AZEPINONES

II.* SYNTHESES OF SUBSTITUTED PYRIDAZINES

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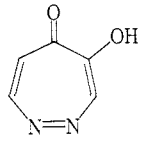
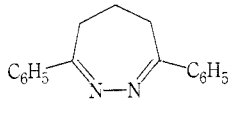
Summary

Two attempted synthetic routes to diphenyldiazatropones are described. Cyclization with hydrazine of 2-oximino-1,5-diphenylpentane-1,5-dione (IV) yielded substituted pyridazines rather than perhydrodiazepines. Oximination of the diphenyldihydrodiazepine (II) was successful, but attempts to dehydrogenate the ring proved only promising. A new and fully conjugated 10 π-electron system, the pyridazotriazole (VII), is described, as well as some unexpected rearrangements of the oxime (V).

Diazatropolones of type (I) as well as azatropolone itself are as yet unknown despite numerous reported attempts to synthesize them. There are two major synthetic routes which might be expected to yield workable quantities of precursors for diazatropolones. These are (i) cyclization of acyclic precursors of suitable chain length and substitution pattern, and (ii) conversion of a preformed perhydrodiazepine system. Of the two possibilities, the latter would seem more likely to succeed in the synthesis of compounds such as (I). The dihydrodiazepine (II) has been synthesized by Overberger[1] in good yield by cyclizing 1,5-diphenylpentane-1,5-dione (III) with



(I)



(II)

$C_6H_5COCH_2CH_2CH_2COC_6H_5$

(III)

$C_6H_5COC(NOH)CH_2CH_2COC_6H_5$

(IV)

aqueous hydrazine, and attempts to utilize (II) in further transformations to a tropolonoid system are outlined here.

Direct allylic oxidation of (II) by conventional reagents such as manganese dioxide under a variety of reaction conditions gave unchanged material and small yields of (III), whilst selenium dioxide produced high yields of (III) but no oxidation products with the ring intact. Allylic halogenation resulted in rearrangements of the ring system.[2]

* Part I, *J. chem. Soc.*, 1962, 3712.

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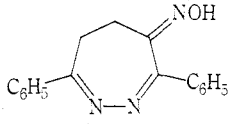
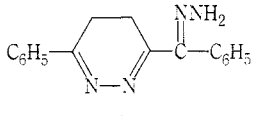
[1] Overberger, C. G., and Monagle, J. J., *J. Am. chem. Soc.*, 1956, **78**, 4470.

[2] Amiet, R. G., Johns, R. B., and Markham, K. R., *Chem. Commun.*, 1965, 128.

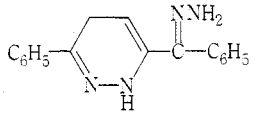
Oxime groups have commonly been used as potential carbonyl groups and hence the acyclic diketone (III) was oximinated before cyclization. Oximination was later used to substitute the preformed ring in (II). The diketone (III) was most readily oximinated under alkaline conditions to give the solid oxime (IV); acid conditions invariably yielded an oil, although this oil gave all the reactions of the solid oxime and in the infrared differed only in that the carbonyl at 1656 cm^{-1} was shifted from 1669 cm^{-1} in the solid oxime. Varying cyclization procedures carried out with hydrazine led not to the desired compound (V), but instead to pyridazine derivatives in high yields.



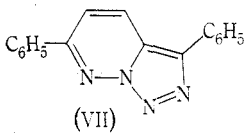
(V)



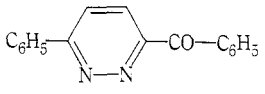
(VI)



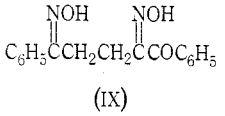
(VIa)



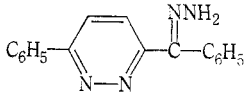
(VII)



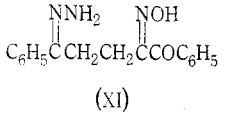
(VIII)



(IX)



(X)



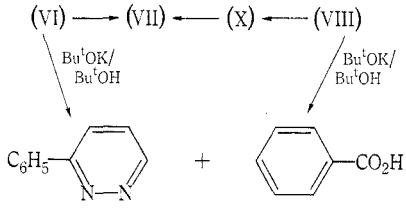
(XI)

