Iminyls. Part 9.[1] Intramolecular Addition of an Iminyl to an Alkene

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Phenyl *o*-styrylphenyl iminyl, generated by oxidation of the corresponding *O*-carboxymethyloxime with persulphate and by thermolysis of the perester of that acid, cyclises to give a mixture of isoquinoline and 1*H*-isoindole derivatives. The intermediate radicals have been investigated by e.s.r.

PREVIOUSLY we reported [2] that iminyls cyclised efficiently onto an adjacent aromatic ring, given favourable molecular geometry, although they did not react with benzene or substituted benzenes under ordinary conditions. We describe here a further intramolecular reaction of iminyls for which there is no intermolecular analogy. Although the parent iminyl (CH_2=N·) does not react with liquid ethylene [3] at 260 K, intramolecular addition of an iminyl onto an adjacent alkenyl group has now been observed.

The iminyl (2; R = Ph) was generated by oxidation of the acids (1; R = Ph, X = H, R′ = H and Me) with persulphate in boiling aqueous solution, and by decomposition of the corresponding perester (1; R = Ph, R′ = H, X = OBu^t) in boiling benzene, both established routes to iminyls.[4]

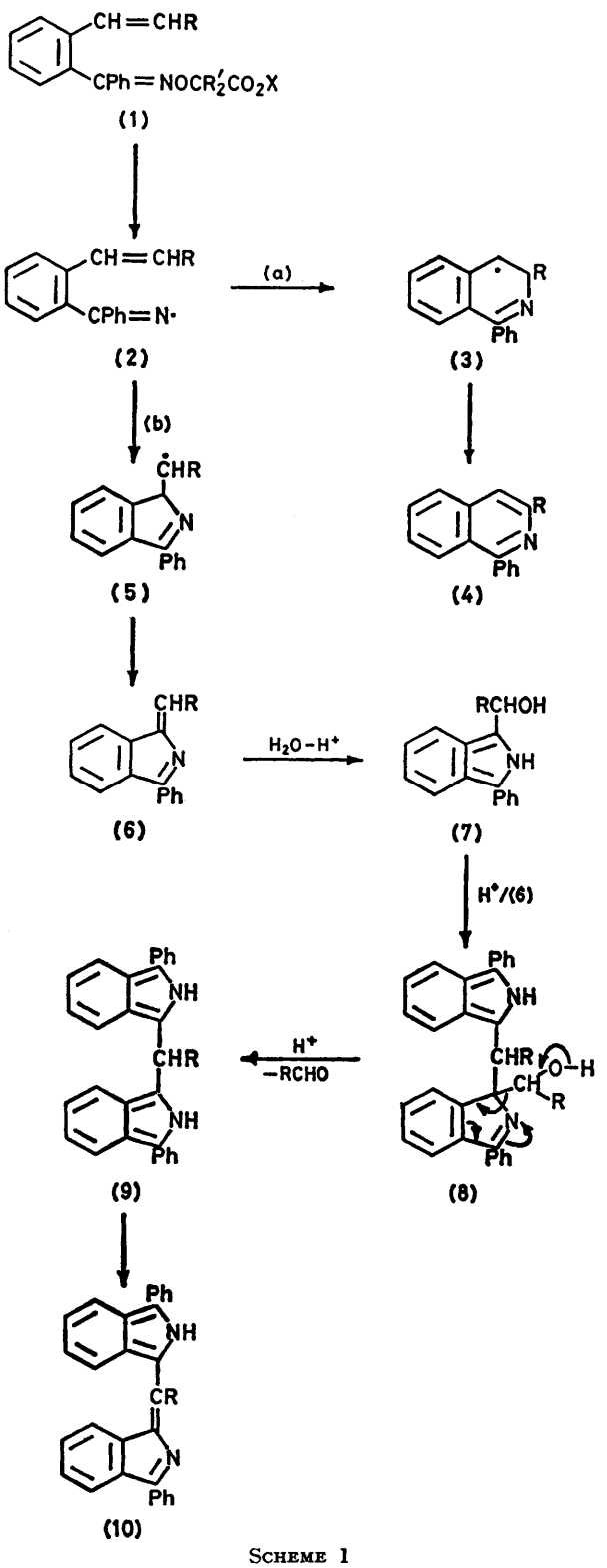
From the blue mixture obtained from the persulphate oxidation four products were separated. An intensely blue pigment was identified as the known [5] isoindolyl derivative (10; R = Ph) (24%) the methylene analogue (10; R = H) of which we had previously obtained from phenyl *o*-tolyl iminyl and formaldehyde.[6] The phenyl analogue (10; R = Ph) was prepared from benzaldehyde and 1-phenyl-1*H*-isoindole.[5] The other products were the red 2,3-diphenylindenone [7] (14; R = Ph) (5%) and two isomeric materials ($C_{21}H_{15}N$). One of these was the diphenylisoquinoline [8] (4; R = Ph) (39%) and the other is tentatively assigned the isoindole structure (6; R = Ph) (6%).

