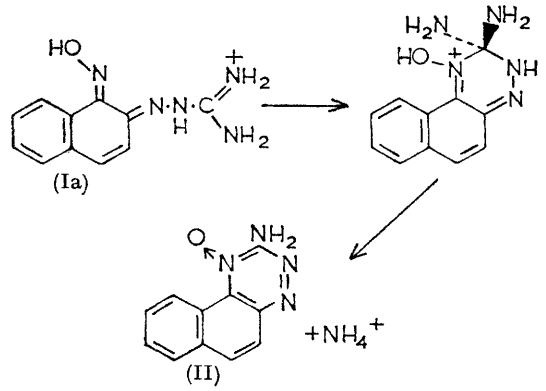
Intramolecular Oxime–Acyl Attack: New Routes to 1,2,4-Triazine 4-Oxides and 1,2,3-Triazoles

By F. J. Lalor and F. L. Scott,* Chemistry Department, University College, Cork, Ireland

A number of 3-substituted 1,2,4-triazine 4-oxides and their deoxy-analogues have been synthesised *via* an intramolecular condensation between neighbouring oxime and acylhydrazone functions. The condensation takes place only in molecules of rigidly favourable geometry, such as the oxime-acylhydrazones of 1,2-naphthaquinone, in which oxime and acyl group are rigidly held in positions sterically favourable for interaction. In molecules of less rigid geometry, oxime-acylhydrazones derived from benzil, for example, ring-closure does not take place. The exact nature of the product of cyclisation depends on the structure of the acyl group. Thus oxime-guanylhydrazones yield 3-amino-1,2,4-triazine 4-oxides, and oxime-semicarbazones cyclise to the analogous 3-hydroxy-compounds. On the other hand, the 3-amino-triazine oxides formed on cyclisation of oxime-thiosemicarbazones undergo deoxygenation concurrently with formation, and the ultimate products are the analogous deoxy-compounds. The ring-closure process, which is formally an addition–elimination reaction at acyl carbon, is subject to catalysis by either acid or base, or both.

Replacement of the acyl group in the oxime-acylhydrazone by structures which bear an electron-deficient atom other than carbon causes a considerable modification in the chemistry of the compounds. Thus oxime-*OO'*-diphenylphosphorohydrazones undergo a base-induced ring-closure to 1,2,3-triazoles while the analogous oxime-toluene-*p*-sulphonylhydrazones decompose spontaneously with the formation of the related 1-hydroxy-1,2,3-triazoles. Mechanisms are suggested for the ring-closure processes discussed.

OXIME groups behave as ambident nucleophiles,[1] their overall potency depending upon the electrophilic centre with which they interact. They are particularly reactive, for example, towards unsaturated phosphorus centres,[2] a reaction which has important biomedical implications.[3] We have now been able to examine the donor properties of oximes towards a variety of acyl receptor sites,[4] largely as a result of an earlier structural investigation. This work [5a] involved our recognition (later confirmed by Fusco and Bianchetti [5b]) that 1,2-naphthaquinone 1-oxime 2-guanylhydrazone nitrate (Ia) when briefly refluxed with water, loses ammonium nitrate and forms



(Ia)

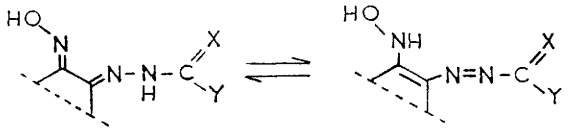
(II)

2-aminonaphtho[1,2-*e*][1,2,4]triazine 1-oxide (II). This reaction was originally noted by Thiele and Barlow [6] but (despite statements to the contrary in a recent review [7]) these authors did not assign a structure to the organic product of the decomposition. Compound (II) is most probably formed by nucleophilic attack of the oxime nitrogen on the guanidinium function in compound (Ia) *via* an addition–elimination process,[8a] in which the acyl carbon becomes tetrahedrally hybridised in the intermediate.[8b]

In the intermolecular reaction of oximes with acylating agents, reaction is primarily at the oxygen atom.[9] In our present work, considerations of ring-size confine nucleophilic reactivity to the nitrogen centre, while we have elsewhere discussed [10] processes where ring-size forces reaction at the oxygen ambident site only. To investigate the effect of variations in the structure of the electrophilic centre of compound (Ia) on interaction with the oxime group, and to explore the synthetic scope of the reaction, a variety of analogues of hydrazone (Ia) were synthesised in which the guanyl function was replaced by substituted guanyl or carbamoyl, ethoxycarbonyl, acyl, thiocarbamoyl, and isothiocarbamoyl structures. Generally we used the naphthaquinone-based system referred to above as a model compound because of the convenience of synthesis and properties of the materials thus obtained. The behaviour of these compounds was studied under some or all of a variety of conditions, *i.e.*, heating alone in aqueous or aqueous-alcoholic solvents, treatment with boiling dilute aqueous acid or base, or treatment with boiling glacial acetic acid. Analytical and physical data for the hydrazones are summarised in Table 1, together with the conditions and products of cyclization.

[1] P. A. S. Smith and J. E. Robertson, *J. Amer. Chem. Soc.*, 1962, **84**, 1197; E. Buehler, *J. Org. Chem.*, 1967, **32**, 261.
[2] R. O'Brien, 'Toxic Phosphorus Esters,' Academic Press, New York, 1960, p. 194.
[3] J. I. G. Cadogan and J. A. Maynard, *Chem. Comm.*, 1966, 854, and references therein.
[4] Some of the work reported here has been published in preliminary form: F. L. Scott and F. J. Lalor, *Tetrahedron Letters*, 1964, 641; F. L. Scott and F. J. Lalor, *Chem. and Ind.*, 1966, 420.
[5] (*a*) F. L. Scott and J. Reilly, *Nature*, 1952, **169**, 584; (*b*) R. Fusco and G. Bianchetti, *Gazzetta*, 1957, **87**, 446.
[6] J. Thiele and W. Barlow, *Annalen*, 1898, **302**, 311.
[7] F. Kurzer and L. Godfrey, *Angew. Chem. Internat. Edn.*, 1963, **2**, 459.
[8] (*a*) W. P. Jencks, *Progr. Phys. Org. Chem.*, 1964, **2**, 63; (*b*) D. R. Robinson, *Tetrahedron Letters*, 1968, 5007.
[9] J. W. Churchill, M. Lapkin, F. Martinez, and J. A. Zaslowsky, *J. Amer. Chem. Soc.*, 1959, **81**, 2110.
[10] F. L. Scott, J. C. Riordan, and A. F. Hegarty, *Tetrahedron Letters*, 1963, 537; F. L. Scott, R. J. MacConaill, and J. C. Riordan, *J. Chem. Soc.* (*C*), 1967, 44; F. L. Scott and R. J. MacConaill, *Tetrahedron Letters*, 1967, 3685.

Since compound (Ia) and its substituted analogues constitute a potential α-hydrazone-oxime to α-azo-hydroxylamine tautomeric system, we cannot altogether



exclude the possibility that ring-closure takes place *via* the hydroxyamino-tautomer. Evidence on this point is provided by the 2-methyl-semicarbazone (IIIe). This compound (which cannot tautomerise to an azo-compound) cyclises even more readily than its potentially tautomeric analogues (IIIa—d) inasmuch as reaction of 1,2-naphthaquinone 1-oxime with 2-methylsemicarbazide leads directly to the ring-closure product (IX) under conditions where compounds (IIIa—d) are completely stable. This would seem to indicate that the oximino-tautomer is at least no less reactive towards ring-closure than the hydroxyamino-form. Furthermore, the yellow colour of compounds (Ia)—(IVd) [the red compound (Ib) is a special case; see below] indicates that in the solid form at least tautomers containing azo-chromophores probably do not predominate. In the absence of more conclusive evidence we are assuming for the purposes of this communication that cyclisation takes place exclusively *via* the oximino-tautomers.

