General Procedure for Preparation of 2-Oxazolines 7-10 and 23-26. 2-(o-Bromophenyl)-2-oxazoline (10).[18] To a stirred (250 mL) methylene chloride solution of ethanolamine (42.06 g, 0.69) was added dropwise 0.5 equiv (0.34 mol) of o-bromobenzoyl chloride in methylene chloride while the temperature was maintained at 5 °C. The resulting suspension was then allowed to stir at ambient temperature 0.5 h. At the end of this time 200 mL of water was added and the organic layer was separated and the aqueous layer extracted with methylene chloride several times. The combined and dried organic layer was concentrated to yield 92.0 g of crude N-(β-hydroxyethyl)-o-bromobenzamide (**34**): mp 93-95 °C (petroleum ether-ether).

The amide **34** (88.0 g, 0.36 mol) was treated with 53 mL of thionyl chloride in chloroform under reflux 0.5 h. At the end of this time the solvent and excess thionyl chloride were removed under vacuum. The residue was treated with K_2CO_3(aq) and extracted with chloroform several times. The combined and dried organic layer was concentrated to yield 67.34 g (0.25 mol, 71%) of N-(β-chloroethyl)-o-bromobenzamide (**35**): mp 73-75 °C (petroleum ether-ether).

Amide **35** (63.34 g, 0.24 mol) was treated with NaH (8.17 g, 0.34 mol) in THF at reflux 0.5 h. At the end of this time the suspension was filtered and the filtrate dried ($MgSO_4$) and concentrated to yield 43.1 g (0.19 mol, 79%) of the desired product **10**: bp 94 °C (0.05 mm); IR (film) 2940, 1650, 1090, 940, 760, 725 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.9-7.2 (m, 4 H), 4.3 (octet, 2 H); high-resolution mass spectrum, m/e 224.979 (M^+, 1 Br; C_9H_8BrNO requires 224.979).

2-(o-Chlorophenyl)-2-oxazoline (7) was prepared as described above: bp 90 °C (0.015 mm); IR (film) 1650, 1090, 1040, 940 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.9-7.1 (m, 4 H), 4.25 (octet, 2 H); mass spectrum, m/e 181 (M^+, 1 Cl).

Anal. Calcd for $C_9H_8ClNO \cdot 0.33H_2O$: C, 57.61; H, 4.48; N, 7.46. Found: C, 57.70; H, 4.27; N, 7.20.

2-(m-Chlorophenyl)-2-oxazoline (8) was prepared as described above: mp 46 °C; IR (film) 1650, 1350, 1250, 940, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.90 (m, 2 H), 7.35 (m, 2 H), 4.2 (m, 4 H); mass spectrum, m/e 181 (M^+, 1 Cl).

Anal. Calcd for C_9H_8ClNO: C, 59.52; H, 4.44; N, 7.71. Found: C, 59.38; H, 4.56; N, 7.69.

2-(p-Chlorophenyl)-2-oxazoline (9) was prepared as described above: mp 77-78 °C; IR (film) 1650 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.65 (q, 4 H), 4.15 (m, 4 H); mass spectrum, m/e 181 (M^+, 1 Cl).

Anal. Calcd for C_9H_8ClNO: C, 59.52; H, 4.44; N, 7.71. Found: C, 59.70; H, 4.54; N, 7.54.

2-(2,4-Dichlorophenyl)-2-oxazoline (23) was prepared as described above: bp 95 °C (0.2 mm); IR (film) 1650, 1590, 1480, 1100, 1040, 950, 805 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.8-7.1 (m, 3 H), 4.25 (octet, 4 H); mass spectrum, m/e 215 (M^+, 2 Cl).

Anal. Calcd for $C_9H_7Cl_2NO$: C, 50.03; H, 3.27; N, 6.48. Found: C, 49.85; H, 3.26; N, 6.49.