We consider that these products arise by (i) cyclisation [routes (a) and (b) Scheme 1] and (ii) hydrogen abstraction [route (c) Scheme 2] by the first-formed phenyl *o*-styrylphenyl iminyl (2; R = Ph). A measure of the competitive cyclisation to give 6- and 5-membered rings is given by the 4 : 3 ratio of (4; R = Ph) to (6 and 10; R = Ph). Significantly, in Scheme 1 the 1*H*-isoindole (6; R = Ph) is an intermediate *en route* to (10; R = Ph). The route to 2,3-diphenylindenone is less obvious but it probably involves the imine (11) as shown in Scheme 2. We have frequently isolated imines and their hydrolysis products, the corresponding ketones, from oxidations of iminoxyacetic acids (*O*-carboxymethyloximes) with persulphates.[2,4,6] The source of abstractable hydrogen has not been fully established (formaldehyde?) but the occurrence of the reaction is not in doubt.

A similar set of products was isolated when a solution of the t-butyl perester (1; R = Ph, R′ = H, X = OBu^t) in benzene was heated under reflux. Yields were lower but products with 6-membered and 5-membered rings were again isolated. However, in this case 2,3-diphenylindenone was absent. Instead, *o*-styrylbenzophenone was isolated. This result is consistent with Scheme 2, the water and acid necessary for diphenylindenone (14; R = Ph) formation being absent in the perester decomposition. The ketone presumably arises from the imine (11; R = Ph) by hydrolysis during work-up.

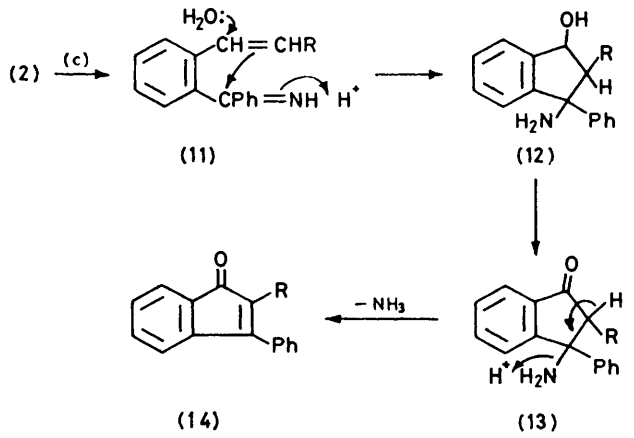
When the perester (1; R = Ph, R′ = H, X = OBu^t) was decomposed in benzene solution in the cavity of an e.s.r. spectrometer, the iminyl (2; R = Ph) was not detected. An intense spectrum consisting of a triplet of triplets rapidly developed. We have encountered such spectra previously [2,4,6] during decomposition of related peresters which were attributed to alkoxy-aminyls. In this case the spectrum showed a_N = 14.1 and a_H = 2.0 G (2 H), g = 2.0053 and is assigned to the radical (15; X is unknown). Iminyl radicals cannot be trapped by nitroso-compounds. Usually when an oximinoperester, *e.g.* (16), is decomposed in the presence of nitrosobutane the spectrum of t-butoxy t-butyl nitroxide accumulates rapidly and then as it wanes that of di-t-butyl nitroxide develops. In an attempt to trap the intermediate radicals (3) and (5) the perester (1; R = Ph, R′ = H, X = OBu^t) in benzene at 50 °C was treated with nitrosobutane. Complex and rapidly changing spectra developed initially which gave way finally to spectra of di-t-butyl and t-butyl t-butoxy nitroxides. Of the several signals to appear initially a triplet (a_N = 15.1 G) of double (a_H = 2.0 G) doublets (a_H = 0.7 G) predominated. This is more likely to be due to the spin adduct of (5) rather than of (3) by comparison with the model nitroxides (17) [9] and (18) [10] which have $a_{\alpha\text{-H}}$ values of 2.26 and 0.86 G, respectively. The relative concentration of the spin adducts, of course, does not necessarily reflect the relative concentration of the radicals present in solution. Hence this result is not at variance with the product analysis.

