351. *Pyrone Series. Part V.*[1] *A Synthesis of 6-Phenyl-2,3-cyclopenteno-4-pyrone, and a Study of the Action of Carbonyl Reagents on 2,6-Diphenyl-4-pyrone.*

By Ibrahim El-Sayed El-Kholy, Fathi Kamel Rafla, and Gabra Soliman.

6-Phenyl-2,3-cyclopenteno-4-pyrone has been prepared and converted into the thio-analogue and oxime. 2,6-Diphenyl-4-pyrone gives with hydroxylamine the oxime, 1-hydroxypyridone, and 4-hydroxyamino-2,6-diphenylpyridine 1-oxide (IX). 5-Phenacyl-3-phenylpyrazole hydrazone (XI) has been converted into the complex hydrazine (XIII). The infrared spectra of these compounds are discussed.

Light and Hauser [2] recently described an elegant synthesis of a series of 2,6-diaryl-4-pyrones by cyclisation of 1,3,5-triketones which were obtained by aroylation of the terminal methyl group in β-diketones. This series includes 6-*p*-methoxyphenyl-2,3-cyclopenteno-4-pyrone and some of the diaryl-4-pyrones previously prepared by Soliman and El-Kholy.[3]

In this paper, however, we report the preparation of 6-phenyl-2,3-cyclopenteno-4-pyrone (I) by the condensation of ethyl phenylpropiolate with cyclopentanone. So far, we have failed to obtain the homologous pyrone by using cyclohexanone, probably owing to steric factors.

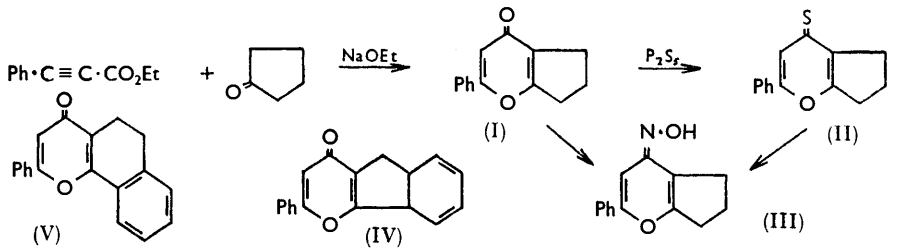
The 1,4-pyrone structure of compound (I), 6-phenyl-4-indeno(3′,2′-2,3)pyrone [3] (IV), and 5,6-dihydro-7,8-benzoflavone [4] (V) was established by alkaline hydrolysis to benzoic acid, acetophenone, and the expected ketones.

These three pyrones, as well as 2,6-diphenyl-4-pyrone (VI), show an infrared band at 1645—1653 cm.$^{-1}$ (Table 1) which is specific for the carbonyl group in 4-pyrones.[2]

[1] Part IV, El-Kholy, Rafla, and Soliman, *J.*, 1961, 4490.
[2] Light and Hauser, *J. Org. Chem.*, 1960, **25**, 538.
[3] Soliman and El-Kholy, *J.*, 1954, 1755.
[4] El-Kholy, Rafla, and Soliman, *J.*, 1959, 2588.

Like other 1,4-pyrones,[4] 6-phenyl-2,3-cyclopenteno-4-pyrone readily gives the corresponding 4-thiopyrone (II) from which the pyrone oxime (III) was obtained with hydroxylamine in neutral medium. This thiopyrone and the thio-analogues of (IV), (V), and (VI) are characterised by strong absorption in the 1075—1111 cm.$^{-1}$ region normally associated with the thiocarbonyl stretching frequency in a variety of sulphur compounds.[1,5,6a]

Unlike 2,6-diaryl-4-pyrones,[3] the polycyclic 4-pyrones (I), (IV), and (V) failed to give the corresponding 1-hydroxy-4-pyridones with hydroxylamine in neutral media; in the presence of pyridine their oximes were the sole products.



The 4-pyrone oximes which we have studied (Table 1) are characterised by strong absorption in the 1681—1656 cm.$^{-1}$ region attributable to the C=N group,[6b] both in the

TABLE 1.

The infrared spectra (cm.$^{-1}$) were measured on Perkin–Elmer spectrophotometer 137 for KBr pellets; for solution spectra, thickness was 0·5 mm.