2-(2,5-Dichlorophenyl)-2-oxazoline (24) was prepared as desired above: bp 107 °C (0.5 mm); IR (film) 1650, 1470, 1405, 1100, 1040, 950, 420 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.8 (m, 1 H), 7.32 (m, 2 H), 4.25 (octet, 4 H); mass spectrum, m/e 215 (M^+, 2 Cl).

Anal. Calcd for $C_9H_7Cl_2NO$: C, 50.03; H, 3.27; N, 6.48. Found: C, 50.02; H, 3.18; N, 6.21.

2-(3,4-Dichlorophenyl)-2-oxazoline (25) was prepared as described above: mp 90-91 °C; IR (film) 1650, 1070, 710, cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.0 (d, 1 H), 7.6 (q, 2 H), 4.6-3.8 (m, 2 H); mass spectrum, m/e (M^+, 2 Cl).

Anal. Calcd for $C_9H_7NOCl_2$: C, 50.03; H, 3.27, N, 6.48. Found: C, 50.19; H, 3.20;, N, 6.24.

2-(3,5-Dichlorophenyl)-2-oxazoline (26) was prepared as described above: mp 61-63 °C; IR (film) 1650, 1560, 800 $cm^{1;}$ ^1H NMR ($CDCl_3$) δ 7.70 (s, 3 H), 4.6-3.75 (m, 4 H); mass spectrum, m/e 215 (M^+, 2 Cl).

Anal. Calcd for $C_9H_7Cl_2NO$: C, 50.03; H, 3.27; N, 6.48. Found: C, 50.20; H, 3.30; N, 6.59.

Acknowledgment. I am indebted to the Analytical and Physical Chemistry Department for the analytical data: Ms. E. Reich for combustion analyses, Mr. David B. Staiger and Mr. Gary E. Zuber for NMR/IR spectra, Mr. Walter P. Johnson and Mr. Gerald D. Roberts for mass spectra, and Mr. Lewis B. Killmer and Ms. Mary Mentzer for GC/MS data.

Registry No. **7**, 82891-76-7; **8**, 82891-77-8; **9**, 7399-68-0; **10**, 51816-27-4; **12**, 82891-78-9; **13**, 82891-79-0; **14**, 82891-80-3; **15**, 82891-81-4; **16**, 82891-82-5; **17**, 43221-62-1; **18**, 82891-83-6; **19**, 82891-84-7; **20**, 15629-92-2; **21**, 38754-20-0; **22**, 14264-16-5; **23**, 82891-85-8; **24**, 82891-86-9; **25**, 82891-87-0; **26**, 82891-88-1; **27**, 82891-89-2; **28**, 82891-90-5; **29**, 82891-91-6; **30**, 82891-92-7; **33**, 82891-93-8; **34**, 82891-94-9; **35**, 51816-16-1; ethanolamine, 141-43-5; o-bromobenzoyl chloride, 7154-66-7.

Supplementary Material Available: Spectral data and physical constants of (β-hydroxyethyl)- and (β-chloroethyl)-benzamides **34-49**, intermediates in the synthesis of oxazolines **7-10** and **23-26** (5 pages). Ordering information is given on any current masthead page.

2-Hydroxyindazoles

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Thermolysis of 2-azidophenyl ketoximes provides 2-hydroxyindazoles, which in aqueous solution usually exist in the alternative 1*H*-indazole 2-oxide tautomeric forms. Both N- and O-substituted derivatives are produced on alkylation.

In the course of a study of a general rearrangement reaction of heterocycles, it was found that the oximes of 4-formylbenzofurazan oxides (**1**) were transformed on heating into 2-hydroxy-7-nitroindazoles (**2**).[1] At that time a search of the literature revealed only two prior examples of 3-unsubstituted 2-hydroxyindazoles: the simplest, **3**, reported by Bamberger and Demuth in 1902,[2] and the 7-methoxy-4-nitro compound **4**.[3] Both had been made by thermal decomposition of the corresponding azides (**5**), and

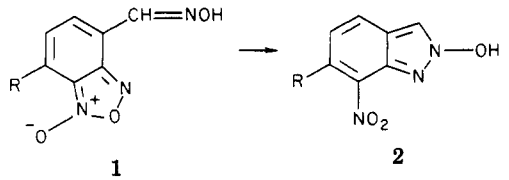
(1) Boulton, A. J.; Thoe K.-W.; Balasubrahmanyam, S.N.; Mallick, I. M.; Radhakrishna, A. S. *J. Org. Chem.* **1980**, *45*, 1653.

