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ALKALINE CLEAVAGE OF SOME (1-PHENYLSULFONYL-2-PYRAZOLIN-5-YL)-METHYL KETONES AND RELATED COMPOUNDS[a]

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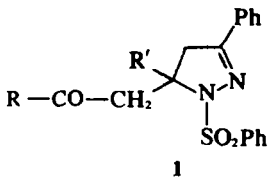
Abstract—The (1-phenylsulfonyl-2-pyrazolin-5-yl)-methyl ketones **1a–c** and the ethylene hemithioketal of **1b** are converted by ethanolic sodium hydroxide into a variety of heterocyclic products such as pyridines, pyrazoles (**2a, 2c,** and the ethylene hemithioketal of **2f**, respectively) and pyridazines (**7a, b**). The formation of part of these products involves a novel variant of the van Alphen rearrangement and a novel 3*H*-pyrazole → pyridazine ring enlargement reaction. The oximes of the ketones **1a–c** as well as the oxime ether **14** are converted under elimination of their side chains and/or the benzenesulfonyl group into aromatic pyrazole derivatives and ring transformation products, viz. derivatives of 2-isoxazoline and pyridine, respectively. The cleavage reactions of the oxime derivatives are compared with those of their parent ketones.

The reaction of pyrylium salts with benzenesulfonohydrazide yielded a series of (1 - phenyl - sulfonyl - 2 - pyrazolin - 5 - yl)-methyl ketones (**1a–c**).[2] We now report the influence of the substituents R and R′ on the course of the alkaline cleavage of ketones **1a–c** and of some of their derivatives.

The reaction of ketones **1a–c** with 0·2 N ethanolic sodium hydroxide solution yielded 2 - [5(3) - phenyl - 3(5) - pyrazolyl] - acetophenone (**2a**) identified on the basis of (1) its elemental composition and its IR and NMR spectra, (2) its oxidation to the known[3] 5(3) - phenyl - 3(5) - pyrazolecarboxylic acid (**2b**) and (3) its synthesis from 1,5 - diphenyl - 1,3,5 - pentanetrione[4] and hydrazine hydrate.



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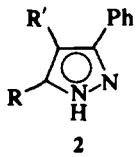
a: R = Ph; R′ = H
b: R = Me; R′ = Ph
c: R = R′ = Ph



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	R	R′
a:	$PhCOCH_2$	H*
b:	COOH	H*
c:	Ph	$PhCOCH_2$
d:	Ph	H
e:	$PhCOCH_2$	Ph*
f:	$MeCOCH_2$	Ph*
g:	COOH	Ph*

*Potentially tautomeric compound. Only one of the tautomeric forms of the pyrazole cycle has been depicted.

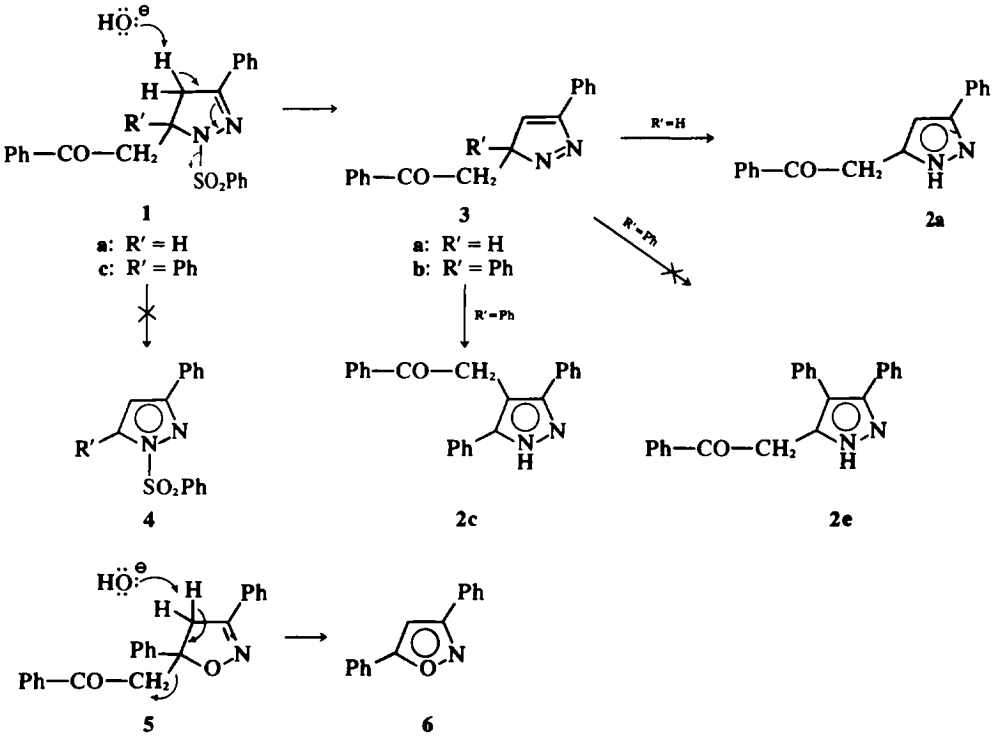
The conversion of **1a** into **2a** may be explained by assuming base-induced elimination of benzenesulfinic acid (either in a concerted of a stepwise manner) to yield the 3*H*-pyrazole **3a** which, subsequently, rearranges into **2a** (Scheme 1). Base-induced elimination of arenesulfinic acids from N - arylsulfonyl - pyrazolines related to **1a** have been earlier observed by Ege.[5] An alternative mode of the base induced fragmentation of **1a** could, in principle, be formation of 3 - phenyl - 1 - phenylsulfonyl-pyrazole (**4**, R′=H) under extrusion of acetophenone since an analogous cleavage of 2 - (3,5 - diphenyl - 2 - isoxazolin-5 - yl) - acetophenone (**5**) to yield 3,5-diphenylisoxazole (**6**) has been observed by Kumler *et al.*[6] (Scheme 1). The course of the alkaline cleavage of **1a** is, apparently, governed by the better leaving group properties of the benzenesulfinate as compared to the acetophenone enolate anion.

