8-diazaazulene.

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