(2) Bamberger, E.; Demuth, E. *Chem. Ber.* **1902**, *35*, 1885.

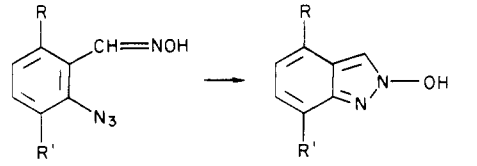
(3) Boulton, A. J.; Ghosh, P. B.; Katritzky, A. R. *J. Chem. Soc. B* **1966**, 1011.

0022-3263/82/1947-4323$01.25/0

both showed a fair degree of thermal stability, as did compounds **2**.

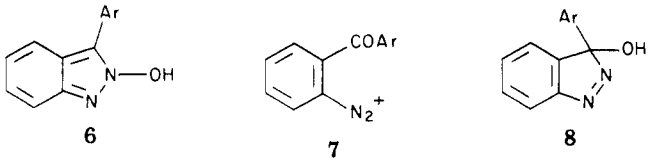


1 **2**



5

3, R = R′ = H
4, R = NO_2; R′ = OMe

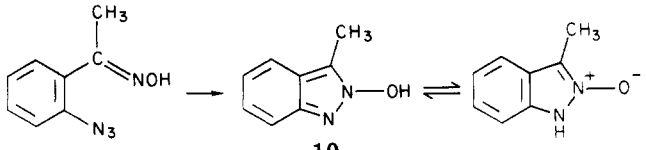


6 **7** **8**

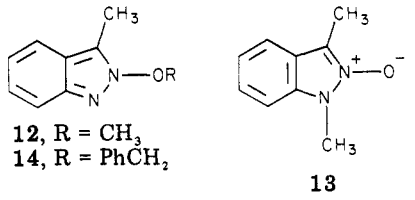
A number of other 2-hydroxyindazoles (**6**), all with 3-aryl substituents, had also been reported, by von Auwers[4] and others.[5] They were prepared by treating diazotized *o*-aminobenzophenones (**7**) with sodium sulfite. However, their chemical properties contrasted so much with those of compounds **3** and **4** that it was evident that the 3-aryl and 3-unsubstituted compounds could not be so closely related as had formerly been supposed. Earlier, we reported arguments and evidence in favor of formula **8** for Auwers' compounds,[6] and although a final proof of structure **8** is still lacking, we are now able to show that the 2-aryl-3-hydroxyindazoles (**6**) that are prepared by the conventional azide pyrolysis method are not the same as the products from the action of sulfite on the benzophenone diazonium salts **7**. The synthesis of the 3-aryl compounds (**6**) proved troublesome, but we found that the 3-methyl analogue was much more easily prepared, and this was subjected to a fuller investigation.

2-Hydroxy-3-methylindazole (10). 2-Azidoacetophenone[7] was prepared by diazotization of the 2-amino compound and treatment with sodium azide and was converted into its oxime (**9**). This oxime had previously been reported in a patent[8] to be formed by reaction of *o*-chloroacetophenone oxime with sodium azide, but the melting point (78–79 °C)[8] did not correspond to that of our product (123–124 °C). The procedure described by the earlier workers did not in our hands provide an azide, and we believe that our route furnished the authentic material.[9]

The oxime **9** on thermolysis provided a white crystalline acidic product, with two remarkably broad hydrogen-bonded OH-stretching bands in the IR spectrum, spanning the 3000–1400-cm^{-1} region, with maxima at ca. 2400 and 1660 cm^{-1}. It is not clear from this whether structure **10** (OH) or **11** (NH form) more accurately describes the