The conversion of **3a** into **2a** may, probably, be best described as a [1, 5] hydrogen shift; in view of the alkalinity of the medium, the possibility of process **3a** → **2a** to occur by prototropy may, however, not be ruled out with complete certainity.

Similarly the product from **1b** proved identical with the known[7] 2 - methyl - 4,6 - diphenylpyridine. The formation of the latter requires fission of the N–N bond of the starting substance. Whether this fission takes place by reduction or by sulfonylnitrene elimination from some intermediate (*cf.* Ref. 8) is not yet clear.

Alkaline cleavage of **1c** proved to be more complex. Four major products (**A–D**) were obtained and were identified as 2,4,6 - triphenylpyridine,[9] 2 - (3,5 - diphenyl - 4 - pyrazolyl) - acetophenone (**2c**), (4,6 - diphenyl - 3 - pyridazinyl) phenyl ketone (**7a**) and α,4,6, - triphenyl - 3 - pyridazinemethanol (**7b**), respectively. The structure assignment of **B** = **2c** is based on (1) its elemental composition and spectral properties, in particular the close resemblance of the UV spectra of **B** and 3,5-diphenylpyrazole (**2d**)[10] and (2) its structure proving synthesis from 2 - benzoyl - 1,4 - diphenyl - 1,4 - butanedione[11] and hydrazine hydrate. The close resemblance of the UV spectra of **C** and **D** whose elemental compositions differed only by two H atoms, suggested closely related structures for these products, which was confirmed by reduction of **C** to **D** and oxidation of **D** to **C**. On the basis of its IR and NMR spectra the structure of a (diphenylpyridazinyl) phenyl ketone was tentatively deduced for **C**. The latter structure assignment was partly confirmed by alkaline degradation of **C** to 3,5-diphenylpyridazine (**7c**)[12] and benzoic acid. The point of attachment of the benzoyl group to the pyridazine ring of

[a]Part of the present work has been published as a preliminary communication, (Ref. 1).



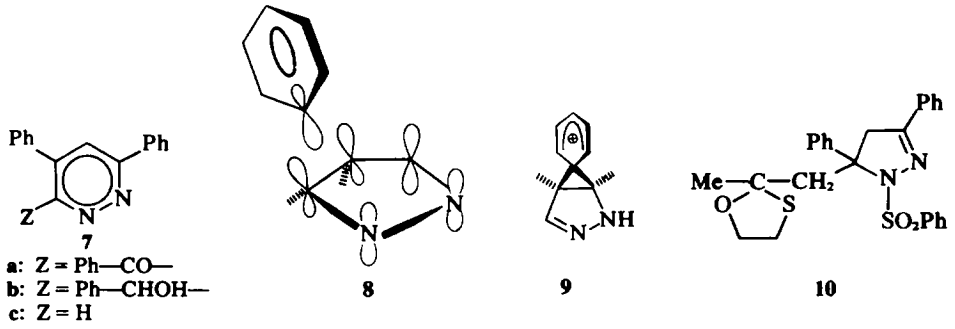
Scheme 1.

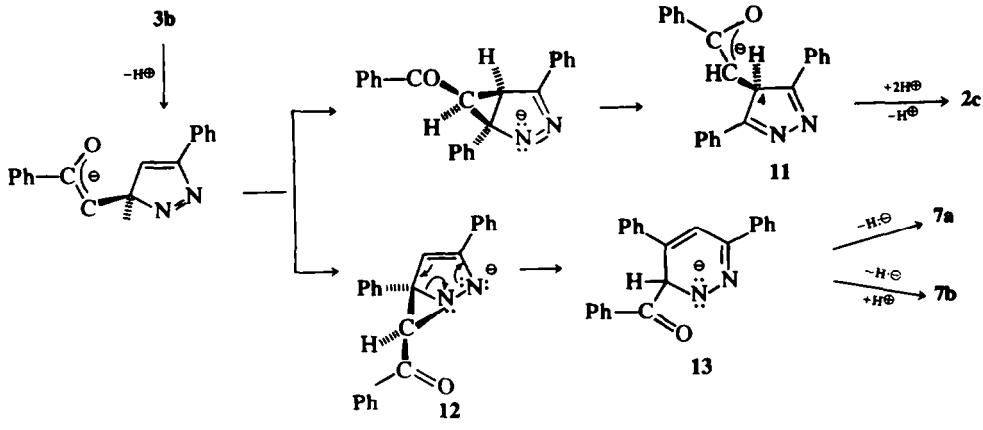
C became apparent by comparison of the NMR spectra of C and **7c**. The NMR spectrum of **7c** in $CDCl_3$ solution exhibited two one-proton-doublets at δ 9·40 and 8·0 ppm (J = 2·3 Hz), corresponding to the pyridazine protons attached to C-6 and C-4, respectively. In the NMR spectrum ($CDCl_3$) of C, on the other hand, the low-field doublet was lacking and the high-field doublet was replaced by a singlet at the same δ value, demonstrating that the benzoyl group of C ≡ **7a** is attached to a C atom in α-position to one of the ring N atoms. Consequently, the structure of **D** must be **7b**.