Virtually all the hydrazones we studied could be prepared in high yield by standard methods: condensation of quinone oxime with the appropriate hydrazine in aqueous alcohol at, or slightly above, room temperature and in the presence of a catalytic trace of acid. Under these conditions, however, we could not prepare the 4-methyl-guanylhydrazone salt (Ic) and both reactants could be recovered in quantitative yield. If the solution was refluxed, on the other hand, both hydrazone formation and cyclisation took place concurrently. The only product was the amino-triazine oxide (II), the methyl-amino-group being eliminated from the presumed tetrahedral intermediate. Both the phenyl- and *p*-tolyl-guanylhydrazones (Id) and (Ie) could be prepared normally. Under either acidic or basic cyclisation conditions these also eliminated the substituted amino-group with formation of (II). By way of contrast 1,2-naphthaquinone 1-oxime reacted with *NN'*-diphenylamino-guanidine in warm acidic aqueous ethanol to yield 2-anilinonaphtho[1,2-*e*][1,2,4]triazine 1-oxide (V) directly, presumably *via* the hydrazone (If). The uneven reactivity of 1,2-naphthaquinone 1-oxime towards substituted guanylhydrazines hampered the development of this latter synthetic route to 2-substituted analogues of (II). For instance, even under forcing conditions, no

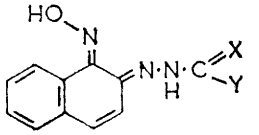
TABLE 1

Hydrazone	Found (%) C	H	N	S	Required (%) C	H	N	S	M.p.	Cyclisation conditions	Product	Yield (%)
(Ia)	44·8	4·45	28·4	—	45·2	4·15	28·8	—	145°	*a*	(II)	89
(Ib)	56·9	5·2	30·1	—	57·6	4·85	30·6	—	152—153	*b*	(II)	91
										c	(II)	98
(Ic)	—	—	—	—	—	—	—	—	—	*d*	(II)	91
(Id)	55·6	4·5	22·3	—	55·4	4·4	22·8	—	132—133	*a*	(II)	91
										e	(II)	77
(Ie)	56·4	4·8	21·6	—	56·5	4·75	22·0	—	160—163	*a*	(II)	100
										e	(II)	63
(If)	—	—	—	—	—	—	—	—	—	*f*	(V)	92
(Ig) *	48·9	3·7	29·3	—	48·2	3·65	30·6	—	165	*b*	(II)	97
										c	(II), (VI)	65, 28
(IIIa)	57·2	4·5	24·1	—	57·4	4·4	24·3	—	190—191	*g*	(VI)	78
										b	(VI)	0
										h	(VI)	90
(IIIb)	66·5	4·3	18·2	—	66·7	4·6	18·3	—	195—196	*c*	(VI)	78
										h	(VI)	93
(IIIc)	60·4	4·9	16·7	—	60·2	5·05	16·2	—	175—176	*c*	(VI)	93
										h	(VI)	0
(IIId)	70·1	4·5	14·2	—	70·1	4·5	14·4	—	185—189	*c*	(VIII)	96
(IIIe)	—	—	—	—	—	—	—	—	—	*f*	(IX)	86
(IVa) *	54·2	4·55	22·9	10·7	53·6	4·1	22·7	13·0	160 (decomp.)	*c*	(II)	64
										g	(X)	65
(IVb)	—	—	—	—	—	—	—	—	—	*d*	(XI)	66
(IVc)	—	—	—	—	—	—	—	—	—	*i*	(V)	53
										j	(XII)	51
(IVd)	—	—	—	—	—	—	—	—	—	*f*	(II)	47

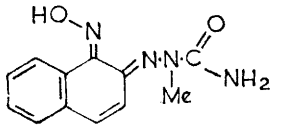
(*a*) Aqueous suspension of hydrazone refluxed for 10—15 min. (*b*) As for (*a*) but with aqueous ethanol as solvent. (*c*) Hydrazone refluxed 15—30 min. with 20% aqueous sodium or potassium carbonate, followed by acidification when product is base-soluble. (*d*) Hydrazine and quinone-oxime did not condense at ambient temperatures in acidified aqueous ethanol. At reflux temperature condensation was followed by cyclisation. (*e*) Hydrazone dissolved in the minimum of ice-cold DMF treated with an excess of ice-cold aqueous sodium or potassium carbonate until precipitation of the free base was complete, then heated to reflux for 15—30 min. (*f*) Cyclisation took place spontaneously at ambient temperatures when quinone-oxime and hydrazine reacted in acidified aqueous ethanol. (*g*) Quinone-oxime, hydrazine, and 1 equiv. of hydrochloric acid refluxed briefly in aqueous ethanol. (*h*) Hydrazone, or quinone-oxime and hydrazine, warmed to *ca.* 60° in glacial acetic acid for *ca.* 15 min. (*i*) As for (*d*), reflux time 15 min. (*j*) As for (*d*), reflux time 45 min.

* These compounds are somewhat unstable, rendering accurate microanalysis difficult.

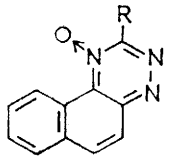
coupling could be effected between this quinone oxime and either 4,4′-dimethylaminoguanidine or 4,4,4′-trimethylaminoguanidine salts. The related 2-methylaminoguanidine nitrate showed a similar lack of reactivity towards 1,2-naphthaquinone 1-oxime.

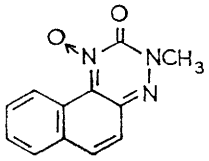


(Ib) X = NH, Y = NH_2
(Ic) X = $NH_2^+NO_3^-$, Y = NHMe
(Id) X = $NH_2^+NO_3^-$, Y = NHPh
(Ie) X = $NH_2^+NO_3^-$, Y = NH·C_6H_4·Me
(If) X = NHPh$^+NO_3$, Y = NHPh
(Ig) X = NH, Y = NH·NO_2
(IIIa) X = O, Y = NH_2
(IIIb) X = O, Y = NHPh
(IIIc) X = O, Y = OEt
(IIId) X = O, Y = Ph
(IVa) X = S, Y = NH_2
(IVb) X = S, Y = NHMe
(IVc) X = S, Y = NHPh
(IVd) X = $NH_2^+I^-$, Y = SMe



(IIIe)

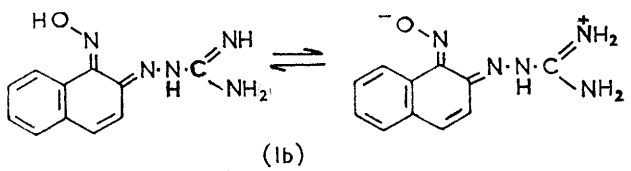




(V) R = NHPh
(VI) R = OH
(VII) R = NH·NO_2
(VIII) R = Ph

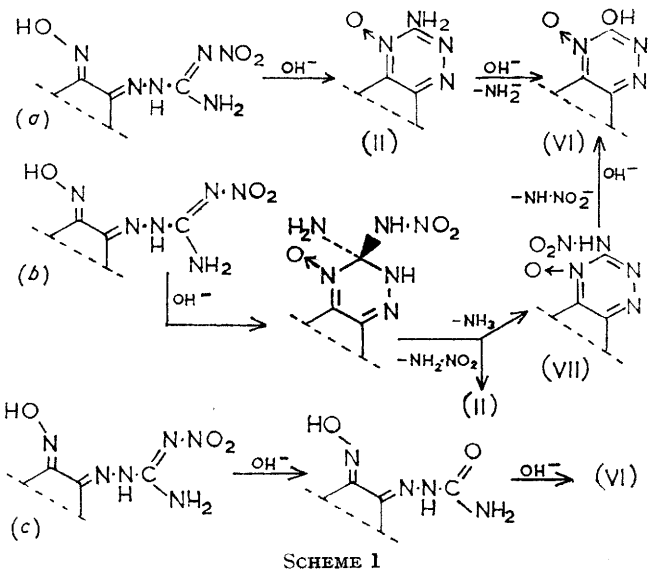
(IX)

Compounds such as hydrazone (Ia) which possess a protonated site for nucleophilic attack can, by analogy with nucleophilic addition to simple carbonyl groups,[11] be said to undergo an 'acid-catalysed' cyclisation. A similar situation exists when cyclisation of a formally neutral hydrazone, such as semicarbazone (IIIa) (see below), is carried out in acidic media. Analogous base catalysis, *i.e.*, conversion of the oxime function into the more nucleophilic conjugate base, operates in alkaline solution. Furthermore, the unexpected reactivity of the guanylhydrazone free base (Ib), which undergoes smooth ring-closure in the absence of any trace of external catalysis (contrast the corresponding semicarbazone below) is probably due to operation of both acid and base catalysis either intermolecularly or *via* a zwitterion of the form:



(Ib)

The ability of the *N*-nitro-substituted guanylhydrazone (Ig) to undergo a similar uncatalysed ring-closure is probably a consequence of the electron-deficient character of the acyl carbon atom, since the low basicity of the nitroguanyl function makes zwitterion formation somewhat unlikely. Another interesting facet of the reactivity of this nitroguanylhydrazone is reflected in the products of its cyclisation. While the 2-amino-heterocycle (II) was the only product of ring-closure in acidic or neutral solution, two products were obtained when compound (Ig) was treated with boiling dilute aqueous potassium carbonate. One of these, obtained in 65% yield, was the expected amino-compound (II), while the other was the analogous 2-hydroxy-triazine oxide (VI), which was isolated in 28% yield.* In theory, all the cyclisations described in this work could yield two products when the presumed tetrahedral intermediate bears a pair of dissimilar exocyclic substituents and hence two different potential leaving groups. With the exception of the nitroguanylhydrazone (Ig), however, an exclusive preference for one or the other of the two leaving groups has been observed within the limits of the experimental product balances.



SCHEME 1

Action of base on nitroguanylhydrazone (Ig) could lead to the formation of both 2-amino-triazine oxide (II) and 2-hydroxy-triazine oxide (VI) by any of three separate pathways (See Scheme 1). (*a*) Initial cyclisation to the amino-triazine oxide (II), followed by a nucleophilic attack of hydroxide ion at the 2-position of the triazine ring, with displacement of the amino-group. (*b*) Collapse of the presumed tetrahedral intermediate in the cyclisation process to give both amino-compound (II) and its 2-nitroamino-analogue (VII). Nucleophilic displacement of the more labile nitroamino-

* Heterocycle (VI) will be shown in a later publication to exist predominantly as the tautomeric triazin-2-one. However, the 'hydroxy'-nomenclature will be used here as a matter of convenience.

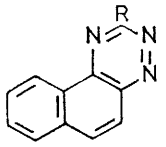
[11] M. L. Bender, *Chem. Rev.*, 1960, **60**, 53.

group (as nitramide anion) would account for the formation of hydroxy-compound (VI). (*c*) As a third possibility, base hydrolysis of the nitroguanyl function in hydrazone (Ig) may compete with formation of compound (II) by ring-closure. The resulting semicarbazone (IIIa) cyclises to hydroxy-triazine oxide (VI) under the conditions of this experiment (see below).

Since the amino-triazine oxide (II) is unaffected by aqueous base of the concentration used to effect ring-closure with compound (Ig), pathway (*a*) can be ruled out. Similarly our inability to convert benzylidene-nitroaminoguanidine to benzylidene-semicarbazide with dilute aqueous carbonate argues against pathway (*c*), and we are forced to the conclusion that route (*b*) seems the most satisfactory.

When the imino-group of the guanyl structure in hydrazone (Ia) was replaced by a carbonyl group, as for example in the semicarbazone (IIIa) and its 2-alkyl and 4-aryl substituted derivatives, or the related ethoxy-carbonyl and benzoyl hydrazones (IIIc) and (IIId), the nature of the product, and to some extent, the reactivity pattern was altered. While the carbonyl group is somewhat more polar than the imino-group, it is also less sensitive to acidic catalysis of nucleophilic attack since the carbonyl oxygen atom is a less basic site than the imino-nitrogen. Hence the fact that none of the compounds in this carbonyl class underwent cyclisation in formally neutral solution is a strong indication that the cyclisation of the free base (Ib) under comparable conditions involves acid catalysis, either intermolecularly or, as already suggested, intramolecularly *via* a zwitterionic structure. In more acidic media, *i.e.*, aqueous-ethanolic solution containing 1 equivalent of hydrochloric acid or in glacial acetic acid, the semicarbazones (but not the ethoxycarbonyl or benzoyl hydrazones) underwent ring-closure, reflecting the lower basicity of the latter two compounds. In contrast, compounds (IIIa—d) underwent a smooth ring-closure in basic solution, the oximate anion thus formed being sufficiently reactive to interact with even the least electrophilic of the neighbouring acyl structures. With the substituted semicarbazones and the ethoxycarbonylhydrazone the product in each case was the 2-hydroxynaphtho[1,2-*e*][1,2,4]triazine 1-oxide (VI), following elimination of an amide anion [in the case of (IIIa) and its derivatives] or ethoxide ion [from (IIIc)]. Fission of a carbon–carbon bond is difficult under the mild conditions employed here (see Table 1) and so it was not surprising that the benzoyl hydrazone (IIId) on treatment with base yielded 2-phenylnaphtho-[1,2-*e*][1,2,4]triazine 1-oxide (VIII) instead of the hydroxy-triazine (VI). In view of our inability to effect condensation between 1,2-naphthaquinone 1-oxime and 2-methylaminoguanidine it was surprising to find that as mentioned earlier the analogous condensation with 2-methylsemicarbazide proceeded quite smoothly, though the 2-methylsemicarbazone (IIIe) could not itself be isolated, the ultimate product being the triazinone oxide (IX).

Thiosemicarbazones derived from 1,2-naphthaquinone 1-oxime were found to be very reactive; only the parent unsubstituted compound (IVa) could be isolated and even this compound lost hydrogen sulphide slowly at room temperature. In basic solution, thiosemicarbazone (IVa) cyclised rapidly to amino-triazine *N*-oxide (II). In acidic solution, however, formation of compound (II) was followed by an *in situ* deoxygenation, so that only 2-aminonaphtho[1,2-*e*][1,2,4]triazine (X) was isolated, together with tarry materials. It was found impossible to isolate the 4-methyl- or 4-phenyl-substituted thiosemicarbazone analogues of (IVa), *i.e.*, (IVb) and (IVc). Reaction between 1,2-naphthaquinone 1-oxime and the appropriate 4-substituted thiosemicarbazide did not take place in acidified aqueous alcohol at or near room temperature. However, if these solutions were refluxed, condensation was followed by both cyclisation and deoxygenation with formation of the 2-methylamino- and



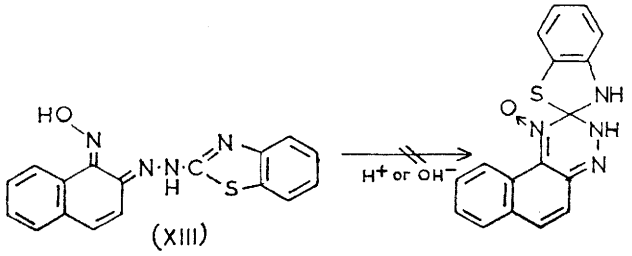
(X) R = NH_2
(XI) R = NHMe
(XII) R = NHPh

2-anilino-triazines (XI) and (XII). In the reaction between 4-phenylthiosemicarbazide and 1,2-naphthaquinone 1-oxime it was possible to isolate the initially formed 2-anilino-triazine 1-oxide (V), since its relatively low solubility in aqueous-alcoholic media removed it from solution before deoxygenation could take place. However, if the oxide was not removed by filtration at an early stage and reflux was prolonged, it slowly redissolved and was replaced by the deoxy-compound (XII). Though evolution of hydrogen sulphide, initially rapid, had ceased long before formation of deoxy-compound (XII) was apparent, it is possible that the removal of the oxide oxygen from (V) involves deoxygenation with hydrogen sulphide remaining in solution. [It can be demonstrated that *N*-oxides such as (V) are deoxygenated by hydrogen sulphide in boiling acidic aqueous alcohol.*] Reaction with 4-methylthiosemicarbazide followed the same pattern but here the oxide was sufficiently soluble to remain in solution until removal of the oxide oxygen was complete. The yields of deoxy-compound rarely exceeded 65%. Further work-up of the reaction mixtures yielded only intractable black tars. The reaction of 1,2-naphthaquinone 1-oxime with *S*-methylisothiosemicarbazide hydriodide in acid solution proceeded smoothly at room temperature, or slightly above it, to yield the expected amino-triazine oxide (II) and methanethiol. In contrast only tarry materials resulted when attempts were made to react the same quinone oxime with either *NS*-dimethyl- or *N*-phenyl-*S*-methylisothiosemicarbazide salts. Cyclisation of 1,2-naphthaquinone 1-oxime

* The ease and modes of deoxygenation of such triazine oxides will be discussed elsewhere.[12]

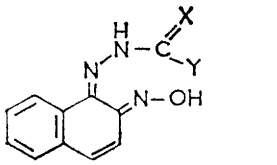
[12] F. J. Lalor and F. L. Scott, to be published.