Compounds	OH	NH	C=N	C=O	C=C		Pyridine band	Phenyl group		C=S	$^{+}N-O^{-}$
Pyrones											
I	—	—	—	1653s	1613s	1587w	—	1497m	1449s	—	—
IV	—	—	—	1645s	1613sh	1587sh	—	1493m	1443s	—	—
V	—	—	—	1645s	1613s	1590sh	—	1493m	1447s	—	—
VI	—	—	—	1645s	1613s	1587w	—	1493s	1449s	—	—
Thiopyrones											
II	—	—	—	—	1626s	1587m	—	1493s	1453s	1107s	—
from IV	—	—	—	—	1623s	1597s	—	1493m	1449s	1075s	—
from V	—	—	—	—	1613s	1575s	—	1493s	1445s	1111s	—
from VI	—	—	—	—	1613s	1580s	—	1488s	1443s	1111s	—
Pyrone oximes											
III	3125vb	—	1672s	—	1605w	1580w	—	1493s	1449s	—	—
III *	3650m	—	1681s	—	1613m	1587sh	—	1493w	1499m	—	—
from IV	3175vb	—	1656s	—	1616m	1587sh	—	1488s	1449s	—	—
from V	3125vb	—	1658s	—	1608w	1582m	—	1488s	1441s	—	—
VII	3125vb	—	1664s	—	1608m	1587sh	—	1493s	1449s	—	—
VII *	3636m	—	1667s	—	1613m	1587m	—	1493m	1449s	—	—
Pyridine 1-oxides											
VIII	3115vb	—	—	1645s	1605sh	1587s	1563s	1493m	1451s	—	1258m
VIII *	3636m	—	—	1645s	1608s	1580sh	—	1490w	1449s	—	—
IX	3279vb	—	—	—	1608s	1580s	1538m	1499m	1449s	—	1325s
IX *	3650s	3041s	—	—	1613s	1582m	—	1493sh	1445s	—	1274s
Pyrazoles											
XII	—	3425s	—	1684s	1605m	1585m	—	1515m	1451s	—	—
XIII	—	3195vb	—	—	1608s	1572s	—	1488s	1449s	—	—

* In chloroform.

solid state and in solution (cf. Fig. 1). The medium absorption between 3650 and 3636 cm.$^{-1}$ in chloroform solution is associated with the free hydroxyl group, whereas the broad

[5] Spinner, *J. Org. Chem.*, 1958, **23**, 2037; *J.*, 1960, 1237.

[6] Bellamy, " The Infrared Spectra of Complex Molecules," Methuen, London, 1959, pp. (*a*) 350, (*b*) 268, (*c*) 96, (*d*) 308, (*e*) 277, (*f*) 249.

absorption between 3·1 and 3·3 μ in the solid state indicates intermolecular hydrogen bonding.[6c]

In Part IV of this series,[1] we reported that pyridine catalyses the condensation of hydroxylamine with 5-methoxy- and 5-aryloxy-4,6-diaryl-2-pyrones giving the corresponding 1-hydroxy-2-pyridones. This reaction has been extended to 2,6-diphenyl-4-pyrone (VI), from which 2,6-diphenyl-4-pyrone oxime (VII) and 4-hydroxyamino-2,6-diphenylpyridine 1-oxide (IX) have been prepared. Under identical conditions, the oxide

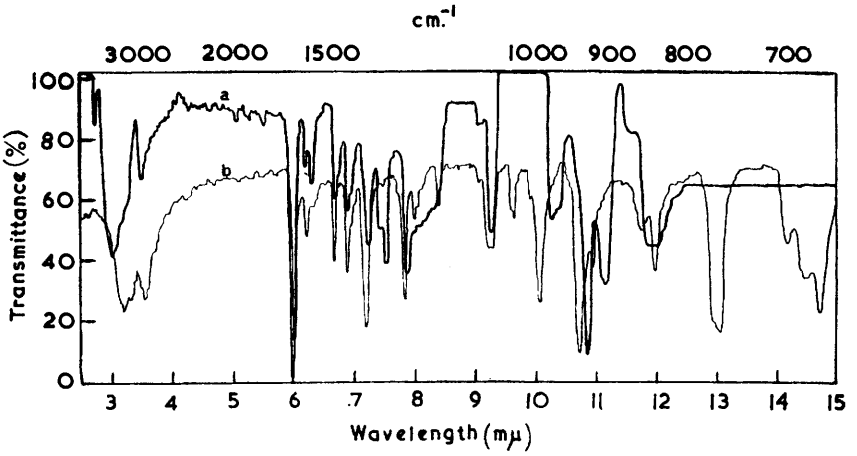


FIG. 1.