The formation of **2c** on alkaline cleavage of **1c** is similar to the conversion of **1a** to **2a**. In the present case, however, a 3,3-*di*substituted (**3b**) rather than a 3-monosubstituted 3*H*-pyrazole has to be assumed as the intermediate. In contrast to **3a**, **3b** can not undergo prototropy, and either a phenacyl or a phenyl shift must take place in order that an aromatic pyrazole derivative (**2c** and **2e**, respectively) may be formed. Rearrangements of 3,3-disubstituted 3*H*-pyrazoles are known as van Alphen rearrangements[13] and they may be brought about by acid or pure thermal treatment. In the course of these rearrangements aryl groups were always found to migrate in preference to alkyl and aralkyl groups which—irrespective of whether the rearrangements take place by a concerted [1, 5] aryl shift or (as is perhaps the case in the presence of acid catalysts) in a stepwise manner, i.e. through **8** (transition state) or **9** (intermediate)—appears to be the result of the higher electron density available in the migrating aryl groups.

If the rearrangement of **3b** involved migration of the phenyl group, 2 - [5(3),4 - diphenyl - 3(5) - pyrazolyl] - acetophenone (**2e**) ought to be formed; the product actually obtained, however, was clearly different from **2e**, an authentic sample of which was prepared by allowing 1,2,5 - triphenyl - 1,3,5 - pentanetrione[14] to react with hydrazine hydrate.

The reversal of the usual order of the migratory aptitudes in the case of **3b** appears to be consequence of the alkalinity of the medium and of the presence of an active methylene group in a suitable position of the side chain. The probable course of the rearrangement **3b** → **2c**, depicted as a stepwise rather than a concerted process, is shown in the upper part of Scheme 2. Conversion of the





Scheme 2.

postulated intermediate 4*H*-pyrazole derivative **11** into the final product is thought to take place either by a [1, 5] hydrogen shift or by prototropy, followed by proton uptake of the enolate side chain.

Support for our view concerning the importance of the active methylene group in the alkali induced conversion of **1c** to **2c** comes from the observation that a related 1 - phenylsulfonyl - 2 - pyrazoline, viz. the ethylene hemithioketal (**10**) of **1b**, which does not contain such an acidic group, is converted upon alkaline treatment under migration of the phenyl group originally attached to C-5 into the ethylene hemithioketal of 1 - [5(3),4 - diphenyl - 3(5) - pyrazolyl] - acetone (**2f**). The structure of the latter hemithioketal follows from the mass spectrum of its parent ketone **2f** obtained by chloramine T cleavage[17] of the ketal—in particular from the presence of abundant peaks corresponding to the elimination of ketene and the acetyl radical, respectively, from the molecular ion which are consistent with the attachment of the acetonyl side chain to a ring carbon *adjacent* to a ring N atom—as well as from the formation of the known[15] 5(3),4 - diphenyl - 3(5) - pyrazolecarboxylic acid (**2g**) on oxidation of the ketone.

The formation of the two pyridazine derivatives (**7a, b**) on alkaline treatment of **2c** may also be rationalized through the anion of **3b** as shown in the lower part of Scheme 2. In the present case nucleophilic attack of the enolate side chain takes place at N(2), rather than at C(4) to yield the bicyclic intermediate **12** which subsequently isomerises into the anionic pyridazine species **13**. The latter, finally, becomes stabilized either by hydride anion losss to yield **7a**, or by hydride migration from the tetrahedral ring C atom to the CO carbon and concomitant proton uptake to yield **7b**.

The alkali induced cleavage reactions of the oximes of ketones **1a–c**, as well as of the oxime ether **14** were also studied.

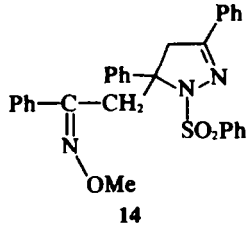
When refluxed with ethanolic sodium hydroxide, **1a**-oxime was converted under elimination of benzenesulfinic acid into 2 - [5(3) - phenyl - 3(5) - pyrazolyl] - acetophenone oxime whose structure was established by comparison with an authentic sample prepared from the corresponding ketone **2a**. Thus, the ketone **1a** and its oxime behave similarly upon alkaline treatment.

The behaviour of ketone **1b** and its oxime upon refluxing with ethanolic sodium hydroxide proved, on the other hand, different, the latter being converted, under elimination of both its side chain and the phenylsulfonyl group, into 3,5-diphenylpyrazole. The first step of this sequence appears to be elimination of acetone oxime to yield 3,5 - diphenyl - 1 - phenylsulfonylpyrazole, since the latter is rapidly converted by sodium hydroxide into the final product. The first step is analogous to the alkali induced conversion of 2 - (3,5 - diphenyl - 2 - isoxazolin - 5 - yl) - acetophenone (**5**) into 3,5-diphenylisoxazole.[6]

When treated with ethanolic potassium hydroxide, the oxime of **1c** furnished the phenylsulfonylhydrazone of **5**. The structure of the product follows from its conversion into 3,5-diphenylisoxazole by perchloric acid treatment.