Employing excess hydrazine and reaction conditions most favourable to the formation of (II), the hydrazone (VI) was obtained (22% yield) as well as the bicyclic compound (VII) (45% yield). Benzaldehyde condensed with (VI) to give an azine in which the heterocyclic ring had oxidized to the fully aromatic pyridazine system. The dihydropyridazine (VI) has been isolated only from reactions in which excess hydrazine, engendering reducing conditions, was present. Dihydropyridazines are known to be sensitive to mild oxidizing conditions[3] and, in keeping with the formulation for (VI), warming in solvent oxidized this compound, but because of the hydrazone substituent the end product isolated was always the bicyclic system (VII). The n.m.r. spectrum of (VI) suggests that the true structure is (VIa), at least in deuterochloroform solution, and the resonance assignments are as follows: τ 2·2–2·9 (10 benzenoid protons); τ 0·5 (ring NH); a broad maximum τ 5–5·75 (NH_2 protons) with a superimposed multiplet at τ 5·63 (HC=C); the doublet at τ 6·87 (J 3 c/s) is assigned to the methylene group at position 5 on the assumption that the methylene group at position 4 in (II) resonates at τ 6·76. The mass spectrum of (VI) confirms

[3] Zimmermann, B. G., and Lochte, H. L., *J. Am. chem. Soc.*, 1938, **60**, 2456; Elderfield, R. C., "Heterocyclic Compounds." Vol. 6, p. 110. (John Wiley: New York 1957.); Rodd, E. H., "Chemistry of Carbon Compounds." Vol. 4B, p. 1204. (Elsevier: Amsterdam 1959.)

the molecular weight; the fragmentation pattern is explicable in terms of the proposed structure and will be reported on fully in a later paper.

When 1 equiv. of hydrazine was employed in the cyclization of (IV), the ketone (VIII) and compound (VII) were isolated. If acetic acid was substituted for mineral acid in the cyclization reaction, the mixture of products was more promising in that a 3% yield of the required oxime (V) was obtained together with a 20% yield of each of (VIII) and (IX), and a 15% yield of (VII). The ketone (VIII) has not been previously reported. It readily formed an hydrazone (X) which reacted with benzaldehyde to give the same azine as was prepared from (VI). The hydrazone (X) was reduced to the known[4] 3-benzyl-6-phenylpyridazine. These interconversions summarized in Scheme 1, together with the data described below for the alcohol (XV),



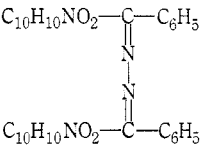
Scheme 1

substantiate structure (VIII). Acid hydrolyses of (VI) and (X) yielded only (VII), a reaction path energetically favoured over that leading to (VIII); but in strongly basic hydrolyses an alternative mechanism was found to operate. When (VI) was treated with potassium t-butoxide in t-butanol for a short time only, the ketone was isolated almost quantitatively, but if the reaction was prolonged in the presence of oxygen, both (VI) and (VIII) reacted to give the known[5] 3-phenylpyridazine and benzoic acid. The mechanism of oxidation by oxygen under these experimental conditions has been well established[6] and the reaction, in this case, should lead to 3-phenyl-6-pyridazone. It is suggested, therefore, that the actual mechanism is one of a reverse Claisen condensation facilitated by the electron-deficient pyridazine ring stabilizing the intermediate anion.

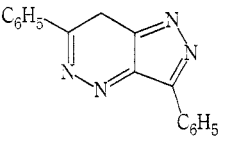
The formation of the pyridazine derivatives in these condensations is understandable mechanistically. The first step is hydrazone formation by reaction at position 5 of (IV) and confirmed by the isolation of (XI) from a reaction under slightly acid conditions at 0°, or better at a basic pH when up to an 80% yield was obtained. Compound (XII) was obtained if alkaline conditions, which led preferentially to azine formation,[7] were used. The second step in the cyclization involves ring closure at position 1 in (XI) to form (V), and this did occur to a maximum yield of 5%. The preferred reaction is to take the alternative pathway leading to the sterically favoured six-membered ring. Displacement of the oximino group is

[4] Borsche, W., and Klein, A., *Liebigs Ann.*, 1941, **548**, 74.
[5] Gabriel, S., and Coleman, J., *Ber. dt. chem. Ges.*, 1899, **32**, 395.
[6] Doering, W. von E., and Haines, R. N., *J. Am. chem. Soc.*, 1954, **76**, 482.
[7] Barton, D. H. R., O'Brien, R. E., and Sternhell, S., *J. chem. Soc.*, 1962, 470.