We proposed to extend the scope of these cyclisations by varying the group R in (2) and observing the effect on the ratio of 5-membered- to 6-membered-ring products. However, this was not practicable because of the ease with which persulphate attacked allylic hydrogen. For example, oxidation of the acid (1; R = Me, R′ = H, X = H) gave a bright-blue mixture of products containing many components only one of which, anthraquinone,



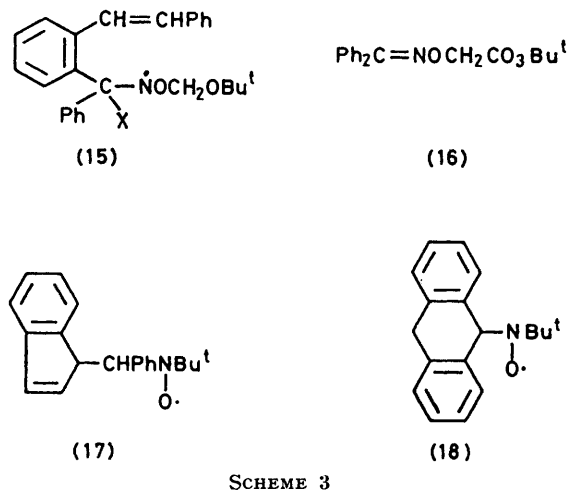
SCHEME 1

was adequately identified. The blue material, presumably an analogue of (10), faded rapidly and decomposed during separation. We were unable to establish satisfactorily the presence of the isoquinoline (4; R = Me) or indenone (14; R = Me) in the mixture although authentic samples of these were to hand. We have obtained anthraquinones previously[6] from *ortho*-substituted iminyls; presumably the course of the reaction in this case is similar.



SCHEME 2

Intramolecular addition of iminyls to C≡C (*cf.* ref. 1) could not be tested using models analogous to (2; R = Ph). Reaction of 1-(2-cyanophenyl)-2-phenylacetylene [11] with phenylmagnesium bromide gave a dark green mixture of several products whose i.r. spectra



SCHEME 3

showed no ν(C≡N) or ν(C≡C) absorption. Reaction of the Grignard reagent of 1-(2-bromophenyl)-2-phenylacetylene [12] and benzonitrile gave a similar result. We presume that reaction of C≡C with C=NH or $C=\overset{+}{N}H_2$ occurs during work-up thus preventing access to the required ketone/oxime substrates.

EXPERIMENTAL

I.r. spectra were measured as KBr discs and n.m.r. spectra in deuteriochloroform, unless stated otherwise. Petroleum refers to light petroleum, b.p. 60—80 °C. Merck GF_{254} silica was used for chromatographic separations.

Preparation of Starting Materials.—o-*Styrylbenzophenone.* To a stirred and cooled solution of benzylmagnesium chloride [prepared from benzyl chloride (83.5 g, 0.66 mol) and magnesium (16.0 g, 0.83 mol) in ether (300 ml)] a solution of *o*-bromobenzaldehyde (116 g, 0.63 mol) in ether (500 ml) was added. After 2 h the product was hydrolysed with ice and acetic acid and the mixture was extracted with ether. The extracts were washed with aqueous sodium hydrogen carbonate and water and then dried ($MgSO_4$). Evaporation of the solvent and distillation of the residue gave 1-(o-*bromophenyl*)-2-*phenylethanol* (70 g, 40%) as an oil, b.p. 209—218 °C/0.35 mmHg, which rapidly crystallised. Recrystallisation from hexane gave needles, m.p. 82—86 °C (Found: C, 60.7; H, 4.9; Br, 29.0%. $C_{14}H_{13}BrO$ requires C, 60.65; H, 4.7; Br, 28.9%), $\nu_{max.}$ 3 320 and 3 255br cm^{-1}; δ 2.22 (1 H, bs, OH), 2.67 (1 H, dd, *J* 9 and 13.8 Hz, CH_aH_bCHOH), 3.17 (1 H, dd, *J* 3 and 13.8 Hz, CH_aH_bCH-OH), and 5.18 (1 H, dd, *J* 9 and 3 Hz, CH_aH_bCHOH).