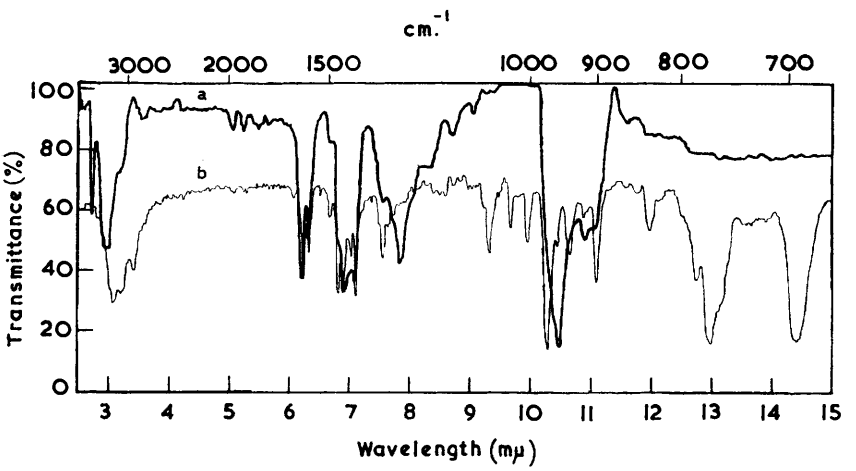


FIG. 2.

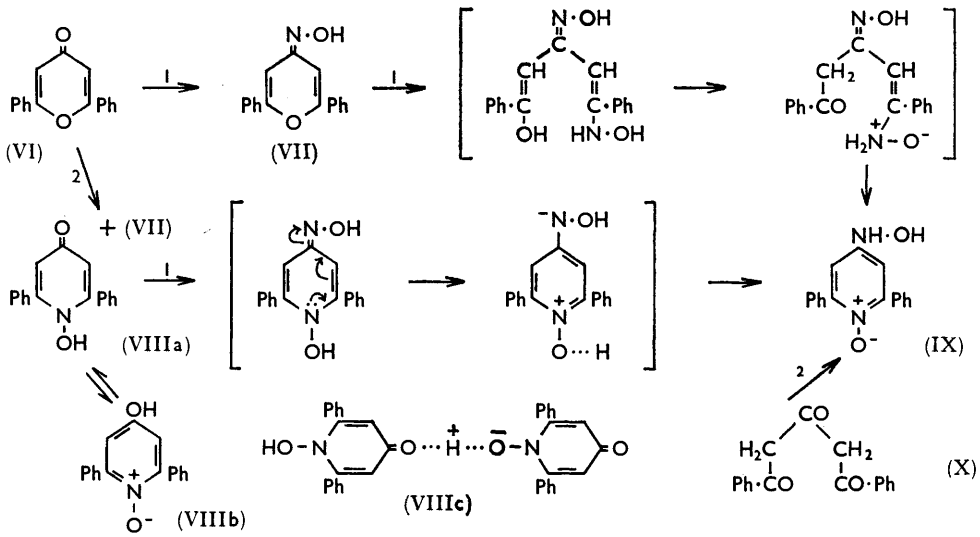
Infrared spectra of (FIG. 1) 2,6-diphenyl-4-pyrone oxime and (FIG. 2) 4-hydroxyamino-2,6-diphenylpyridine 1-oxide: (a) in $CHCl_3$; (b) in KBr discs.

(IX) is more readily obtained by the action of hydroxylamine on 1-hydroxy-2,6-diphenyl-4-pyridone (VIII) than on the oxime (VII).

In an attempt to prepare 1-hydroxy-2,6-diphenyl-4-pyridone in larger quantities by the action of hydroxylamine on 2,6-diphenyl-4-pyrone in a neutral medium,[3] the reaction mixture was fractionated by using picric acid. This formed insoluble picrates with the pyrone (VI) and its oxime (VII), but not with the hydroxypyridone (VIII). In this way analytically and spectroscopically pure 1-hydroxy-2,6-diphenyl-4-pyridone and 2,6-diphenyl-4-pyrone oxime were obtained.