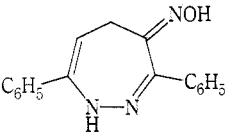
aided here by the reduced electrophilicity of the carbonyl at position 1, and the formation of a fully stabilized heteroaromatic ring system. Accordingly, (VIII) is a major product of cyclization reactions. The formation of the dioxime (IX) can be rationalized by an increase in concentration of hydroxylamine, liberated by displacement from (IV) through the preferential formation during reaction of (VII), which alters the initial ratio of hydrazine/(IV). Clearly, oximination α to the carbonyl group, with consequent changes in hybridization, predisposes the system on several grounds to cyclize to a six-membered ring.



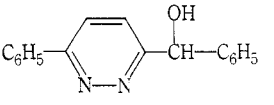
(XII)



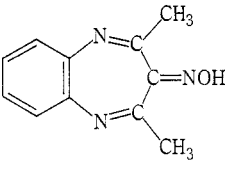
(XIII)



(XIV)



(XV)



(XVI)

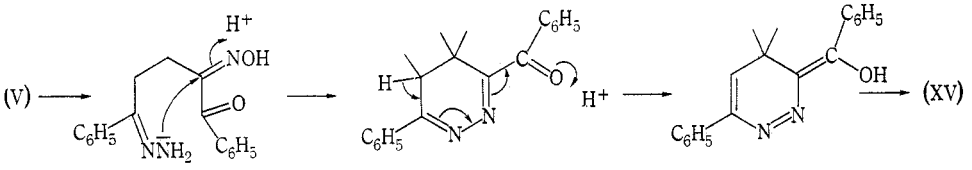
Compound (VII), 3,6-diphenylpyridazo[3,2-*c*]-[1,2,3]-triazole, is novel and arises from reactions, amongst others, when either (VI) or the hydrazone (X) are heated in ethanol. The high yields suggest the favourable nature of this intramolecular reaction. The molecular weight was confirmed by mass spectrometry. The i.r. spectrum contains no NH absorption and the u.v. spectrum shows a shift to longer wavelengths over a compound such as (X). Two structures, (VII) and (XIII), may be written to account for these facts. Structure (XIII) is eliminated by the n.m.r. spectrum which shows no protons resonating above τ 3·0. The pyridazine ring is preformed in (X), and it is unlikely that ring opening would occur in the nucleophilic addition of the hydrazone group to form the bicyclic system. The n.m.r. spectrum ($CDCl_3$ and $(CD_3)_2SO$ mixture) shows two singlets at τ 1·24 and 1·40 which together integrate for one proton, and a complex series of multiplets from τ 1·8 to 2·6 integrating as expected for 11 protons. Structure (VII) best accounts for the physical data and represents a fully conjugated, bicyclic system of 10 π-electrons.

When cyclization of suitable acyclic precursors failed to provide a synthetic route to derivatives of (I), oximination of the preformed ring in (II) was tried. Oximination of (II) was achieved by using butyl nitrite and acetyl chloride or concentrated hydrochloric acid in benzene to yield (V). The u.v. spectrum of (V) (maxima at 259–271 and 275–308 mμ) showed only a slight movement to longer wavelengths when compared with that for (II) (maximum at 260–290 mμ). The i.r. spectrum showed absorption at 3247 cm^{-1} ascribed to the >NOH group, and

this was not present in the spectrum of the derived acetate; instead there was a new absorption at 1770 cm^{-1} consistent with an *O*-acetyl of an oxime.[8] The n.m.r. spectrum of (V) could not be determined because of solubility difficulties, but the spectrum of the acetate showed, besides the benzenoid protons, a three-proton singlet at τ 8·00 (CH_3CO); the expected triplet at τ 7·26 (J 6·9 c/s) for the methylene at position 5 as well as a broad two-proton absorption about τ 6·7 for the methylene at position 6. It is suggested that the broadening of this last absorption results from proton exchange through an intermediate such as (XIV).