2-benzthiazolylhydrazone (XIII) could lead to a 2-spiro-1,2,4-triazine 1-oxide or products derived therefrom, but hydrazone (XIII) did not cyclise under our acidic or basic conditions.

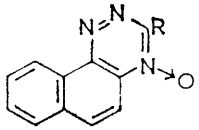


(XIII)

Attempts were also made to apply this synthetic procedure to triazine oxide formation from derivatives of other α-oximino-carbonyl compounds. The 1-carbonyl group in 1,2-naphthaquinone 2-oxime was very sluggish in its reactivity towards hydrazines. While 1,2-naphthaquinone 1-oxime condenses smoothly with aminoguanidine nitrate in the presence of a trace of acid, the 2-oxime is inert under these conditions. However, we were able to effect a clean synthesis of 1,2-naphthaquinone 1-guanylhydrazone nitrate 2-oxime (XIV) by carrying out the coupling reaction in aqueous alcohol approximately normal with respect to hydrogen ion. The action of boiling water on hydrazone (XIV) converted it smoothly into the corresponding 3-amino-naphtho[2,1-*e*][1,2,4]triazine 4-oxide (XV).

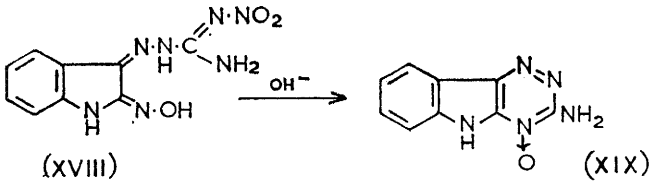


(XIV) X = $NH_2^+NO_3^-$, Y = NH_2
(XVI) X = O, Y = NH_2



(XV) R = NH_2
(XVII) R = OH

A similar procedure was applied to the synthesis of 1,2-naphthaquinone 1-semicarbazone 2-oxime (XVI) but here it was found more convenient to use the more reactive 1,2-naphthaquinone 1-imine 2-oxime as the starting material, a procedure that has parallels in Jencks's use of aniline as a nucleophilic catalyst for semicarbazone formation.[13] Cyclisation of the semicarbazone proceeded normally under basic conditions to yield triazine oxide (XVII).



(XVIII) (XIX)

Isatin 2-oxime 3-nitroguanylhydrazone (XVIII) proved to be stable in acidic solution but with dilute base was rapidly converted into 3-amino[1,2,4]triazino[5,6-*b*]-indole 4-oxide (XIX) in excellent yield. Aminoguanidine nitrate did not react with 1,2-benzoquinone 1-oxime, and reaction with 4-nitrosoresorcinol (4-hydroxy-1,2-benzoquinone 1-oxime) yielded only totally intractable solids.

In all cases of successful cyclisation, so far discussed, the electrophilic and nucleophilic centres of the reacting molecule are attached to a rigid molecular framework which holds them in relative positions highly favourable to intramolecular interaction. Just how important is this steric assistance was demonstrated by our inability to bring about oxime–acyl interaction in its absence. Two kinds of experiment were performed in this regard. First, an attempt was made to produce an intermolecular oxime–guanyl interaction. Thus, benzylideneaminoguanidine nitrate and benzylidenenitroaminoguanidine were separately refluxed for long periods in ethanolic solution containing equimolar amounts of acetophenone oxime or 1,2-naphthaquinone 1-oxime. No evidence for interaction could be detected and both oximes and hydrazones were recovered in quantitative yield. In the second group of experiments the oxime and guanyl functions were maintained in the same molecule but were not constrained in positions sterically favourable for interaction. Here, butane-2,3-dione 2-oxime 3-guanylhydrazone nitrate, α-benzil monoxime guanylhydrazone nitrate, and α-benzil monoxime benzoylhydrazone (in all of which there is a limited degree of steric assistance towards triazine formation) underwent no cyclisation. The butane-2,3-dione derivative underwent a complex disproportionation in refluxing aqueous solution, but the recovery of 58% unreacted hydrazone after 6 hours left no doubt that triazine formation was not being obscured by a more rapid disproportionation process. The products of disproportionation were butane-2,3-dione 2-oxime, the analogous dioxime and the guanylosazone (see Experimental section).

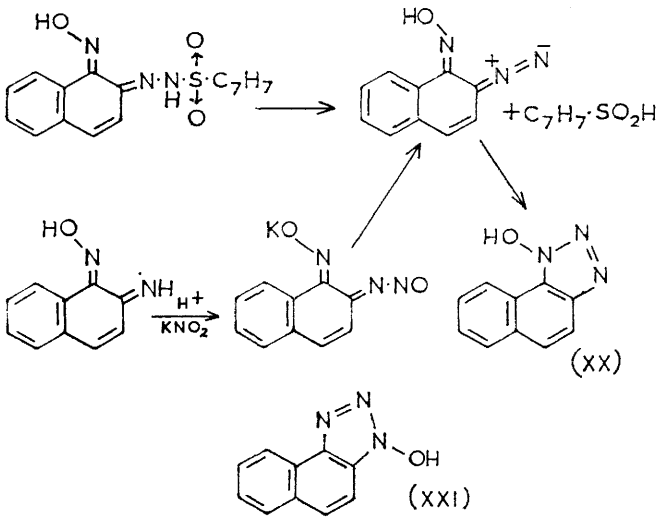
The two benzil derivatives were similarly resistant to cyclisation, though in the case of the benzoylhydrazone, which occurs in two isomeric forms (see Experimental section) aqueous base was observed to convert the higher-melting isomer into the lower-melting form. It is interesting to compare the high degree of steric assistance which the triazine *N*-oxide ring closure obviously requires with the far less rigid requirements of the somewhat related formation of 1,2,4-triazines from α-carbonyl-guanylhydrazones or thiosemicarbazones.[14]

Replacement of carbon at the electrophilic centre of our model compound (Ia) by elements of different electrophilicity produced drastic modifications in the observed chemistry. For instance, toluene-*p*-sulphonylhydrazide reacted with either 1,2-naphthaquinone 1-oxime or the isomeric 2-oxime, in neutral or acidic solution, to give 1-hydroxynaphtho[2,1-*d*][1,2,3]triazole (XX) and the isomeric 3-hydroxynaphtho[1,2-*d*][1,2,3]triazole (XXI)

[13] W. P. Jencks and E. H. Cordes, *J. Amer. Chem. Soc.*, 1962, **84**, 826.

[14] J. G. Erickson, P. F. Wiley, and V. P. Wystrach, 'The Chemistry of Heterocyclic Compounds; the 1,2,3- and 1,2,4-Triazines, Tetrazines and Pentazines,' Interscience, New York, 1956, p. 44.

respectively instead of the expected hydrazones. Formation of these compounds can be explained by initial formation of the toluene-*p*-sulphonylhydrazones followed by their decomposition to α-diazoquinone oximes *via* a spontaneous uncatalysed Bamford–Stevens [15] fission. The α-diazo-oxime so formed would be expected to undergo a rapid ring-closure with formation of the 1-hydroxy-1,2,3-triazole system. A precedent for the first step of this scheme is provided by Cava's observation [16] of the direct formation of 9-diazo-10-phenanthrone from the reaction of 9,10-phenanthrenequinone with toluene-*p*-sulphonylhydrazine in boiling ethanol. Evidently quinonoid structures are capable of exerting a powerful labilising effect towards cleavage of the Bamford–Stevens type. A previous report [17] of the