1-Hydroxy-2,6-diphenyl-4-pyridone differs from the polysubstituted 1-hydroxy-2-pyridones [1] in failing to give a characteristic colour with ferric chloride. Such a difference is known between 1-hydroxy-4-pyridone and 1-hydroxy-2-pyridone,[7] but it is not considered as evidence against the existence of the hydroxypyridine oxide form (VIIIb).[8]

The infrared spectrum (Table 1) of this hydroxypyridone (VIII) in chloroform is characterised by strong carbonyl absorption at 1645 cm.$^{-1}$ and hydroxyl absorption at 3636 cm.$^{-1}$, but it lacks the $^{+}N–O^{-}$ band in the 1300—1240 cm.$^{-1}$ region.[6d,9,10] Unless the latter band is masked by the solvent, this compound exists exclusively as the pyridone (VIIIa) in chloroform. On the other hand, the solid pyridone shows a strong carbonyl band at 1645 cm.$^{-1}$, a pyridine oxide band at 1258 cm.$^{-1}$, and a broad band at 3·1—3·3 μ signifying polymeric association (VIIIc).[11]



Unlike 2,6-diphenyl-4-pyrone oxime (VII), 4-hydroxyamino-2,6-diphenylpyridine 1-oxide is colourless and fails to give a colour with ferric chloride or form a picrate, and its spectrum (cf. Fig. 2) lacks the strong C=N band between 1681 and 1656 cm.$^{-1}$. On the other hand, its spectrum in the solid state is characterised by the band at 1325 cm.$^{-1}$ associated with the $^{+}N–O^{-}$ group and by the bands at 1608, 1580, and 1538 cm.$^{-1}$ associated with the pyridine structure.[6e] It appears that the two phenyl groups adjacent to the heteroatom in (IX) shift the $^{+}N–O^{-}$ band towards higher frequency.[6d,10] Further, the broad absorption at 3·1—3·3 μ indicates intermolecular association, but in solution the bands at 3650, 3401, and 1274 cm.$^{-1}$ signify the presence of the free OH, NH, and the $^{+}N–O^{-}$ groups in this compound.

The sequence of the reactions leading to 4-hydroxyamino-2,6-diphenylpyridine 1-oxide (IX) from the pyrone or the oxime (VII) demands fission of the oxide ring to an acyclic intermediate hydroxyamino-derivative which undergoes cyclisation by rearrangement and elimination of water as illustrated. On the other hand, its formation from the hydroxypyridone (VIII) with comparative ease appears to proceed by oximation and subsequent rearrangement.

The product obtained by the action of hydroxylamine on 1,3-dibenzoylacetone (X),

[7] Shaw, *J. Amer. Chem. Soc.*, 1949, **71**, 67.
[8] Albert, " Heterocyclic Chemistry," Essential Books, Fair Lawn, N. Jersey, 1959, 55.
[9] Wiley and Slaymaker, *J. Amer. Chem. Soc.*, 1957, **79**, 2233.
[10] Katritzky and Gardner, *J.*, 1958, 2192.
[11] Costa, Blasina, and Sartori, *Z. phys. Chem.* (*Leipzig*), 1956, **7**, 123.

previously considered to be 5-(2-hydroxyimino-2-phenethyl)-3-phenylisoxazole,[3] proved to be identical with the pyridine 1-oxide (IX).

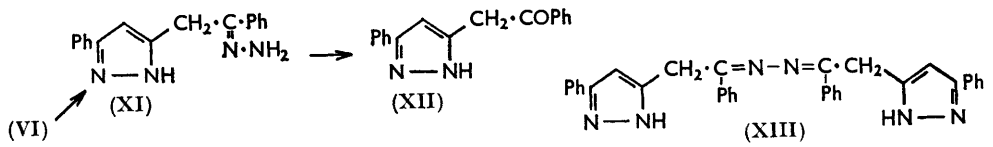
Quite recently, Parisi, Bovina, and Quilico [12] prepared 4-hydroxyaminopyridine 1-oxide by the action of hydroxylamine on 4-pyrone in the presence of sodium hydrogen carbonate and determined its structure chemically and spectroscopically.

The mechanism proposed by these authors involves addition of a molecule of hydroxylamine to the carbonyl group before fission of the oxide link.

2,6-Diphenyl-4-pyrone and its thio-analogue could not be converted into the hydrazone or phenylhydrazone by the action of the respective reagents in neutral media. Further, 2,6-diphenyl-4-pyrone oxime did not react with hydrazine hydrate.

Ainsworth and Jones,[13] however, found that 2,6-diphenyl-4-pyrone readily gives 5-phenacyl-3-phenylpyrazole hydrazone (XI) by the action of hydrazine hydrate.