Attempts to provide chemical evidence that no rearrangements had occurred during oximination revealed the sensitivity of (V) to both acid and base. Aqueous alkaline hydrolysis of (V) gave a 70% yield of the oxime of 2,3-diphenylcyclopent-2-enone. This rearrangement requires initial hydrolysis at C6 with elimination of nitrogen and a final condensation to form the cyclopentenone oxime. Acid hydrolysis did not lead to the expected pentanetrione, but instead to the alcohol (XV). The following evidence is the basis for its formulation. The u.v. spectrum (max. 255 mμ) suggests a system less conjugated than 3,6-diphenylpyridazine (max. 262 mμ). The i.r. spectrum possessed all the maxima typical of the pyridazine ring[9] as well as one at 3185 cm^{-1} consistent with an hydroxyl group. The n.m.r. spectrum, apart from the benzenoid protons and the two assigned to the pyridazine ring, showed broad singlets at τ 4·2 and τ 6·67 assigned to the methine and hydroxyl protons respectively. The mass spectrum confirmed the molecular weight and showed a metastable peak proving the transformation, by loss of H_2 from the parent ion, to M−2, a transformation characteristic of a secondary hydroxyl group. The alcohol (XV) was oxidized to the ketone (VIII), which in turn could be reduced back to (XV).

The formation, by acid hydrolysis of (V), of the fully oxidized pyridazine ring system with the reduced secondary alcohol substituent, contrasts with the situation found in the cyclization reactions. In the former case the reaction conditions are not reducing and a reasonable pathway for the transformation is outlined in Scheme 2 in which an oxidation step is not invoked.



Scheme 2

Compound (V) is formally one oxidation step away from the oxime of a diazepinone. Since acid hydrolysis of the oxime could not be readily achieved, and in view of the failure[10] to hydrolyse the oxime (XVI), this step was not pursued but rather attempts were made to dehydrogenate the system in the expectation

[8] Exner, O., and Horak, M., *Collin Czech. chem. Commun.*, 1959, **24**, 2992.

[9] Amiet, R. G., and Johns, R. B., unpublished data.

[10] Barltrop, J. A., Richards, C. G., Russell, D. M., and Ryback, G., *J. chem. Soc.*, 1959, 1132.

that greater chemical stability might be found in the fully conjugated triene. Neither selenium dioxide nor bromine proved useful oxidizing agents. The most promising reaction was oxidation with chloranil in refluxing toluene. The isolated solid was shown to be a mixture by thin-layer chromatography, and a mass spectral analysis suggested 30% of the solids to be (V). In the spectrum there was a mass peak two units less than for (V), which was absent in the mass spectrum of purified (V). Alternative oxidation procedures are under consideration.

Experimental

Oximation of 1,5-Diphenylpentane-1,5-dione (III)

(i) The diketone (III) (3 g) was dissolved in ethanol (80 ml) in which sodium (0·3 g) had been dissolved. The solution was cooled to 10° and freshly prepared butyl nitrite (1·25 g) added slowly. The mixture was allowed to react for 3 hr at 0° and overnight at 20° and then poured on crushed ice (150 g). The unchanged diketone was filtered off, the solution neutralized with HCl, and after standing a further 12 hr the precipitate of *oxime* (IV) (2·6 g) was collected, chromatographed in benzene over silica, and crystallized from benzene/light petroleum (b.p. 40–60°) for analysis, m.p. 94° (Found: C, 72·7; H, 5·55; N, 5·0. $C_{17}H_{15}NO_3$ requires C, 72·6; H, 5·4; N, 5·0%). ν_{max} (KCl disk) 3257m, 3100w, 2940w, 1689s, 1669s, 1597w, and 1582w cm^{-1}.

(ii) Freshly distilled amyl nitrite (0·52 g) in diethyl ether (10 ml) was added dropwise over a period of 1 hr to the diketone (III) (1·0 g) dissolved in a mixture of ethanol (18 ml), diethyl ether (10 ml), and conc. HCl (6 ml). The temperature was kept at 40°. The precipitated ammonium chloride formed by neutralization with ammonia (*d* 0·880) was filtered off and water added. The aqueous layer was separated, ether extracted, and the solvent ether removed to give an oil which distilled at 90° (10^{-3} mm). This oil gave all the reactions of the solid oxime (IV) described above.

Reaction of the Oxime (IV) with Hydrazine

(i) The oxime (1·0 g) was added to a mixture of ethanol (25 ml), conc. HCl (0·2 ml), and 100% hydrazine hydrate (0·4 ml), and the whole refluxed for 2 hr, after which the resultant solution was poured on crushed ice (600 g). The fine precipitate of *hydrazone* (VI) was filtered off and crystallized from ethanol for analysis, m.p. 156–157°. (VI) gave a red colour with $FeCl_3$ solution (Found: C, 73·6, 73·4; H, 6·0, 6·0; N, 20·2, 20·4. $C_{17}H_{16}N_4$ requires C, 73·9; H, 5·8; N, 20·3%). ν_{max} (KCl disk) 3407m, 3311w, 3226w, 1620w, 1592w, 1563w, 1490w, and 1447m cm^{-1}. λ_{max} (EtOH) (at 5°) 257, 295sh mμ (log ϵ 4·27, 3·95). λ_{max} (EtOH) (70° for 3 days) 270, 323sh mμ (log ϵ 4·38, 3·63). A mass spectral determination of the molecular weight gave 276.