The transformation of a 2-pyrazoline ring into a 2-isoxazoline ring appears to be a novel type of reaction (the reverse reaction is well known from literature) and it is apparently brought about by nucleophilic attack of the anionized oxime O atom at C-5 of the 2-pyrazoline ring. The driving force of the rearrangement is probably the greater stability of the anionized phenylsulfonylhydrazone as compared to that of the anionized hydroximino group.

In agreement with the above consideration, the oxime ether **14** behaves differently from the oxime of **1c**, being converted upon alkaline treatment in almost quantitative yield into 2,4,6-triphenylpyridine which was also one of the products obtained on similar treatment of ketone **1c**.



14

EXPERIMENTAL

Hydrolysis of 2 - (3 - *phenyl* - 1 - *phenysulfonyl* - 2 - *pyrazolin* - 5 - *yl*) - *acetophenone* (**1a**). A mixture of **1a**[2] (0·4 g; 1 mmole), EtOH (160 ml) and 2 N ethanolic NaOH (16 ml) was refluxed until the starting substance was shown by TLC to have been completely used (8 min), and subsequently evaporated to dryness *in vacuo*. The residue was taken up in water and the mixture was extracted with chloroform; the organic layer was washed with dil. HCl and water, dried over $MgSO_4$, and evaporated to dryness. The residue was recrystallized from EtOH to yield 0·14 g (53%) of **2a**, colourless crystals, m.p. 153–4°. (Found: C, 77·62; H, 5·30; N, 10·70. Calc for $C_{17}H_{14}N_2O$ (262·30); C, 77·84; H, 5·38; N, 10·68%); IR (KBr): νNH 3330, νC=O 1665 cm^{-1}; NMR (DMSO-d_6): NH δ 12·75 (b); Ph δ 8·3–7·0 (10 H); 4–H δ 6·58; $\diagdown$C–CH_2–CO $\diagup$ δ 4·43 ppm, s; UV (EtOH); ~200 (~4·7); 249 (4·47); ~314 (2·46), sh.

The product proved identical in all respects with an authentic sample, see below.

Oxidation of 2 - [5(3) - *phenyl* - 3(5) - *pyrazolyl*] - *acetophenone* (**2a**). A mixture of **2a** (0·26 g; 1 mmole), t-BuOH (6 ml) and an aqueous (5 ml) soln of $KMnO_4$ (0·5 g) was heated for 4 hr on a steam bath under continuous stirring, an additional amount (0·5 g) of $KMnO_4$, dissolved in 3 ml water, being added after 3 hr. The MnO_2 ppt was removed and the t-BuOH distilled off from the filtrate. The resulting clear soln was acidified to yield 0·12 g (64%) of **2b**, m.p. and m.m.p. with an authentic sample[3] 232–4°, lit.[3] 231–2°.

2 - [5(3) - *Phenyl* - 3(5) - *pyrazolyl*] - *acetophenone* (**2a**). A mixture of 1,5 - diphenyl - 1,3,5 - pentanetrione[4] (0·5 g; 1·9 mmoles), EtOH (5 ml) and hydrazine hydrate (0·25 g) was refluxed for 2 hr to yield on cooling, 0·17 g (36%) of **2a**, m.p. 150°–2. By concentrating the mother liquor, 0·18 g (35%) of the hydrazone of **2a**, m.p. 167–9° was obtained. (Found: C, 73·90; H, 6·11; N, 20·50. Calc. for $C_{17}H_{16}N_4$ (276·33): C, 73·89; H, 5·84; N, 20·28%).

Hydrolysis of (3,5 - *diphenyl* - 1 - *phenylsulfonyl* - 2 - *pyrazolin* - 5 - *yl*) - *acetone* (**1b**). A mixture of **1b**[2] (0·41 g; 1 mmole), EtOH (160 ml) and 2 N ethanolic NaOH (16 ml) was refluxed for 30 min and subsequently evaporated to dryness *in vacuo*. The residue was taken up in water and the mixture was extracted with ether. The dry residue of the ethereal soln was recrystallized from MeOH to yield 0·10–0·13 g (40–50%) of 2 - methyl - 4,6 - diphenylpyridine, m.p. and m.m.p. with an authentic sample[7] 72–3° (ligroin), lit.[7]: 73–4°.

1b was transformed into 2 - methyl - 4,6 - diphenylpyridine also when treated with sodium dimsylate at r.t., and no intermediate could be detected when following the reaction by TLC.