In the course of the preparation of 5-phenacyl-3-phenylpyrazole (XII) by acid-catalysed hydrolysis of the hydrazone (XI), a yellow crystalline product separated at an intermediate stage, but gradually dissolved. This product was shown to be *NN'*-di-[1-phenyl-2-(3-phenylpyrazol-5-yl)ethylidene]hydrazine (XIII) by analysis and by condensation of the hydrazone (XI) with the ketone (XII) in ethanol. Whereas 5-phenacyl-3-phenylpyrazole



(XII) is characterised by NH absorption at 3425 cm.$^{-1}$ and C=O absorption at 1684 cm.$^{-1}$ (Table 1), the hydrazine (XIII) exhibits broad absorption at 3·1—3·3 μ ascribed to hydrogen bonding.

Experimental

Light petroleum had b. p. 50—70°.

6-Phenyl-2,3-cyclopenteno-4-pyrone.—This was prepared by condensation of cyclopentanone (1·7 g., 1 mol.) with ethyl phenylpropiolate (3·5 g., 1 mol.) in presence of sodium ethoxide (1·45 g., 1 mol.) in ice-cold dry ether (150 ml.). The mixture was kept at 0° for 3 days, then mixed with water and worked up as usual. The brown oil (2·2 g.) recovered from the neutral ethereal solution deposited the pyrone (0·2 g.), m. p. 155—160°. More of the *pyrone* (0·6 g.) was recovered from the alkaline solution after acidification, extraction with ether, and removal of phenylpropiolic acid (1·5 g.). It crystallised from benzene–light petroleum in needles, m. p. 165° (Found: C, 79·25; H, 5·8. $C_{14}H_{12}O_2$ requires C, 79·2; H, 5·7%). Its *picrate* crystallised from methanol in yellow needles, m. p. 162—163° (Found: N, 9·5. $C_{20}H_{15}N_3O_9$ requires N, 9·5%).

The pyrone was recovered unchanged after being heated with hydroxylamine hydrochloride and sodium acetate in ethanol for 5 hr.

Most of this pyrone was degraded by boiling 20% aqueous potassium hydroxide in 2 hr., as previously described.[3] It yielded benzoic acid, acetophenone (2,4-dinitrophenylhydrazone, m. p. 246—248°), and cyclopentanone (2,4-dinitrophenylhydrazone, m. p. 146°).[14]

About 50% of 6-phenyl-4-indeno(3',2'-2,3)pyrone was degraded by the same method to benzoic acid, acetophenone, and inden-1-one which was identified as 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 258°.[14]

5,6-Dihydro-7,8-benzoflavone was also degraded to benzoic acid, acetophenone, and 1-tetralone (2,4-dinitrophenylhydrazone, m. p. 257°).[14]

6-Phenyl-2,3-cyclopenteno-4-thiopyrone.—This *thiopyrone* was prepared by boiling the pyrone with phosphorus pentasulphide in dry benzene for 3 hr. and crystallised from methanol in pale brown needles, m. p. 160—161° (Found: C, 73·35; H, 5·2; S, 14·0. $C_{14}H_{12}OS$ requires C, 73·7; H, 5·3; S, 14·05%).

[12] Parisi, Bovina, and Quilico, *Gazzetta*, 1960, **90**, 903.
[13] Ainsworth and Jones, *J. Amer. Chem. Soc.*, 1954, **76**, 3172.
[14] Vogel, "Elementary Practical Organic Chemistry," Longmans Green, London, 1957, Part II, pp. 587—589.

6-Phenyl-2,3-cyclopenteno-4-pyrone oxime. A solution of the foregoing thiopyrone (0·5 g.) in ethanol was refluxed with a solution of hydroxylamine hydrochloride (0·5 g.) and sodium acetate (0·5 g.) in water (2 ml.) for 4 hr. When the mixture was carefully diluted with water, the *oxime* separated. It crystallised from methanol in yellow needles, m. p. 216—218° (decomp.), which gave a brown colour with ferric chloride and reduced Tollens's reagent (Found: C, 74·0; H, 5·8; N, 6·35. $C_{14}H_{13}NO_2$ requires C, 74·0; H, 5·8; N, 6·2%). Its *picrate* was prepared in methanol and crystallised from benzene in yellow needles, m. p. 202° (decomp.) (Found: N, 12·25. $C_{20}H_{16}N_4O_9$ requires N, 12·3%).