The alcohol (2.77 g) was heated under reflux for 0.5 h with acetic acid (10 ml) containing concentrated sulphuric acid (1 ml) to give *o*-bromostilbene, b.p. 154—160 °C/0.4 mmHg (lit.,[13] 145 °C/0.15 mmHg).

To a solution of *o*-styrylphenylmagnesium bromide [prepared from *o*-bromostilbene (14.63 g, 0.07 mol) and magnesium (1.82 g, 0.075 mol)] in tetrahydrofuran (100 ml), benzonitrile (6.5 g, 0.063 mol) in tetrahydrofuran (25 ml) was added with vigorous stirring. The mixture was heated under reflux overnight before the deep yellow solution was filtered, and the filtrate was poured into hydrochloric acid (75 ml) and ice. The greenish yellow solid which separated was dissolved in chloroform and the solution was dried ($MgSO_4$). Concentration followed by addition of petroleum to the concentrate gave o-*styrylbenzophenone imine hydrochloride hemihydrate* (14 g, 70%) as a yellow powder, m.p. 223—226 °C (from chloroform–petroleum) (Found: C, 76.4; H, 5.7; Cl, 10.8; N, 4.3. $C_{21}H_{18}ClN \cdot \frac{1}{2}H_2O$ requires C, 76.7; H, 5.8; Cl, 10.8; N, 4.25%), $\nu_{max.}$ 2 750br and 1 645 cm^{-1}.

A suspension of the imine hydrochloride (2 g) in water (15 ml) was heated under reflux for 15 min. The mixture was extracted with ether and the dried extracts were evaporated to give o-*styrylbenzophenone* (1.14 g, 80%) as a yellow oil, b.p. 194—196 °C/0.35 mmHg which eventually crystallised to give rhombs, m.p. 36—42 °C (Found: C, 88.7; H, 5.5. $C_{21}H_{16}O$ requires C, 88.7; H, 5.65%), $\nu_{max.}$ 1 660 cm^{-1}. Its 2,4-*dinitrophenylhydrazone* gave orange–red needles, m.p. 210—213 °C (from acetic acid) (Found: C, 70.1; H, 4.2; N, 11.8. $C_{27}H_{20}N_4O_4$ requires C, 69.8; H, 4.35; N, 12.05%).

o-*Prop*-1-*enylbenzophenone.* o-*Prop*-1-*enylbromobenzene* was prepared by reaction of *o*-bromobenzaldehyde with ethylmagnesium bromide and dehydration of the resulting alcohol as described for its styryl analogue. It was an oil, b.p. 110—112 °C/0.5 mmHg (Found: C, 54.6; H, 4.6; Br, 39.8%; M^+, 195.9888. C_9H_9Br requires C, 54.8; H, 4.6; Br, 40.6%; *M*, 195.9887), δ 1.85 (3 H, d, *J* 7 Hz, CH_3), 6.13 (1 H, dq, *J* 15 and 7 Hz, $CHCH_3$), 6.7 (1 H, d, *J* 15 Hz, CH=$CHCH_3$), and 7.0—7.5 (4 H, m, ArH).