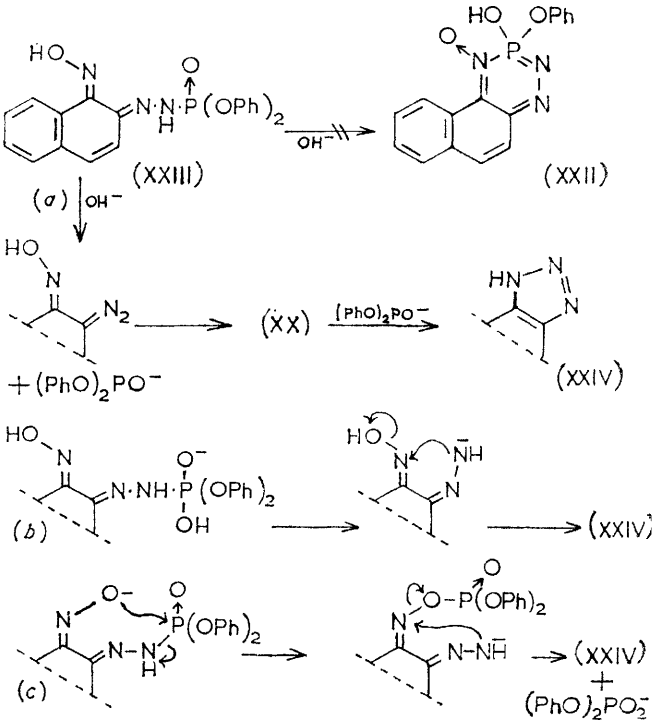


synthesis of triazoles (XX) and (XXI) *via* the stannous chloride reduction of the potassium salts of the two isomeric α-naphthaquinone oxime (*N*-nitroso)imines, which however lacked experimental details, has been confirmed. It is probable that the same pair of α-diazo-oximes intervene as intermediates in this reaction also. Euler and Euler [18] have claimed that a similar reduction of the ammonium salt of ethyl α-oximino-β-(*N*-nitroso)-iminobutyrate, followed by hydrolysis of the product, yields 2-hydroxy-4-methyl-1,2,3-triazole-5-carboxylic acid. In the light of our results it would seem that this compound is almost certainly the 1-hydroxy-isomer.

It is well known that oximes exhibit a considerably enhanced nucleophilicity towards unsaturated phosphorus centres.[2] It has hoped that the novel 2-hydroxy-2-phenoxynaphtho[1,2-*e*][1,2,4]triaza[3]phosphorine 1-oxide (XXII) would result from the action of base on 1,2-naphthaquinone 1-oxime 2-(*OO'*-diphenyl)-phosphorohydrazone (XXIII). However, refluxing with dilute aqueous potassium carbonate converted hydrazone (XXIII) into 1*H*-naphtho[2,1-*d*][1,2,3]triazole (XXIV) in excellent yield.

More than one pathway can be postulated to account for the formation of triazole (XXIV) in this reaction (Scheme 2). In scheme (*a*) a Bamford–Stevens cleavage [15] of hydrazone (XXIII) leads to hydroxy-triazole (XX) *via* the previously postulated α-diazo-oxime intermediate. As 1-hydroxy-triazoles are known to exist in equilibrium with the tautomeric *N*-oxides [19] the oxide form of compound (XX) might then be reduced to triazole (XXIV) by diphenylphosphonate anion formed in the initial cleavage. Since the hydroxy-triazole (XX) was recovered quantitatively after refluxing with diphenyl phosphite in aqueous potassium carbonate, scheme (*a*) had to be rejected.

The simplest remaining solution, (*b*) in Scheme 2, involves an initial degradation of hydrazone (XXIII) to an unsubstituted hydrazide anion followed by a



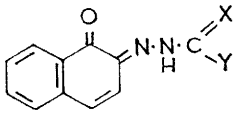
SCHEME 2

nucleophilic displacement of hydroxide ion from the neighbouring oxime group by this hydrazide anion. The first step of this pathway parallels the mechanism suggested [20] for the Wolff–Kishner reduction of semicarbazones, while the second is similar to that proposed by Rapoport and Nilsson [21] to account for the formation of triazoles in the Wolff–Kishner reduction of α-oximino-hydrazones. Further investigation of this reaction at

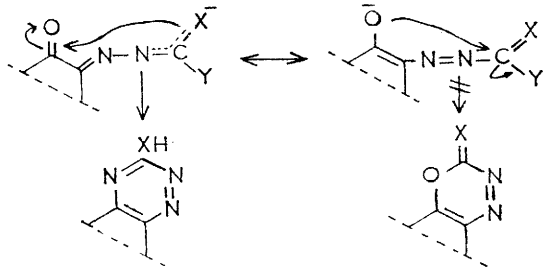
[15] W. R. Bamford and T. S. Stevens, *J. Chem. Soc.*, 1952, 4735.
[16] M. P. Cava, R. L. Litle, and D. R. Napier, *J. Amer. Chem. Soc.*, 1958, **80**, 2257.
[17] A. Harden, *Annalen*, 1889, **255**, 148; A. Harden and J. Okell, *Chem. News*, 1901, 45.
[18] H. Euler and A. Euler, *Ber.*, 1903, **36**, 4253; 1904, **37**, 47.
[19] A. K. McBeth and J. R. Price, *J. Chem. Soc.*, 1936, 111.
[20] T. Nishikawa and T. Ando, *J. Chem. Soc. Japan*, 1962, **83**, 578.
[21] H. Rapoport and W. Nilsson, *J. Amer. Chem. Soc.*, 1961, **83**, 4262.

present under way in these laboratories suggests that the actual process may be more involved. A possible alternative mechanism is suggested in (*c*).

It has long been known that the action of acid or base on acyclic or alicyclic α-carbonyl-guanylhydrazones, semicarbazones, or thiosemicarbazones induces an intramolecular nucleophilic attack of the terminal amino-group of the hydrazone chain on the neighbouring carbonyl function, with formation of the 1,2,4-triazine ring system.[14] In the case of the related 1,2-quinone mono-acylhydrazones only the acid-induced ring-closure has received detailed attention. The anions derived from compounds of this type were of potential interest since they should involve extensive contributions from an azo-phenoxide canonical form. Since the azo-phenoxide anion is closely related structurally to the anion derived from the analogous α-oximino-hydrazones, it was interesting to determine whether intramolecular attack of the phenoxide anion on the acyl group would take place in a manner similar to that demonstrated by Rosenblum *et al.*[22] for the conjugate bases of α-ketol ethoxycarbonylhydrazones.

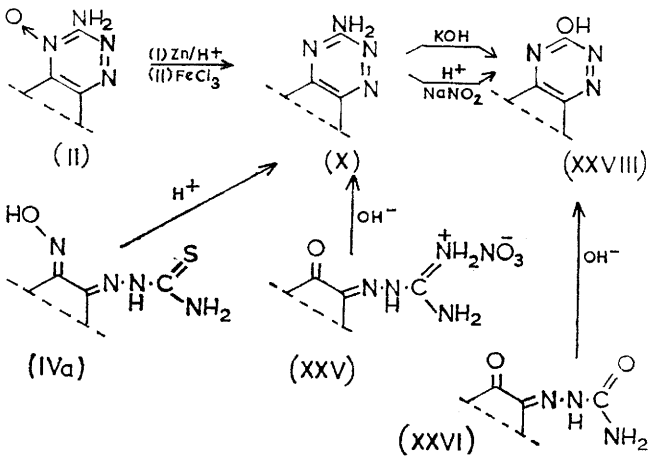


(XXV) X = $NH_2^+NO_3^-$, Y = NH_2
(XXVI) X = O, Y = NH_2
(XXVII) X = S, Y = NH_2



(XXVIII) X = O
(XXIX) X = S

While action of dilute aqueous base on 1,2-naphthaquinone 2-guanylhydrazone nitrate (XXV) or the analogous semicarbazone (XXVI) or thiosemicarbazone (XXVII) yields deep red solutions, suggesting the presence of contributions from azo-type chromophores, no evidence for oxadiazine formation could be found. Instead, the acyl function itself acted as a nucleophile towards the quinonoid carbonyl group and the products were the 2-amino-, -hydroxy-, and -mercapto-derivatives of naphtho[1,2-*e*][1,2,4]triazine, (X), (XXVIII), and (XXIX) respectively. Hydroxy-triazine (XXVIII) is of particular interest since, although it has previously been reported twice in the literature,[5b,23] neither group of workers properly characterised the compound. As 1,2-naphthaquinone could conceivably react with semicarbazide (and the other hydrazines referred to above) at the 1- rather than the 2-carbonyl group, it was felt necessary to establish conclusively the structure of triazine (XXVIII) and its analogues. This was achieved by the sequence of reactions shown in Scheme 3.