Hydrolysis of 2 - (3,5 - *diphenyl* - 1 - *phenylsulfonyl* - 2 - *pyrazolin* - 5 - *yl*) - *acetophenone* (**1c**). A mixture of **1c**[2] (6·0 g; 12·5 mmoles), EtOH (2000 ml) and 2 N ethanolic NaOH (200 ml) was refluxed for 10 min and subsequently evaporated to dryness *in vacuo*. The dry residue was triturated with about 100 ml of water at r.t. to obtain 3·85 g of a colourless powder as an insoluble residue. The latter was extracted with 100 ml hot MeOH. On cooling, 0·98 g (25·5%) of 2,4,6 - triphenylpyridine[9], m.p. 138–140° (MeOH), was deposited from the methanolic soln. The dry residue of the mother liquor was dissolved in the minimum amount of hot benzene to deposit, on cooling, 0·45 g (10·5%) of almost pure **2c**, m.p. 177–8° (MeOH), identical according to its IR and NMR spectrum with an authentic sample. (Found: C, 81·19; H, 5·43; N, 8·57. Calc. For $C_{23}H_{18}N_2O$ (388·41): C, 81·63; H, 5·36; N, 8·28%); IR (KBr): νNH 3400–2800, with a local maximum at 3190; νC=O 1688 cm^{-1}; NMR ($CDCl_3$): NH δ 8·6(b), Ph δ 8·15–7·15 (15 H); $\rangle$C–CH_2–CO δ 4·3 ppm (s); UV (EtOH): 202 (4·76); 243 (4·56); ~310 (2·15), sh.

The mother liquor of **2c** was chromatographed through a column of Brockmann alumina, benzene-EtOAc mixtures, containing gradually increasing amounts of the latter, being used as the eluent, and the composition of the eluate being checked at appropriate intervals by TLC (absorbent: Kieselgel G, Merck, activated according to Stahl; development: benzene-chloroform-EtOAc, 8:1:1; detection: UV light). The following products were obtained (in the order of decreasing migration rates both through the column and in the TLC experiments): an additional amount of 0·27 g (6·5%) of 2,4,6-triphenylpyridine, 0·35 g (5·8%) of unreacted starting substance, 0·22 g (5%) of **7a**, m.p. 141–143° (EtOH), and 0·47 g (11%) of **7b**, m.p. 140–142° (EtOH). Finally the adsorbent was extracted with boiling EtOH to yield an additional amount of 0·55 g (13%) of **7b**.

Compound **7a**, (Found: C, 81·97; H, 4·90; N, 8·70; Calc for $C_{23}H_{16}N_2O$ (336·40): C, 82·12; H, 4·79; N, 8·33%); IR (KBr): νC=O 1665 cm^{-1}; *no* NH band; NMR ($CDCl_3$): 6-Ph, *o*-protons δ 8·3–8·15; Ph–CO, *o*-protons δ 8·1–7·9; 5–H δ 8·00; 6-Ph and Ph–CO, *m* - and *p*-protons δ 7·7–7·5 (6H); 4-Ph δ 7·42 ppm (5 H); UV (EtOH): ~200 (~4·75); 263 (4·53); ~330 (~3·0), sh.

Compound **7b** (Found: C, 81·57; H, 5·42; N, 8·51. Calc. for $C_{23}H_{18}N_2O$ (338·41): C, 81·63; H, 5·36; N, 8·28%); IR (KBr): νOH 3400–3100 cm^{-1}; *no* νC=O band; NMR ($CDCl_3$): ArH δ 8·3–6·75 (16 H); $\rangle$CH–OH δ 6·05 (s); OH δ 5·1 ppm (b); UV (EtOH): ~200 (~4·7); 255 (4·43); ~326 (~2·75), sh.

When **1c** was treated with sodium dimsylate at r.t., the formation of the pyridizine derivatives **7a** and **b** could be detected by TLC. According to TLC, *no* 2,4,6-triphenylpyridine or **2c** were formed under these conditions; nor could any intermediate be detected by following the reaction with TLC.

2 - (3,5 - *Diphenyl* - 4 - *pyrazolyl*) - *acetophenone* (**2c**). A suspension of 2 - benzoyl - 1,4 - diphenyl - 1,4 - butanedione[11] (2·0 g; 5·85 mmoles) in EtOH (12 ml) was treated with hydrazine hydrate (0·3 g) and refluxed for 2 min. A clear yellow soln was first formed from which a crystalline ppt soon deposited. The latter was separated and, in order to hydrolyse any azine of **2c** formed as a by-product, refluxed for 5 min with 4ml EtOH containing 3 drops of conc HCl. On cooling, 0·56 g (28%) of creme coloured crystals of **2c** separated, m.p. 174–6° from EtOH. (Found: N, 8·21; 8·14. Calc. for $C_{23}H_{18}N_2O$ (338·41): N, 8·28%).

2 - [4,5(3) - *Diphenyl* - 3(5) - *pyrazolyl*] - *acetophenone* (**2e**). 70% hydrazine hydrate (0·15 g) was added to a boiling methanolic (10 ml) soln of 1,2,5 - triphenyl - 1,3,5 - pentanetrione[14] (0·5 g; 1·45 mmoles). The yellow colour of the soln disappeared immediately, and the product (0·22 g; 45%) crystallized on cooling, m.p. 188–9° from EtOH (Found: N, 8·07, 8·12. Calc. for $C_{23}H_{18}N_2O$ (338·41): N, 8·28%); IR (KBr): νNH 3250 (b); νC=O 1695 cm^{-1}; NMR (DMSO-d_6): Ph δ 8·15–6·9 (15 H); $\rangle$$CH_2$–CO δ 4·37 ppm (s); UV (EtOH): 201 (4·78); 242 (4·41); 320 (2·62), sh.