Continuous ether extraction of the filtrate above gave, on removal of the solvent, a yellow crystalline *solid* (0·4 g) which crystallized from ethanol/chloroform to give an analytical sample of (VII), m.p. 254° (Found: C, 74·7, 75·0; H, 4·4, 4·6; N, 20·6. $C_{17}H_{12}N_4$ requires C, 75·0; H, 4·4; N, 20·6%). ν_{max} (KCl disk) 3100w, 1600m, 1555m, 1515m, 1475m, 1447m, 1416m, 1316m, 1235m, 1143m, 1071w, 1026w, 1003m, 993m, 925w, 913w, 833w, 777m, 768m, 750w, 735s. and 690s cm^{-1}. λ_{max} (EtOH) 242, 275, 355 mμ (log ϵ 4·1, 4·4, 3·3). The n.m.r. spectrum determined in $(CD_3)_2SO$ (60 mc/s) showed maxima at τ 0·9, 1·08, (1 proton) and τ 1·56–2·40 (11 protons). A mass spectral molecular weight determination gave a value of 272.

(ii) (1) The liquid oxime (3·5 g) in ethanol (80 ml) was refluxed for 1½ hr with conc. HCl (0·16 ml) and 100% hydrazine hydrate (0·6 ml; 1 mol. propn.) and the reaction mixture was then poured on crushed ice (500 g). The semi-solid brown precipitate was dissolved in benzene and chromatographed over silica gel. Unchanged oxime (0·3 g) was followed in successive fractions by a pale yellow crystalline solid. This solid, *6-benzoyl-3-phenylpyridazine* (VIII), sublimed at 100° (10^{-3} mm) and was crystallized from benzene/light petroleum (b.p. 60–80°) for analysis, m.p. 126° (Found: C, 78·2; H, 4·7; N, 10·7. $C_{17}H_{12}N_2O$ requires C, 78·4; H, 4·7; N, 10·8%). ν_{max} (KCl disk) 3067w, 1669s, 1595m, 1570m, 1490w, 1447m, 1403m. λ_{max} (EtOH)

203, 220sh, 280–288 mμ (log ε 4·46, 4·05, 4·20). Increasing the polarity of the eluent to chloroform/benzene (4 : 1) yielded compound (VII) (0·2 g), and more polar solvent mixtures eluted intractable oils (1·6 g).

(ii) (2) When the crystalline oxime (0·6 g), ethanol (20 ml), 100% hydrazine hydrate (0·12 ml; 1 mol. propn.), and glacial acetic acid (1 ml) were refluxed together and worked up as for method (ii) (1), the following were isolated: ketone (VIII) (0·2 g) and compound (VII) (0·1 g).

(iii) The oxime (0·2 g) was dissolved in ethanol (7 ml) and glacial acetic acid (0·3 ml). To this solution, 100% hydrazine hydrate (0·04 ml) was added and the solution was stood aside for 3 days at room temperature. The solution was then neutralized, solvent removed under vacuum, and the residue taken up in benzene and chromatographed over silica gel. Benzene eluted ketone (VIII) (0·04 g) and compound (VII) (0·03 g). Chloroform/benzene (1 : 1) eluted a white crystalline solid (0·006 g), m.p. 237°, which proved to be identical with compound (V) described fully below. Subsequent fractions, using this eluent, contained the *dioxime* (IX) (0·04 g) which crystallized well from benzene for analysis, m.p. 158° (Found: C, 69·0; H, 5·5; N, 9·4. $C_{17}H_{16}N_2O_3$ requires C, 68·9; H, 5·4; N, 9·4%). ν_{max} (KCl disk) 3330m, 3086w, 2920w, 1661s, 1592w, 1570w cm^{-1}. More polar solvents eluted only oils.