SCHEME 3

The 2-amino-compound (X) was synthesised by a slight modification of the two-step reduction and re-oxidation of oxide (II) originally described by Thiele and Barlow,[6] and, as earlier described, by the acid-induced cyclisation of thiosemicarbazone (IVa). There can therefore be no doubt as to the orientation of the triazine ring in (X). Compound (X) prepared by either of these routes was shown (by mixed melting point and infrared spectrum) to be identical with that resulting from the action of base on guanylhydrazone (XXV), thus establishing the latter to be the 2- rather than the 1-guanylhydrazone. The action of strong base [23] or nitrous acid [5b] on amino-compound (X) converted it in high yield into a compound which both analysed satisfactorily for hydroxy-triazine (XXVIII) and was identical with the product previously obtained from semicarbazone (XXVI), thus confirming the structure originally assigned to compound (XXVIII). By analogy with these results we feel it is reasonable to assume that the product obtained by

TABLE 2

	Found (%)			Required (%)			
No.	C	H	N	C	H	N	M.p.
(*a*) 1,2,4-Triazine oxides							
(II)	61·9	3·65	26·4	62·3	3·8	26·4	241°
(V)	71·0	4·5	19·8	70·8	4·2	19·4	222—223
(VI)*	61·7	3·4	19·9	62·0	3·3	19·7	217
(VIII)	74·7	3·95	15·5	74·7	4·05	15·4	164—165
(IX)	63·7	4·1	18·0	63·4	4·0	18·5	184
(*b*) 1,2,4-Triazines							
(X)	67·1	4·1	28·7	67·3	4·1	28·5	198—199
(XI)	68·5	4·95	26·3	68·6	4·8	26·6	222—224
(XII)	75·4	4·75	19·9	75·0	4·45	20·6	268—270
(XXVIII)	66·9	3·85	21·2	67·0	3·6	21·3	272—273

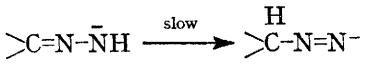
* Compound (VI) readily forms a monohydrate in moist air or when recrystallised from aqueous solvents, m.p. 167° (decomp.) (Found: C, 57·2; H, 3·95; N, 17·7; $C_{11}H_7N_3O_2,H_2O$ requires C, 57·1; H, 3·9; N, 18·2%).

[22] M. Rosenblum, V. Nayak, S. K. DasGupta, and A. Longroy, *J. Amer. Chem. Soc.*, 1963, **85**, 3874.
[23] S. C. De, *J. Indian Chem. Soc.*, 1927, **4**, 183.

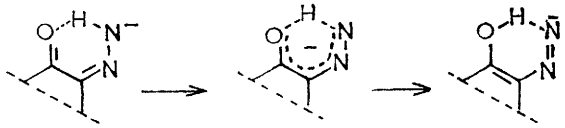
the action of base on the thiosemicarbazone (XXVII) is the 2-thio-analogue of compound (XXVIII), *i.e.*, triazine (XXIX).

In an attempt to force oxadiazine formation we examined the behaviour towards dilute base of 9,10-phenanthraquinone 9-ethoxycarbonylhydrazone, an analogue of hydrazone (XXVI) in which the acyl terminus of the hydrazone chain cannot function as a nucleophile. We were able to confirm Rosenblum's observations [22] that this reaction does not lead to oxadiazine formation and to extend them in that we were able to isolate, apart from unreacted hydrazone, a 30% yield of 9-phenanthrol. Laasko *et al.*[24] have also observed 9-phenanthrol as the product of the action of base on 9,10-phenanthraquinone 9-benzoylhydrazone. In the latter case, however, the absence of a potential leaving group on the acyl terminus precludes oxadiazine formation.

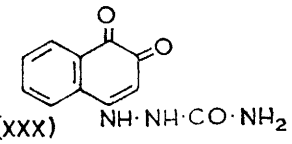
Formation of 9-phenanthrol in the above reaction presumably takes place *via* a Wolff–Kishner reduction taking place under very mild conditions. 'Activation' of the Wolff–Kishner reaction of α-carbonyl-hydrazones has been ascribed [25] to the acid-strengthening effect of the α-carbonyl group. However, if Szmant *et al.*[26] are correct in suggesting that the rate-determining step of the Wolff–Kishner reaction involves transfer of a proton from the terminal nitrogen of a hydrazide ion to the carbonyl of the original carbonyl group:



it is also possible that the α-carbonyl group participates in this proton transfer *via* a cyclic transition state:



which would also account for the 'activation' phenomenon. Subsequent to our initial recognition of this possibility,[27] a similar suggestion has appeared in print.[28]



During this investigation an interesting effect of pH on the reaction of 1,2-naphthaquinone with semicarbazide was observed. In the presence of the usual catalytic trace of acid, the reaction with semicarbazide proceeded normally to give a quantitative yield of semicarbazone. However, in solutions buffered with 1 equivalent of sodium acetate the yield of semicarbazone dropped to and a 20% yield of 4-(1′-semicarbazido)-1,2-naphthaquinone (XXX) was isolated as a highly insoluble precipitate. Compound (XXX) was also formed by the action of semicarbazide on 1,2-naphthaquinone-4-sulphonic acid, so its structure is not in doubt. This reaction appears to be general and is being further investigated.

EXPERIMENTAL

Melting points were determined on an Electrothermal melting point apparatus. All the hydrazines and most of the hydrazones used were prepared by standard methods that are adequately described in the literature. As the majority of the ring-closure reactions studied involved only minor variations of the same experimental procedure, these data are summarised in Table 1 together with physical and analytical data for the hydrazones involved. Reactions which could not be conveniently included in the Tables or had some point of special interest are described below.

Hydrazone Formation.—*1,2-Naphthaquinone 1-guanylhydrazone nitrate 2-oxime* (XIV). A solution of 1,2-naphthaquinone 2-oxime in 95% ethanol was treated at room temperature with 1 equiv. of aminoguanidine nitrate in aqueous solution, followed by enough 30% aqueous nitric acid to make the solution approximately 1N with respect to hydrogen ion. After 48 hr., the *guanylhydrazone salt* had separated (79%) as light yellow crystals, m.p. 159—160° (from ice-cold DMF–ether) (Found: C, 45·5; H, 4·3; N, 28·6. $C_{11}H_{11}N_5O,HNO_3$ requires C, 45·2; H, 4·15; N, 28·8%).

1,2-Naphthaquinone 1-semicarbazone 2-oxime (XVI). An aqueous-ethanolic solution of 1,2-naphthaquinone 1-imine 2-oxime and semicarbazide hydrochloride, acidified with a drop of dilute hydrochloric acid, deposited yellow crystals of the *semicarbazone* after 48 hr. at room temperature. It had m.p. 214—216° (from aqueous ethanol). Yield 80% (Found: C, 57·7; H, 4·45. $C_{11}H_{10}N_4O_2$ requires C, 57·4; H, 4·4%).

Isatin 2-oxime 3-nitroguanylhydrazone (XVIII). Condensation of isatin 2-oxime with nitroaminoguanidine yielded the *nitroguanylhydrazone* (XVIII) as the monohydrate, yellow crystals from aqueous ethanol, m.p. 197° with slight explosion (Found: C, 37·9; H, 3·9; N, 35·4. $C_9H_9N_7O_3,H_2O$ requires C, 38·4; H, 3·95; N, 34·9%).

Butane-2,3-dione 2-oxime 3-guanylhydrazone nitrate. The *guanylhydrazone* crystallised from aqueous ethanol in colourless needles, m.p. 215° (Found: C, 27·7; H, 5·65; N, 37·9. $C_5H_{11}N_5O,HNO_3$ requires C, 27·3; H, 5·5; N, 38·2%).

Benzil 1-oxime 2-guanylhydrazone nitrate. This was obtained as colourless *crystals* (from water), m.p. 186—186·5 (Found: C, 52·3; H, 4·55; N, 24·1. $C_{15}H_{15}N_5O,HNO_3$ requires C, 52·3; H, 4·7; N, 24·4%).