Addition of benzonitrile (6.18 g, 0.06 mol) to a stirred solution of *o*-prop-1-enylphenylmagnesium bromide [prepared from *o*-prop-1-enylbromobenzene (11.82 g, 0.06 mol) and magnesium (2 g)] and work-up as before gave *o*-prop-1-enylbenzophenone imine hydrochloride, hydrolysis of which gave *o*-prop-1-enylbenzophenone [14] as a thick oil which did not crystallise even after several months (Found: M^+, 222.1044. Calc. for $C_{16}H_{14}O$, *M*, 222.1044), $\nu_{max.}$ (film) 1 660 cm^{-1}; δ 1.75 (3 H, d, *J* 6.5 Hz, CH_3), *ca.* 6.0 (1 H, dq, *J* 15 and 6.5 Hz, $CHCH_3$), 6.4 (1 H, d, *J* 15 Hz, ArC*H*), and 7.1—7.8 (9 H, m, ArH). Its 2,4-*dinitrophenylhydrazone* formed orange needles, m.p. 166—167 °C (from ethanol) (lit.,[12] 165—167 °C) (Found: C, 65.7; H, 4.5; N, 13.3. Calc. for $C_{22}H_{18}N_4O_4$: C, 65.6; H, 4.4; N, 13.8%).

o-*Styrylbenzophenone oxime* formed tablets, m.p. 178—180 °C (from chloroform–petroleum or acetic acid) (Found: C, 84.0; H, 5.5; N, 4.7. $C_{21}H_{17}NO$ requires C, 84.25; H, 5.7; N, 4.7%), $\nu_{max.}$ 3 240br cm^{-1}.

o-*Prop*-1-*enylbenzophenone oxime* formed needles, m.p. 133—137 °C (from aqueous ethanol) (Found: N, 5.8%; M^+, 237.1152. $C_{16}H_{15}NO$ requires N, 5.9%; *M*, 237.1153), $\nu_{max.}$ 3 250br cm^{-1}; δ (two isomers) 1.73 and 1.78 (3 H, d, *J* 6 Hz, Me), 6.1—6.4 (2 H, m, CH=CH), and 7.1—7.8 (9 H, m, ArH).

Imino-oxyacetic and 2-*Imino-oxy*-2-*methylpropionic acids.* These were prepared as previously described.[4] *Phenyl*-(o-*styrylphenyl*)*methyleneamino-oxyacetic acid* formed needles, m.p. 139—141 °C (from aqueous acetic acid) (Found: C, 77.3; H, 5.0; N, 3.9. $C_{23}H_{19}NO_3$ requires C, 77.3; H, 5.35; N, 3.9%), $\nu_{max.}$ 1 731 cm^{-1}; δ 4.68 (2 H, s, OCH_2), 7.08 (2 H, s, CH=CH), 7.32 (14 H, m, ArH), and 9.12 (1 H, bs, CO_2H). *Phenyl*-(o-*prop*-1-*enylphenyl*)*methyleneamino-oxyacetic acid* formed needles, m.p. 120—123 °C (from carbon tetrachloride) (Found: M^+, 295.1206. $C_{18}H_{17}NO_3$ requires *M*, 295.1208), $\nu_{max.}$ 1 722 cm^{-1}; δ 1.74 (3 H, d, *J* 6 Hz, CH_3), 4.7 (2 H, s, OCH_2), *ca.* 6.15 (1 H, dq, *J* 16 and 6 Hz, $CHCH_3$), and *ca.* 6.35 (1 H, d, *J* 16 Hz, C*H*Ar).

2-[*Phenyl*-(o-*styrylphenyl*)*methyleneamino-oxy*]-2-*methylpropionic acid* was prepared from the corresponding oxime and 1,1,1-trichloro-2-methylpropan-2-ol hydrate by the literature method.[15] It formed needles, m.p. 116—120 °C (from chloroform–petroleum) (Found: C, 77.6; H, 6.2; N, 3.8. $C_{25}H_{23}NO_3$ requires C, 77.9; H, 6.0; N, 3.65%), $\nu_{max.}$ 1 715 cm^{-1}; δ 1.51 (6 H, s, 2 × CH_3), 7.07 (2 H, s, CH=CH), 7.30 (14 H, m, ArH), and 9.45 (1 H, bs, CO_2H).