Alkaline cleavage of 4,6 - *diphenyl* - 3 - *pyridazinyl phenyl ketone* (**7a**). Metallic K (0·3 g) was dissolved in anhyd t-BuOH (9 ml), the excess of the latter was distilled off *in vacuo* and the residue was kept for 15 min at 150° *in vacuo*.[16] Anhydrous dioxane (10 ml) was added and, under efficient stirring, water (0·04 ml). Finally **7a** (0·25 g; 0·8 mmole) was added at 20° under N_2. The mixture was stirred for 4 hr, and evaporated to dryness. Water and ether were added, the organic layer was washed with water, dried ($MgSO_4$) and evaporated to dryness to yield 0·15 g (82%) of **7c**, identical, according to its m.p. (144–145°) and IR spectrum, with an authentic sample.[12] The aqueous alkaline layer was acidified with conc HCl and extracted with ether. Conventional work-up furnished 0·05 g (56%) benzoic acid.

Compound **7c**, NMR ($CDCl_3$): 6-H δ 9·40 (d, J = 2·3 Hz); 3-Ph, *o*-protons δ 8·3–8·1; 4-H δ 8·0 (d, J = 2·3 Hz), other ArH δ 7·85–7·15 ppm (13 H).

Reduction of 4,6 - *diphenyl* - 3 - *pyridazinyl phenyl ketone* (**7a**). A solution of LAH (0·12 g) in anhyd THF (5 ml) was added under continuous stirring to a soln of **7a** (0·12 g; 0·36 mmoles) in anhyd THF (3 ml). A vigorous reaction resulted and a thick red paste, which later turned green, was obtained. After being allowed to stand overnight, the mixture was decomposed by treatment with aqueous EtOH and 10% H_2SO_4. The organic layer was washed with Na_2CO_3 aq to yield a faint yellow soln, the dry residue of which was recrystallized from MeOH to yield 0·06 g (50%) of **7b**, m.p. 140–2° (MeOH), identical according to its IR spectrum with the product obtained by alkaline hydrolysis of **1c**.

Oxidation of α,4,6 - *triphenyl* - 3 - *pyridazinemethanol* (**7b**). A mixture of **7b** (0·2 g; 0·6 mmoles), t-BuOH (3 ml), $KMnO_4$ (0·25 g; 1·6 mmoles) and water (2·5 ml) was heated for 5 hr on a steam bath, an equal amount of $KMnO_4$ aq being added after 3 hr. The mixture was allowed to cool, and the insoluble materials were separated,* dried and extracted with boiling EtOH. From the resulting ethanolic soln 0·11 g (54%) of **7a** separated on cooling as colourless crystals, m.p. 141–142° (EtOH). (Found: C, 82·20; H, 4·77; N, 8·67. Calc. for $C_{23}H_{16}N_2O$ (336·40): C, 82·12; H, 4·79; N, 8·33).

1 - (3,5 - *Diphenyl* - 1 - *phenysulfonyl* - 2 - *pyrazolin* - 5 - *yl*) - *acetone ethylene hemithioketal* (**10**). BF_3-etherate (0·42 g; 3 mmoles) was added at r.t. to a soln of **1b** (0·42 g; 1 mmole) and 2-mercapto-ethanol (0·24 g; 3 mmole) in anhyd THF (2 ml). The mixture was allowed to stand for 24 hr at r.t. Water and chloroform were added, the organic layer was washed with 5% Na_2CO_3 aq and water, and evaporated to dryness. The residue was crystallized from MeOH to yield 0·3 g (62%) of **10**, m.p. 155–156°.

*On acidification of the filtrate, 0·01 g of benzoic acid was obtained.

(Found C, 64·68; H, 5·60; N, 5·58. Calc. for $C_{26}H_{26}N_2O_3S_2$ (478·4): C, 65·27; H, 5·48; N, 5·86%).

Alkali induced cleavage of **10**. A mixture of **10** (0·24 g; 0·5 mmoles), EtOH (100 ml) and 2 N ethanolic NaOH (10 ml) was either refluxed for 2 hr or allowed to stand for 4 weeks, and subsequently evaporated to dryness. Water and ether were added. The organic layer was washed with water, evaporated to dryness and the residue was crystallized from MeOH to yield 0·15 g (89%) of the ethylene hemithioketal of ketone **2f**, m.p. 159–160°. (Found C, 71·52; H, 6·39; N, 8·52; S, 9·51. Calc. for $C_{20}H_{20}N_2OS$ (336·4): C, 71·40; H, 6·00; N, 8·33; S, 9·52%); NMR ($CDCl_3$): 2 Ph δ 7·3 (12 H); $-O-CH_2-CH_2$ m, centered around δ 4·15; CH_2 δ 3·2 (s); $-S-CH_2-CH_2$ m, centered around δ 3·05; CH_3 δ 1·55 ppm.

Conversion of **10** into the hemithioketal of **2f** was brought about also with sodium hydride in benzene or THF at r.t. and sodium dimsylate in DMSO at 100°.