Reaction of Hydrazine with 6-Benzoyl-3-phenylpyridazine

The ketone (VIII) (0·1 g) in ethanol (20 ml) was refluxed with 100% hydrazine hydrate (0·15 ml) for 1½ hr. When the resulting solution was subsequently evaporated, white crystals of the derived *hydrazone* (X) were isolated and crystallized for analysis to m.p. 161° (Found: C, 73·4; H, 5·25. $C_{17}H_{14}N_4$ requires C, 74·4; H, 5·15%). ν_{max} (KCl disk) 3413m, 3322w. 3226w, 1626w, 1570m, 1534m. λ_{max} (EtOH) 264, 303 mμ (log ε 4·27, 4·20).

When refluxing was prolonged for 6 hr the compound (VII) was isolated, but no hydrazone. The hydrazones (X) and (VI) were converted quantitatively into (VII) by refluxing in ethanol for from 2 to 6 hr.

Reaction of Benzaldehyde with Compounds (VI) and (X)

A solution of (VI) (0·2 g) in ethanol (15 ml) was refluxed with benzaldehyde (0·1 g) for 20 min. On working up, the azine was obtained as yellow *needles* which were crystallized from aqueous ethanol for analysis, m.p. 173° (Found: C, 79·1; H, 5·25; N, 15·2. $C_{24}H_{18}N_4$ requires C, 79·5; H, 5·1; N, 15·5%). ν_{max} (KCl disk) 1613m, 1580m cm^{-1}. This azine was identical with that obtained from allowing (VIII), benzaldehyde, and 100% hydrazine hydrate to react together.

When hydrazone (X) was treated with benzaldehyde as above, the same azine was obtained as described above. Their identity was established by m.p., mixed m.p., and the coincidence of their i.r. spectra.

Wolf–Kishner Reduction of (VIII)

The ketone (VIII) (0·1 g) was refluxed in ethylene glycol (8 ml) with 100% hydrazine hydrate (0·25 ml) and sodium (0·4 g) for 10 hr. The mixture was diluted with water, the precipitate (0·005 g) was filtered off, and was recrystallized from light petroleum, b.p. 40–60°, to give colourless crystals of 3-benzyl-6-phenylpyridazine of m.p. 145° (lit.[4] m.p. 142°). ν_{max} (KCl disk) 3096w, 1585w, 1543w, 1493m, 1449m, 1418s, 1111w, 1074w, 1031w, 1010w, 913w, 863w. 833w, 780w, 762m, 748s, 710s, 700s, 695s cm^{-1}. λ_{max} (EtOH) 253 mμ (log ε 4·0).

Hydrolysis of (VI) to (VIII)

The hydrazone (VI) (0·08 g) was dissolved in t-butanol (6 ml) and KOBu^t solution (2 ml; 0·001M in Bu^{t}OH) added. The reaction solution was stood for 1 hr in a nitrogen atmosphere. After neutralization and working-up, the precipitate (0·07 g) had m.p. 125° and showed no depression of m.p. when admixed with authentic (VIII).

Potassium t-Butoxide Oxidation of (VI) and (VIII)

(i) The hydrazone (VI) (0·3 g) was dissolved in Bu^tOH (15 ml) and $KOBu^t$ solution (5 ml) was added to give an orange solution through which a stream of oxygen was bubbled for 1½ hr. A strong smell of NH_3 was apparent in the effluent gases. The reaction solution was stood aside overnight, the solvent was then removed under vacuum, water added, and the solution ether-extracted. From the ether extract 3-phenylpyridazine (0·17 g) was obtained and which was crystallized from hot light petroleum (b.p. 40–60°) as white platelets, m.p. 105° (picrate m.p. 130°). These data agreed with those in the literature[5] for 3-phenylpyridazine (Found: C, 77·4; H, 5·2; mol. wt. (Rast), 156. Calc. for $C_{10}H_8N_2$: C, 76·9; H, 5·2%; mol. wt., 156). ν_{max} (KCl disk) 1572m, 1493w, 1449m, 1429m, 1370m, 1312w, 1153w, 1100m, 980m, 925w, 826m, 763s, 746s, 696s cm^{-1}. λ_{max} (EtOH) 250 mμ (log ϵ 4·14). N.m.r. spectrum $(CD_3)_2SO$ at 60 Mc/s showed maxima at τ 0·62, 0·65, 0·71, 0·73 (doublet of doublets) (2 protons), and multiplets (10 protons) between 1·48 and 1·95, and 2·08 and 2·65.