The pyrone oxime was also obtained when the pyrone (0·5 g.) was heated with hydroxylamine hydrochloride (0·5 g.) in pyridine (10 ml.) for 20 min. On dilution, the oxime (0·15 g.), m. p. and mixed m. p. 216—218° (decomp.), was recovered.

6-Phenyl-4-indeno(3′,2′-2,3)pyrone oxime and 5,6-dihydro-7,8-benzoflavone oxime[4] were also obtained by the pyridine method on refluxing for 5 hr.; the pyridine mother-liquors yielded traces of the unchanged pyrones.

6-Phenyl-4-indeno(3′,2′-2,3)pyrone oxime picrate was prepared in, and crystallised from, ethanol in yellow needles, m. p. 225—226° (decomp.) (Found: N, 11·55. $C_{24}H_{16}N_4O_9$ requires N, 11·1%).

5,6-Dihydro-7,8-benzoflavone oxime picrate, m. p. 217—218° (decomp.), formed yellow needles from ethanol (Found: N, 10·54. $C_{25}H_{18}N_4O_9$ requires N, 10·8%).

Action of Hydroxylamine on 2,6-Diphenyl-4-pyrone in Ethanol.—A solution of the pyrone (5 g.) in ethanol (60 ml.) was refluxed with hydroxylamine hydrochloride (5 g.) and sodium acetate (5 g.) in water (5 ml.) for 10 hr. The mixture was then diluted with water and the yellowish-white product (5·2 g.) separated and dried. Its solution in ethanol (200 ml.) was mixed with hot saturated ethanolic picric acid (50 ml.) and, after cooling, the mixed picrates (5·5 g.), m. p. 173—180°, were separated and washed with ethanol. They were suspended in hot ethanol (100 ml.), mixed with 25% aqueous ammonia (30 ml.), diluted with water, and extracted with chloroform. The residue recovered from the solvent was extracted with cold methanol which removed 2,6-diphenyl-4-pyrone (1·5 g.), m. p. and mixed m. p. 140°. The undissolved pyrone oxime (0·75 g.) crystallised from ethanol in yellow needles, m. p. 205° (decomp.) [lit.,[3,15] 197° (decomp.)].

2,6-Diphenyl-4-pyrone oxime picrate, prepared from the pure oxime, crystallised from methanol in yellow needles, m. p. 220—221° (decomp.) (lit.,[16] m. p. 200°) (Found: N, 11·5. Calc. for $C_{23}H_{16}N_4O_9$: N, 11·4%). Hydrolysis of this picrate led to the oxime, m. p. and mixed m. p. 205° (decomp.).

The ethanolic solution left after separation of the picrates of 2,6-diphenyl-4-pyrone and its oxime was mixed with 25% aqueous ammonia (50 ml.), warmed, diluted with water, and extracted with chloroform. 1-Hydroxy-2,6-diphenyl-4-pyridone (0·75 g.), m. p. 185—190°, was recovered from the solvent and crystallised from methanol in needles, m. p. 194—195° (cf. ref. 3), which gave a negative ferric chloride test (Found: C, 77·5; H, 4·85; N, 5·4. Calc. for $C_{17}H_{13}NO_2$: C, 77·5; H, 5·0; N, 5·3%).

1-Hydroxy-2,6-diphenyl-4-pyridone and 2,6-diphenyl-4-pyrone oxime were recovered unchanged after being boiled with hydroxylamine hydrochloride and sodium acetate in ethanol.

4-Hydroxyamino-2,6-diphenylpyridine 1-Oxide (IX).—A solution of 1-hydroxy-2,6-diphenyl-4-pyridone (0·5 g.) in pyridine (10 ml.) was refluxed with hydroxylamine hydrochloride (0·5 g.) for 2 hr. After dilution with ice-cold water, the *oxide* was isolated and crystallised from dilute methanol in needles, m. p. 152° (Found: C, 73·0; H, 5·0; N, 10·1. $C_{17}H_{14}N_2O_2$ requires C, 73·4; H, 5·1; N, 10·1%). This compound was also obtained when 2,6-diphenyl-4-pyrone oxime was heated for 5 hr. under identical conditions.

4-Hydroxyamino-2,6-diphenylpyridine 1-oxide was quantitatively prepared by refluxing 1,3-dibenzoylacetone with hydroxylamine hydrochloride and sodium acetate in ethanol and crystallised from dilute methanol in needles, m. p. and mixed m. p. 152°.