1 - [5(3),4 - *Diphenyl* - 3(5) - *pyrazolyl*] - *acetone* (**2f**). The suspension of the above hemithioketal (0·17 g; 0·5 mmole) in MeOH (6 ml) was treated with chloroamine T[17] (0·17 g; 0·7 mmole). A clear soln resulted and, after 15 min, the starting compound was shown by TLC to have been completely cleaved. The soln was evaporated to dryness. Water and $CHCl_3$ were added, the organic layer was washed with water and evaporated to dryness. The residue was crystallized from MeOH to yield 0·11 g (79%) of **2f**, m.p. 126–128°. MS*: *m/e* 276 (74·4%; M = $C_{18}H_{16}N_2O$); 261 (0·3%; M − 15); 249 (2·9%); 247 (3·6%); 234 (51·7%; M − CH_2CO); 233 (100%; M − CH_3CO); 218 (3·1%); 206 (4·8%); 204 (3·5%); 203 (3·1%); 202 (4·8%); 165 (4·2%; $C_{13}H_9^+$); 130 (10·7%; $C_9H_8NT^{\cdot}$); 103 (6·7%); 91 (4·2%); 89 (4·2%); 77 (8·1%); 51 (3·1%); 43 (19·2%); metastable peaks for transformations 234 $\xrightarrow{-H\cdot}$ 233, 276 $\xrightarrow{-CH_2CO}$ 234, 203 $\xrightarrow{-27}$ 206, 233 $\xrightarrow{-C_3H_3N}$ 130, 130 $\xrightarrow{-27}$ 103. IR (KBr): νNH 3500–2500 (b) with a local maximum at 3270; νC=O 1725 with a shoulder at 1715 cm^{-1}; NMR ($CDCl_3$): NH δ 9·4 (b); Ph δ 7·3 (12 H); CH_2 δ 3·75; CH δ 2·15 ppm.

4,5(3) - *Diphenyl* - 3(5) - *pyrazolecarboxylic acid* (**2g**). (a) **2f** (0·1 g; 0·36 mmole) was oxidized with $KMnO_4$ in aqueous t-BuOH as described for the oxidation of **2a** to yield 0·054 g (57%) of **2g** which, according to its IR spectrum and the m.m.p., proved identical with an authentic sample prepared according to lit.[15] (b) **2e** on similar treatment furnished 39% of **2g**, m.p. 260–261°, lit.[15] m.p. 261°.

Synthesis of the oximes of ketones **1a–c**. The oximes were prepared by refluxing the parent ketones[2] with hydroxylammonium chloride (100% excess) in ethanol-pyridine (1:1) solns.

Compound **1a**-*oxime* m.p. 153–154° (MeOH)†. (Found: N, 9·92. Calc. for $C_{23}H_{21}N_3O_3S$ (419·5, established by high resolution mass spectrometry): N, 10·01%); MS‡: *m/e* 419 (2·7%; M), 402 (0·3%; M − $\dot{O}H$), 401 (0·5%; M − 18), 285 (84%; M − PhC[=NOH]$\dot{C}H_2$), 277 (6·2%; M − $PhSO_2H$), 261 (5·3%; M − $\dot{O}H$ − $PhSO_2\dot{T}$), 260 (6·7%), 248 (3·2%), 220 (6·5%), 158 (9·7%), 157 (12%), 146 (8·0%), 145 (7·5%), 144 (15·0%; M − PhC[=NOH]$\dot{C}H_2$ − $PhSO_2\dot{T}$), 142 (15·0%), 141 (35%; $PhSO_2$), 130 (18%), 129 (16·0%), 128 (13%), 119 (8·5%), 118 (8·8%), 115 (14%), 105 (19%), 104 (23%), 103 (22%), 91 (10%), 77 (100%), 18 (80%); metastable peaks: 193·9 (419 $\xrightarrow{-134}$ 285), 69·8 (285 $\xrightarrow{-144}$ 141).

Compound **1b**-*oxime*, m.p. 168–169° (EtOAc) (Found: N, 9·50. Calc. for $C_{24}H_{23}N_3O_3S$ (433·4): N, 9·69%); MS§: *m/e* 433 (1·2%; M), 416 (0·15%; M − $\dot{O}H$), 415 (0·3%; M − 18), 375 (0·08%; M − MeĊ=NOH), 361 (100%; M − MeC[=NOH]$\dot{C}H_2$), 296 (1·6%), 292 (2·0%), 275 (3·6%; M − $\dot{O}H$ − $PhSO_2\dot{T}$), 264 (1·7%), 247 (3·2%), 246 (3·2%), 233 (4·7%; M − MeC=NOH − $PhSO_2H$), 220 (82%; M − Me-C[=NOH]$\dot{C}H_2$ − $PhSO_2\dot{T}$), 192 (6·0%), 191 (16%), 141 (12%; $PhSO_2$), 91 (6·8%), 77 (35%); metastable peaks: 301 (433 $\xrightarrow{-72}$ 361), 134·1 (361 $\xrightarrow{-141}$ 220).