When the remaining aqueous layer was acidified and again ether-extracted, removal of the solvent and crystallization of the solid from light petroleum (b.p. 40–60°) yielded benzoic acid (0·06 g), m.p. 121°, undepressed on admixture with an authentic sample.

(ii) Using the method described above, the ketone (VIII) (0·075 g) yielded 3-phenylpyridazine (0·045 g) and benzoic acid (0·025 g). Both compounds were identified by m.p. and mixed m.p., and comparison of i.r. spectra with samples obtained from reaction (i), above.

Preparation of Hydrazone (XI) and Azine (XII)

(i) The oxime (IV) (0·2 g), triethylamine (2·5 ml), and 100% hydrazine hydrate (0·05 ml) were refluxed in ethanol for 2½ hr. Evaporation of the solvent and crystallization of the solid (0·2 g) from ethanol for analysis yielded pale yellow crystals of *hydrazone* (XI), m.p. 170° (Found: C, 69·0; H, 5·8; N, 14·1. $C_{17}H_{17}N_3O_2$ requires C, 69·1; H, 5·8; N, 14·2%). ν_{max} (KCl disk) 3450m, 3322w, 3226w, 3077w, 2778m (br), 1663s, 1640m, 1592w cm^{-1}.

(ii) The oxime (IV) (0·3 g), 100% hydrazine hydrate (0·06 ml), and acetic acid (0·05 ml), were brought to solution in ethanol and were stood at 0° for 15 hr. Working-up in the usual way yielded (XI) (0·18 g) and (VII) (0·04 g).

(iii) When the oxime (IV) (0·35 g) and 100% hydrazine hydrate (0·08 ml) in ethanol (8 ml) were refluxed for 1½ hr the only product isolated, in an 80% yield, was (XI).

(iv) In method (i) above, if 0·66% ethanolic KOH replaced the triethylamine, and the product was isolated by extraction with ether, the *azine* (XII) (0·13 g) was obtained and was crystallized from benzene/ethanol for analysis to m.p. 196° (dec.) (Found: C, 73·3; H, 5·7; N, 10·0. $C_{34}H_{30}N_4O_4$ requires C, 73·1; H, 5·4; N, 10·0%). ν_{max} (KCl disk) 3226m, 3086w, 2915w, 1663s, 1600m, 1567w cm^{-1}.

Cyclization of (XI)

A solution of (XI) (0·1 g) in ethanol (10 ml) containing glacial acetic acid (0·4 ml) was stood at room temperature for 4 days. After working up in the usual way, the residue was chromatographed in benzene over silica gel. The ketone (VIII) (0·31 g) was isolated from the benzene-eluted fractions, and compound (V) (0·005 g) was eluted when chloroform/benzene (1 : 4) was used. The latter compound, m.p. 237°, had an i.r. spectrum identical with compound (V) described below.

Preparation of (V)

The diazepine (II) (0·73 g) was dissolved in benzene (25 ml), acetyl chloride (10 drops) added, and to the mixture butyl nitrite (0·3 g) in benzene (25 ml) was added dropwise over 30 min. The reaction mixture was stirred for 1 hr and then the precipitate of *5,6-dihydro-4-oximino-3,7-diphenyl-4H-1,2-diazepine* (V) (0·57 g) was collected and crystallized from benzene for analysis, to m.p. 238° (dec.) (Found: C, 73·4; H, 5·3; N, 14·7. $C_{17}H_{15}N_3O$ requires C, 73·6; H, 5·4; N, 15·2%). The molecular weight found by mass spectral determination was 277. ν_{max} (KCl disk) 3247s, 3077w, 2915w, 1585w, 1558m, 1538m cm^{-1}. λ_{max} (EtOH) 259–271 and

275–308 mμ (log ε 4·08, 4·07). The same product was obtained if conc. HCl (7 drops) replaced the acetyl chloride. The yield was then 63%.

Acetylation of (V) was achieved with acetic anhydride/pyridine in the usual way. The *acetate* crystallized from ethanol for analysis to m.p. 176° (Found: C, 71·0; H, 5·4; N, 12·8. $C_{19}H_{17}N_3O_2$ requires C, 71·4; H, 5·4; N, 13·2%). ν_{max} (KCl disk) 3077w, 2907w, 1770s, 1618w, 1580w, 1550m cm^{-1}. λ_{max} (EtOH) 256–262, and 300–308 mμ (log ε 4·29, 4·31).