Benzil 1-oxime 2-benzoylhydrazone. On refluxing equimolar amounts of benzil α-oxime and benzhydrazide in boiling ethanol (in the presence of a drop of dilute hydrochloric acid), followed by cooling, a sparingly soluble high-melting point isomer of *benzil 1-oxime 2-benzoylhydrazone*, m.p. 248·9° (28%) separates (Found: C, 73·4; H, 5·05;

[24] P. V. Laasko, R. Robinson, and H. P. Vanderwala, *Tetrahedron*, 1957, **1**, 103.
[25] W. Seibert, *Chem. Ber.*, 1947, **80**, 494.
[26] H. H. Szmant, H. F. Harnsberger, T. J. Butler, and W. P. Barie, *J. Amer. Chem. Soc.*, 1952, **74**, 2724.
[27] F. J. Lalor, Ph.D. Thesis, National University of Ireland, 1965.
[28] H. H. Szmant, *Angew. Chem. Internat. Edn.*, 1968, **7**, 120.

N, 12·0. $C_{21}H_{17}N_3O_2$ requires C, 73·4; H, 5·0; N, 12·2%). Concentration of the filtrate and dilution with water yielded 61% of a relatively soluble isomer, m.p. 233° (Found: C, 73·7; H, 5·1; N, 12·3%). A mixture of the two isomers melted below the m.p. of the low-melting form.

1,2-*Naphthaquinone* 1-*oxime* 2-(OO′-*diphenyl*)*phosphorohydrazone* (XXIII). The *diphenylphosphorohydrazone* (XXIII) was obtained (75%) as pale yellow leaflets from aqueous methanol, m.p. 151—152° (Found: C, 62·9; H, 4·25; N, 10·0; P, 7·4. $C_{22}H_{18}N_3O_4P$ requires C, 63·0; H, 4·35; N, 10·0; P, 7·4%).

4-1′-*Semicarbazido*-1,2-*naphthaquinone* (XXX). (a) *From* 1,2-*naphthaquinone*. 1,2-Naphthaquinone (1·58 g.) in the minimum volume of hot 95% ethanol was treated with an aqueous solution of semicarbazide hydrochloride (1·10 g.) previously neutralised with sodium acetate (0·82 g.). The *semicarbazido-quinone* (XXX) immediately precipitated and was collected by filtration (0·47 g., 20%), m.p. >300°, yellow needles from dilute acetic acid (Found: C, 56·8; H, 3·95; N, 17·9. $C_{11}H_9N_3O_3$ requires C, 57·1; H, 3·9; N, 18·2%). Dilution of the remaining filtrate with water yielded the normal coupling product, 1,2-naphthaquinone 2-semicarbazone, in 70% yield.

(b) *From* 1,2-*naphthaquinone*-4-*sulphonic acid*. An aqueous solution of 1,2-naphthaquinone-4-sulphonic acid, treated with equivalent amounts of semicarbazide hydrochloride and sodium acetate, yielded an immediate precipitate of compound (XXX) (60%), m.p. >300°, with infrared spectrum superimposable on that of material prepared by method (a) above.

1,2-*Naphthaquinone* 2-*thiosemicarbazone* (XXVII). *Quinone thiosemicarbazone* (XXVII) was obtained (86%) as large scarlet needles, m.p. 187—188° (from aqueous ethanol) (Found: C, 56·9; H, 4·05; N, 18·4; S, 13·3. $C_{11}H_9N_3OS$ requires C, 57·1; H, 3·9; N, 18·2; S, 13·9%).

Cyclisation Reactions: Triazine Formation and Related Reactions.—3-*Aminonaphtho*[2,1-e][1,2,4]*triazine* 4-*oxide* (XV). Hydrazone (XIV) (0·43 g.) was suspended in water (30 ml.) and the suspension gently refluxed for 30 min. [condition (*a*), Table 1]. The solution was cooled and the yellow *amino-triazine oxide* (0·28 g., 89%), yellow crystals, m.p. 279—281° from aqueous ethanol, was collected by filtration (Found: C, 62·6; H, 3·95; N, 26·4. $C_{11}H_8N_4O$ requires C, 62·3; H, 3·8; N, 26·4%).

3-*Hydroxynaphtho*[2,1-e][1,2,4]*triazine* 4-*oxide* (XVII). The semicarbazone (XVI) (0·20 g.) was warmed to reflux with 20% aqueous potassium carbonate (30 ml.) [*i.e.*, conditions (*c*), Table 1]. After 10 min. the solution was cooled and acidified with dilute hydrochloric acid, yielding the *hydroxy-triazine oxide* as the yellow monohydrate (0·14 g., 69%), m.p. 222° (from aqueous ethanol) [Found (after drying): C, 61·9; H, 3·5; N, 19·7. $C_{11}H_7N_3O_2$ requires C, 62·0; H, 3·3; N, 19·7%] (loss in weight on drying at 100° *in vacuo*, 7·17; $C_{11}H_7N_3O_2,H_2O$ requires 7·79%).

3-*Amino*[1,2,4]*triazino*[5,6-b]*indole* 4-*oxide* (XIX). Treatment of the nitroguanylhydrazone (XVIII) with aqueous base [as described for the semicarbazone (XVI) above] yielded the yellow *triazino-indole oxide* (XIX), crystals from aqueous acetic acid (sublimes slowly at 290—300°) (72%) (Found: C, 53·2; H, 3·25; N, 35·1. $C_9H_7N_5O$ requires C, 53·7; H, 3·5; N, 34·8%).

Disproportionation of butane-2,3-dione 2-*oxime* 3-*guanylhydrazone nitrate in boiling water*. A solution of the guanylhydrazone (3·0 g.) in boiling water (600 ml.) was refluxed for 6 hr. On cooling, a white infusible solid (0·45 g.), m.p. >310°, separates. Comparison with authentic material [29] identified this material as butane-2,3-dione 2,3-guanylosazone dinitrate. The aqueous filtrate was extracted with ether (4 × 20 ml.), and the dried (anhydrous magnesium sulphate) evaporated extracts yielded 0·25 g. of tan solid. Manual separation followed by sublimation *in vacuo* separated this residue into 0·05 g. of white solid, m.p. 72—74° identified (mixed m.p., infrared spectrum) as butane-2,3-dione 2-oxime,[30] and 0·17 g. of white solid, m.p. 229°, identified [mixed m.p., infrared spectrum, and red complex with Ni^{II} as butane-2,3-dione 2,3-dioxime.[31] Concentration of the remaining aqueous filtrate to dryness *in vacuo* gave 1·93 g. of material which could be separated into an alcohol-soluble fraction (1·75 g.), m.p. 112° (mixed m.p. and infrared spectrum showed this fraction to be unreacted starting material) and an insoluble fraction (0·17 g.), infusible <300°, identified as a second crop of butane-2,3-dione 2,3-guanylosazone dinitrate. The overall product balance was as follows. Recovered starting material, 58%. Yields of disproportionation products (based on 42% reacted guanylhydrazone = 100%) were butane-2,3-dione 2-oxime 10%, butane-2,3-dione 2,3-dioxime 52%, and butane-2,3-dione 2,3-guanylhydrazone dinitrate 67%.

2-*Aminonaphtho*[1,2-e][1,2,4]*triazine* (X). (a) *From* 2-*aminonaphtho*[1,2-e][1,2,4]*triazine* 1-*oxide* (II). The triazine oxide (II) (2·0 g.), in boiling acetic acid (20 ml.) and water (5 ml.), was treated portionwise with zinc dust until the solution became colourless. The filtered solution was then diluted with water and 10% aqueous ferric chloride added dropwise until precipitation of the product was complete. Triazine (X) was obtained in 90% yield and was purified by recrystallisation from aqueous ethanol. Analytical and physical data are summarised in Table 2(b).

(b) *From* 1,2-*naphthaquinone* 2-*guanylhydrazone nitrate* (XXV). The guanylhydrazone salt was treated with 20% aqueous potassium carbonate as for conditions (*c*), Table 1. Amino-triazine (X) precipitated directly from solution in *ca.* 70% yield. The infrared spectrum of material thus obtained was superimposable on that prepared as in (a) above, or from 1,2-naphthaquinone 1-oxime 2-thiosemicarbazone (see Table 1), and mixtures of compounds showed no depression of melting point.