Compound **1c**-*oxime*, m.p. 197–199° (EtOAc + EtOH), (Found: C, 70·14; H, 5·33; N, 8·65; Calc for $C_{29}H_{23}N_3O_3S$ (495·6): C, 70·27; H, 5·09; N, 8·68%); MS¶: *m/e* 495 (2%; M), 477 (0·8%; M − 18); 361 (100%; M − PhC[=NOH]$\dot{C}H_2$), 354 (2%; M − $PhSO_2\dot{T}$), 353 (3%), 337 (4%), 336 (3%), 326 (4%), 325 (3%), 324 (9%), 323 (12%), 322 (14%), 310 (5%), 309 (7%), 308 (30%), 307 (97%; triphenylpyridine radical ion), 297 (1%), 296 (6%), 295 (5%), 282 (12%), 268 (5%), 233 (9%; M − PhĊ=NOH − $PhSO_2H$), 223 (4%), 222 (25%), 221 (40%), 220 (100%; M − PhC[=NOH]$\dot{C}H_2$ − $PhSO_2\dot{T}$), 191 (20%), 142 (10%), 141 (16%; $PhSO_2$), 105 (80%).

3,5 - *Diphenyl* - 5 - (2 - *methoximino* - 2 - *phenylethyl*) - 1 - *phenylsulfonyl* - 2 - *pyrazoline* (**14**). A mixture of **1c**[2] (2·0 g; 4·2 mmole), methoxyammonium chloride[18] (3·5 g; 42 mmole), EtOH and pyridine (20 ml, each) was refluxed for 8 hr. AcOH (10 ml) was added and refluxing was continued for an additional 6 hr. The mixture was evaporated to dryness, the residue was triturated with water to yield crude **14** which was recrystallized from EtOAc, yield: 2·0 g (95%), m.p. 128–130°. The molecular composition ($C_{30}H_{27}N_3O_3S$, 509·6) was established by high resolution mass spectrometry.

Alkaline cleavage of **1a** *oxime*. A mixture of the oxime (0·42 g; 1 mmole), EtOH (100 ml) and 2 N ethanolic NaOH (25 ml) was refluxed for 4 hr. (No reaction took place at r.t. within 72 hr.) The resulting soln was evaporated to dryness. The residue was dissolved in water and the small amount of insoluble impurities was removed by extraction with benzene. The aqueous solution was acidified with HCl and extracted with benzene. The dry residue of the benzene extract was recrystallized from aqueous MeOH to yield 0·22 g (82%) of the oxime of **2a**, m.p. 160–161°, which in all respects proved identical with an authentic sample.

The molecular composition ($C_{17}H_{15}N_3O$, 277·3) was established by high resolution mass spectrometry.

An *authentic* sample of the product was obtained by oximation of **2a**.

Alkaline cleavage of **1b**-*oxime*. The oxime (0·43 g; 1 mmole) was treated with ethanolic NaOH for 2 hr as described for **1a**-oxime. (Again, no reaction took place at r.t. within 96 hr.) The resulting mixture was evaporated to dryness. The residue was triturated with dil HCl to yield 0·2 g (90%) of 3,5-diphenylpyrazole which, according to its m.p. and IR spectrum, proved identical with an authentic sample.[10]

Hydrolysis of 3,5 - *diphenyl* - 1 - *phenylsulfonylpyrazole*. The sulfonylpyrazole (0·1 g) was treated with hot 0·2 N ethanolic NaOH (44 ml). Hydrolysis took place immediately according to TLC. The soln was worked up as above to yield 0·06 g (96%) of 3,5-diphenylpyrazole.

Alkaline cleavage of **1c** *oxime*. (a) A mixture of the oxime (1·0 g; 2·0 mmoles), EtOH (100 ml) and 2 N ethanolic KOH (50 ml) was allowed to stand for 24 hr at r.t. The resulting soln was concentrated to about 1/2 of its original volume and acidified with HCl to yield a crystalline ppt (0·85 g; 85%) of the phenylsulfonylhydrazone of **5**, m.p. 185–187° from EtOAc. (Found: C, 69·83; H, 5·43; N, 8·56; O, 9·77; S, 6·77. Calc. for $C_{29}H_{25}N_3O_3S$ (495·6): C, 70·27; H, 5·09; N, 8·68; O, 9·67; S, 6·48%).

(b) The same result was achieved when the mixture was refluxed for 3 hr. After prolonged refluxing, formation of 3,5-diphenylisoxazole slowly started according to TLC.

(c) A mixture of **5**-phenylsulfonylhydrazone (50 mg), AcOH (1 ml) and 70% perchloric acid (0·2 ml) was heated for 15 min at 110° and subsequently poured into water to yield a crystalline ppt of 22 mg (90%) of 3,5-diphenylisoxazole, m.p. 140–141° (hexane), identical, according to its IR spectrum, with an authentic sample.[19]

Alkaline cleavage of oxime ether **14**. A mixture of **14** (1·5 g; 3 mmoles), EtOH (300 ml) and 2 N ethanolic NaOH (70 ml) was refluxed for 3 hr and subsequently evaporated to dryness. The residue was triturated with water to yield 0·85 g (93%) of 2,4,6-triphenylpyridine, m.p. 138–140°, identical, according to its IR spectrum and its m.p., with an authentic sample.[9]

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*AEI MS 902 instrument, direct inlet system, 70 eV, 160°.

†Earlier a m.p. of 127–129°C (EtOAc) was stated;[2] according to its IR spectrum the lower melting product appeared to be a mixture of *syn-anti* isomers.

‡AEI MS 902 spectrometer, 70 eV, source temp. 200°, direct inlet system.

§AEI MS 902 spectrometer, direct inlet system, 70 eV, source temp. 200°.

¶Instrument as above, source temp. 150°.

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*The UV spectra have been published in full in Ref. 20.