Oxidations with Persulphate.—These reactions were carried out as previously described.[4]

Phenyl-(o-*styrylphenyl*)*methyleneamino-oxyacetic acid* (714 mg) gave (i) 3-phenyl-1-[(3-phenyl-2*H*-isoindol-1-yl)phenylmethylene]-1*H*-isoindole (10; R = Ph) (30 mg, 24%) as blue needles, m.p. 209—212 °C (from ethanol) (lit.,[5] 213—214 °C) (Found: C, 89.1; H, 5.3; N, 5.6. Calc. for $C_{35}H_{24}N_2$: C, 88.95; H, 5.1; N, 5.95%); (ii) 1,3-diphenylisoquinoline (60 mg, 39%) as a pale yellow oil (Found: M^+, 281. Calc. for $C_{21}H_{15}N$: *M*, 281), $\nu_{max.}$ 1 632 cm^{-1}; δ 7.24—7.94 (11 H, m, ArH) and 8.3 (4 H, m, ArH). Its picrate formed orange–brown rods (from ethanol), m.p. 166—170 °C (lit.,[8a] 164—165 °C; lit.,[8b] 168—169 °C) (Found: C, 63.8; H, 3.8; N, 11.2. Calc. for $C_{27}H_{18}N_4O_7$: C, 63.55; H, 3.55; N, 11.0%), (iii) 2,3-diphenylindenone (14; R = Ph) (7 mg, 5%) as red prisms (from methanol), m.p. 148 °C (lit.,[7] 150—151 °C) (Found: M^+, 282.1046. Calc. for $C_{21}H_{14}O$: *M*, 282.1044), $\nu_{max.}$ 1 710 cm^{-1}; $\lambda_{max.}$ (EtOH) 261 and 435 nm and (iv) 1-*benzylidene*-3-*phenyl*-1H-*isoindole* (6; R = Ph) (9.7 mg, 6%) as a yellow oil (Found: M^+, 281.1200. $C_{21}H_{15}N$ requires *M*, 281.1204) whose picrate formed orange plates, m.p. 163—165 °C (from methanol) and (v) unchanged acid (520 mg).

Phenyl-(o-*styrylphenyl*)*methyleneamino-oxy*-2-*methylpropionic acid* (77 mg) gave (i) the isoindole (10; R = Ph) (3 mg, 14%), (ii) 1,3-diphenylisoquinoline (14 mg, 56%), (iii) 2,3-diphenylindenone (1.5 mg, 5%), and (iv) unchanged acid (42 mg).

Phenyl-(o-prop-1-enylphenyl)methyleneamino-oxyacetic acid (1.36 g) on oxidation with persulphate gave a bright blue non-acidic fraction (160 mg) repeated chromatography of which gave anthraquinone (*ca.* 10 mg) identical (mass spec. and n.m.r.) with an authentic sample as the only identifiable product. 3-Methyl-1-phenylisoquinoline,[16] and 2-methyl-3-phenylindenone [17] were not present in the reaction mixture (t.l.c.).

Preparation and Thermolysis of o-*Styrylbenzophenone* O-*t-Butoxycarbonylmethyloxime*.—The perester was prepared from the corresponding acid, t-butyl hydroperoxide, and carbonyldi-imidazole by the literature method.[4,18] It was a pale-yellow oil (Found: C, 75.8; H, 6.4; N, 3.1. $C_{27}H_{27}NO_4$ requires C, 75.35; H, 6.35; N, 3.25%), $\nu_{max.}$ 1 793 cm^{-1}; δ 1.27 (9 H, s, Bu^t), 4.72 (2 H, s, OCH_2), 7.404 (2 H, s, CH=CH), and 7.30 (14 H, m, ArH).

A solution of the peracetate (119 mg) in benzene (5 ml) was heated under reflux in a nitrogen atmosphere for 0.5 h. The solvent was removed and the residue was chromatographed to give (i) 1,3-diphenylisoquinoline (7 mg, 9%), (ii) *o*-styrylbenzophenone *O*-(2,2-dimethylpropyl)oxime (20 mg, 19%) as a colourless oil, δ 5.35 (2 H, s, CH_2), 7.02 (2 H, s, CH=CH), and 7.26 (14 H, m, ArH), (iii) 1-benzylidene-3-phenyl-1*H*-isoindole (2.5 mg, 32%), (iv) *o*-styrylbenzophenone (2.5 mg, 3.2%), and (v) the isoindole (10; R = Ph) which was detected but not isolated.

We thank the S.R.C. for financial support.

[0/1550 *Received*, 10*th October*, 1980]

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