2-*Hydroxynaphtho*[1,2-e][1,2,4]*triazine* (XXVIII). (a) *From the action of nitrous acid on amino-triazine* (X).[5b] A solution of triazine (X) (1·5 g.) in 50% sulphuric acid (150 ml.) was treated at 0—5° with a cold aqueous solution of sodium nitrite (1·0 g.). Gas was evolved and a brilliant cherry-red colour developed. (Spot-testing with alkaline 1-naphthol failed to indicate the presence of any diazonium salt.) The solution was kept at 0—5° for 15 min. and then warmed to 60° for a further 15 min. On cooling to room temperature and dilution with water a 79% yield of 2-*hydroxy-triazine* (XXVIII) precipitated and was recrystallised from aqueous ethanol. Analytical and physical data are in Table 2(b). Comparison of infrared spectra and mixed melting point determinations showed the product of this reaction to be identical with that prepared by either of the alternative syntheses described below.

(b) *From the action of* 3N-*potassium hydroxide on amino-triazine* (X).[23] A suspension of compound (X) (0·5 g.) in 3N-aqueous potassium hydroxide (100 ml.) was refluxed for 10 hr. during which time ammonia was evolved and the

[29] J. Thiele and E. Dralle, *Annalen*, 1898, **302**, 275.
[30] V. Meyer and J. Zublin, *Ber.*, 1878, **11**, 320.
[31] L. Tschugaeff, *Z. anorg. Chem.*, 1905, **46**, 144.

triazine dissolved to give a solution with a brilliant green fluorescence. After cooling the solution and diluting with a large volume of water it was made slightly acid with dilute hydrochloric acid. Hydroxy-triazine (XXVIII) precipitated in *ca.* 83% yield.

(c) *From* 1,2-*naphthaquinone* 2-*semicarbazone* (XXVI). When treated as described above for the corresponding guanylhydrazone nitrate, semicarbazone (XXVI) yielded (on acidification) hydroxy-triazine (XXVIII) (73%).

2-*Mercaptonaphtho*[1,2-e][1,2,4]*triazine* (XXIX). 1,2-Naphthaquinone 2-thiosemicarbazone (1·0 g.) was treated with 20% aqueous potassium carbonate, as in conditions (*c*), Table 1. Acidification of the cooled solution with dilute hydrochloric acid precipitated the *mercapto-triazine* (XXIX) (86%), red-brown needles from aqueous ethanol, m.p. 178—180° (Found: C, 62·0; H, 3·35; N, 20·0. $C_{11}H_7N_3S$ requires C, 61·9; H, 3·3; N, 19·7%).

Action of base on 9,10-*phenanthraquinone* 9-*ethoxycarbonylhydrazone*. The hydrazone [22] (0·5 g.) was dissolved in the minimum volume of boiling absolute ethanol and a few ml. of 20% aqueous potassium carbonate were added. The resulting brilliant red solution was diluted slightly with water and refluxed for 10 min. During this time the red colour faded to brown. The cooled solution was acidified with a little hydrochloric acid. The precipitated solid (0·27 g.), m.p. 172°, was identified as unreacted ethoxycarbonylhydrazone by its infrared spectrum and a mixed m.p. determination (recovery 54%). Dilution of the filtrate with water precipitated a silvery white crystalline solid (0·11 g.), m.p. 145—147°, identified as 9-phenanthrol (lit.,[32] 149·2—154°) by comparison of its infrared spectrum with the published spectrum of 9-phenanthrol,[32] formation of the picrate, red crystals, m.p. 185° (lit.,[33] red crystals, m.p. 185°), the addition compound with phenanthraquinone, red needles, m.p. 156—157° (lit.,[33] red needles, m.p. 156—157°), and deep prussian-blue colour with chloroform–aqueous potassium hydroxide.[34] Yield of 9-phenanthrol, 33%.

Triazole Formation and Related Reactions.—1-*Hydroxynaphtho*[2,1-d][1,2,3]*triazole* (XX). (a) *From* 1,2-*naphthaquinone* 1-*oxime*. A solution of 1,2-naphhaquinone 1-oxime (3·46 g.) and toluene-*p*-sulphonylhydrazide (3·72 g.), in 95% ethanol containing a drop of dilute hydrochloric acid, was refluxed for 15 min. and allowed to cool. A light purple solid (3·14 g.) separated which, after recrystallisation from aqueous ethanol (with activated charcoal) and water, was obtained as fine colourless needles, m.p. 248° (lit.,[17] 248°). Microanalytical data confirmed that this compound was 1-hydroxynaphtho[2,1-*d*][1,2,3]triazole (XX) (Found: C, 64·6; H, 3·45; N, 22·4. Calc. for $C_{10}H_7N_3O$: C, 64·9; H, 3·8; N, 22·7%). The yield was 85%. Compound (XX) gives a deep purple colour with diphenylamine–sulphuric acid.

(b) *From* 1,2-*naphthaquinone* 1-*oxime* (2-(N-*nitroso*)-*imine*.[17] The potassium salt of 1,2-naphthaquinone 1-oxime 2-(*N*-nitroso)imine [17] (1·0 g.) was dissolved in warm water (30 ml.), acidified with dilute hydrochloric acid, and treated immediately with an excess of stannous chloride in dilute hydrochloric acid. The mixture was heated to boiling for a few minutes, and on cooling colourless needles of the triazole (XX) separated (0·5 g., 64%) and were collected by filtration, m.p. 248° not depressed on admixture with material prepared as in (a) above. Addition of stannous chloride to the imine salt without prior acidification yielded extremely impure (XX).

3-*Hydroxy naphtho*[1,2-d][1,2,3]*triazole* (XXI). (a) *From* 1,2-*naphthaquinone* 2-*oxime*. Treatment of 1,2-naphthaquinone 2-oxime with toluene-*p*-sulphonylhydrazide (as described above for the analogous 1-oxime) yielded a red gummy solid, m.p. *ca.* 150°. From this, the triazole (XXI) was isolated (71%) as colourless needles, m.p. 222° (lit.,[17] 222°), by Soxhlet extraction with water [Found (for sample dried at 100° *in vacuo*): C, 65·2; H, 3·65; N, 22·8. Calc. for $C_{10}H_7N_3O$: C, 64·9; H, 3·8; N, 22·7%].

(b) *From* 1,2-*naphthaquinone* 1-(N-*nitroso*)*imine* 2-*oxime*.[17] Using the procedure already described for the isomeric 2-(*N*-nitroso)imine, triazole (XXI) was isolated as colourless needles, m.p. 222°, mixed m.p. with (XXI) prepared by route (a) undepressed. Yield 52%.

Action of base on phosphorohydrazone (XXIII). The phosphorohydrazone (1·0 g.) was suspended in 20% aqueous potassium carbonate (150 ml.), the suspension refluxed for 20 min., and then allowed to cool. After adjusting the pH to *ca.* 2 with dilute hydrochloric acid, a white solid was precipitated (colourless crystals from water, m.p. 185°) (lit.,[35] 188°). Microanalysis and a mixed m.p. determination with authentic [36] material identified the product as 1*H*-naphtho[2,1-*d*][1,2,3]triazole (XXIV). The yield was 89% (Found: C, 70·9; H, 4·2; N, 25·0. Calc. for $C_{10}H_7N_3$: C, 71·0; H, 4·15; N, 24·8%).

This work was carried out during the tenure by one of the authors (F. J. L.) of a State Maintenance Allowance for Research.

[8/563 *Received, April 17th*, 1968]

[32] I. M. Hunsberger, R. Ketcham, and H. S. Gutowsky, *J. Amer. Chem. Soc.*, 1952, **74**, 4839.
[33] F. R. Japp and A. Findlay, *J. Chem. Soc.*, 1897, **71**, 1115.
[34] F. R. Japp and F. Klingemann, *J. Chem. Soc.*, 1893, **63**, 770.
[35] K. Fries, R. Walter, and K. Schilling, *Annalen*, 1935, **516**, 248.
[36] O. Diels, *Ber.*, 1921, **54**, 213.