Action of Hydroxylamine on 2,6-Diphenyl-4-pyrone in Pyridine.—A solution of 2,6-diphenyl-4-pyrone (2 g.) in pyridine (15 ml.) was refluxed with hydroxylamine hydrochloride (2 g.) in water (2 ml.) for 5 hr. The mixture was then diluted with water and the semisolid product separated and washed from pyridine. When its solution in ethanol (150 ml.) was treated with hot saturated ethanolic picric acid (10 ml.), only 2,6-diphenyl-4-pyrone oxime picrate (1·4 g.),

[15] Arndt, Nachtwey, and Scholz, *Ber.*, 1924, **57**, 1903.
[16] Elkaschef and Nosseir, *J. Amer. Chem. Soc.*, 1960, **82**, 4344.

m. p. 220°, was obtained. The residual ethanolic solution was mixed with 25% aqueous ammonia and extracted with chloroform, from which an oily residue (0·9 g.) was recovered. On treatment of this residue with benzene–light petroleum, 4-hydroxyamino-2,6-diphenylpyridine 1-oxide (0·4 g.), m. p. 143—145°, was obtained and crystallised from dilute methanol in needles, m. p. and mixed m. p. 152°.

Action of Hydrazine on 2,6-Diphenyl-4-pyrone and its Thio-analogue.—These two compounds were recovered unchanged after heating with hydrazine hydrochloride and sodium acetate in ethanol for 7 hr.

A suspension of 2,6-diphenyl-4-thiopyrone (0·5 g.) in ethanol (15 ml.) was kept at room temperature with hydrazine hydrate (3 ml.) for 3 hr. with frequent shaking. It gradually went into solution and lost its red colour, and hydrogen sulphide was evolved. On dilution with water, 5-phenacyl-3-phenylpyrazole hydrazone (0·4 g.) was recovered and crystallised from methanol in needles, m. p. and mixed m. p. 176—177°.[13]

5-Phenacyl-3-phenylpyrazole.—A solution of the above-mentioned hydrazone (0·5 g.) in 60% ethanol (30 ml.) containing concentrated hydrochloric acid (1 ml.) was refluxed for 1 hr. A yellow precipitate separated in the course of boiling but it gradually went into solution. On concentration and dilution with water, the *ketone* (0·4 g.) was obtained; it crystallised from dilute methanol in plates, m. p. 154—155°, which gave a green colour with ferric chloride (Found: C, 78·0; H, 5·5; N, 10·6. $C_{17}H_{14}N_2O$ requires C, 77·85; H, 5·4; N, 10·7%). This ketone was converted into the original hydrazone when heated with hydrazine hydrate in ethanol for 2 hr.

5-Phenacyl-3-phenylpyrazole oxime was prepared when the foregoing ketone (0·3 g.) in ethanol (15 ml.) was refluxed with hydroxylamine hydrochloride (0·3 g.) and sodium acetate (0·3 g.) in 2 ml. of water for 3 hr. It was recovered by dilution and extraction with ether and crystallised from benzene–light petroleum in needles, m. p. 160° (Found: C, 74·3; H, 5·6; N, 15·1. $C_{17}H_{15}N_3O$ requires C, 73·6; H, 5·5; N, 15·2%).

NN'-Di-[1-phenyl-2-(3-phenylpyrazol-5-yl)ethylidene]hydrazine.—A solution of 5-phenacyl-3-phenylpyrazole hydrazone (0·6 g.) in 65% methanol (30 ml.) containing 1 ml. of glacial acetic acid or one drop of concentrated hydrochloric acid was heated for 30 min. The yellow *ethylidenehydrazine* (XIII) (0·5 g.), m. p. 235—240°, which crystallised was separated and recrystallised from pyridine–dilute methanol in yellow needles, m. p. 240—241° [Found: C, 78·3; H, 5·5; N, 16·3%; *M* (Rast), 578. $C_{34}H_{28}N_6$ requires C, 78·45; H, 5·4; N, 16·15%; *M*, 520·4]. It was also obtained when 5-phenacyl-3-phenylpyrazole (0·1 g.) and its hydrazone (XI) (0·1 g.) were refluxed in ethanol (15 ml.) for 3 hr. It gradually separated from the solution in yellow needles, m. p. and mixed m. p. 240—241°.

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