Reaction of (V) with Alkali

The oxime (V) (0·2 g) was refluxed with 10% aqueous NaOH (50 ml) for 2½ hr. When the mixture was cold, the solid (0·125 g) was collected and crystallized from ethanol to m.p. 254–258° (dec.). 2,3-Diphenylcyclopent-2-en-1-one oxime[11] is quoted as 257–258° (dec.) (Found: C, 82·1; H, 6·1; N, 5·3. Calc. for $C_{17}H_{15}NO$: C, 81·9; H, 6·1; N, 5·6%). ν_{max} (KCl disk) 3257s, 3077w, 2890w cm^{-1}. λ_{max} (EtOH) 240 and 290 mμ (log ε 4·14, 4·21). N.m.r. ($CDCl_3$ + some $(CD_3)_2SO$): τ 2·78(S); 2·87(S) (aromatic protons); 6·75 (multiplet) (OH); 7·09 (broad singlet) and 7·38 (multiplet) 2 × CH_2. The mass spectrum showed a parent peak at 249 *m/e* which was also the base peak.

Reaction of (V) with Acid

The oxime (V) (0·25 g) was refluxed with 37% HCl (55 ml) for 30 min. The mixture was extracted with ether and dried, and the solvent removed. The residue was taken up in benzene from which solution a solid crystallized. The aqueous mother liquors were basified with solid NaOH and the resulting precipitate added to the previous solid product. The combined solids (0·137 g) were crystallized for analysis from light petroleum (b.p. 60–80°)/benzene to yield the *alcohol* (XV), m.p. 161° (Found: C, 77·95; H, 5·4; N, 10·4. $C_{17}H_{14}N_2O$ requires C, 77·8; H, 5·4; N, 10·7%). ν_{max} (KCl disk) 3185s, 2899w, 1592w, 1553w cm^{-1}. λ_{max} (EtOH) 255 mμ (log ε 4·02). N.m.r. ($CDCl_3$): τ 1·97–2·77 (12H multiplet); 4·20 (1H, broad singlet); 6·67 (1H, broad singlet).

Hydrolysis of the acetate derived from (V) also yielded the same alcohol (XV).

The alcohol (XV) could be acetylated with acetic anhydride in the usual way. The derived *acetate* had m.p. 158–159° (Found: C, 74·4: H, 5·6; N, 9·0. $C_{19}H_{16}N_2O_2$ requires C, 75·0; H, 5·3; N, 9·2%). ν_{max} (KCl disk) 3058w, 1742s, 1603w, 1582m, 1550w cm^{-1}. N.m.r. ($CDCl_3$): τ 1·84–2·66 (12H, multiplet); 2·86 (1H, singlet); 7·73 (3H, singlet).

Oxidation of (XV)

The alcohol (XV) (0·125 g) in acetone (10 ml) was titrated with chromic oxide in aqueous sulphuric acid[12] until a permanent orange colour persisted. On working up, the ketone (VIII) was recovered. The ketone, m.p. 124°, was identified by a comparison of the i.r. spectrum with that of an authentic sample.

Reduction of (VIII)

Sodium was added to a refluxing ethanolic solution of the ketone (VIII) (0·086 g) until the solution turned dark red. Neutralization and ether extraction of the resultant mixture yielded a yellow oil which crystallized from benzene/light petroleum (b.p. 60–80°), to form colourless rosettes of crystals (0·02 g), m.p. 157°. These were found to have an i.r. spectrum identical with the alcohol (XV) described above.

Reaction of (V) with Chloranil

A mixture of (V) (0·2 g), chloranil (0·2 g), and toluene (30 ml) was heated at reflux temperature for 5 hr. When cool, the resulting dark solid was collected (0·29 g) and sublimed

[11] Burton, H., and Shoppee, C. W., *J. chem. Soc.*, 1939, 567.

[12] Bowers, A., Halsall, T. G., Jones, E. R. H., and Lemin, A. J., *J. chem. Soc.*, 1953, 2548.

at 150° (1 mm) to yield a pale yellow solid (0·002 g), m.p. 182–198°. Thin-layer chromatography on silica using the solvent $CHCl_3$+1% CH_3OH showed the mixture to consist of unchanged oxime (V) and an unknown. The mass spectrum of the mixture showed *m/e* 277 and *m/e* 275. The filtrate from the reaction, when analysed by thin-layer chromatography, showed the presence of (V), chloranil, and tetrachlorohydroquinone.

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