9 **10** **11**



12, R = CH_3
14, R = $PhCH_2$

13

product in the solid phase, but in either case a dimer formed by strong hydrogen bonding is indicated. In water, ultraviolet spectral comparison with fixed (methylated) forms suggested that the NH tautomer was predominant, and this was confirmed by pK_a comparison of the methylated derivatives: the methoxy **12** was more basic (pK_a = +0.11) than the *N*-methyl compound **13** (pK_a = −0.16) by 0.27 pK unit, indicating a value of ca. 1.9 for K_T, the ratio of NH/OH forms in the tautomeric equilibrium **10** ⇌ **11**. Since solvents less polar than water are likely to tend to shift the equilibrium in the direction of the less polar hydroxy form (**10**), we prefer to use the hydroxyindazole nomenclature and to depict the tautomeric compounds by structures analogous to **10**, bearing in mind that indazole 2-oxide structures, e.g., **11**, may be predominant in aqueous solutions. An apparent change in tautomeric structure was noted in this series (**2**; R = OMe) earlier, with the solvents water and ethanol.[1] The pK_a value for **10** as an acid was 5.68, in water.

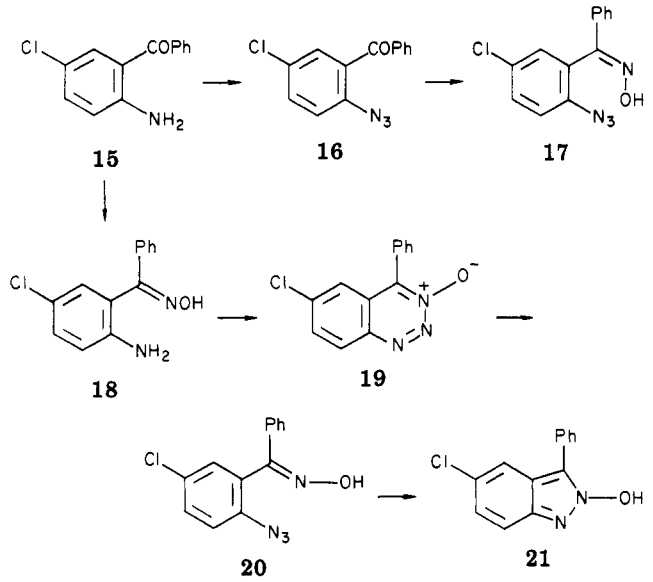
Both the *N*- and *O*-methyl derivatives were formed in the reaction of **10** with diazomethane, the methoxy compound **12** being the major product (ratio 1.4:1). Separation from the *N*-methyl derivative **13** was easily effected by chromatography. The methoxy compound was also formed by methylation of **10** with methyl iodide and alkali, and, unambiguously, by thermolysis of the *O*-methyl ether of **9**. Benzylation ($PhCH_2Br/Na_2CO_3$/DMF) gave the *O*-benzyl derivative **14** exclusively.

3-Aryl-2-hydroxyindazoles (6). The synthesis of a 3-aryl-2-hydroxyindazole was projected for comparison with the products to which structure **6** had been assigned by von Auwers[4] for the reaction of sodium sulfite on the diazonium salts **7**. Accordingly, 2-amino-5-chlorobenzophenone (**15**) was converted into the azide **16**, which formed an oxime, mp 144–146 °C dec, with hydroxylamine.[10] This azido oxime proved surprisingly resistant to heat, and although it was partly decomposed by prolonged reflux in toluene or xylene, TLC examination revealed numerous spots, but none of the authentic 5-chloro-2-hydroxy-3-phenylindazole, prepared as described below, nor any of the (thermally labile) product of the action of sulfite on diazotized **15**, nor any of its thermal decomposition products.

We thought it likely that the cyclization reaction was unsuccessful because of an unfavorable configuration of the oxime group (**17**). We therefore looked for a stereospecific route to the *E* oximes. Diazotization of *o*-amino-

(4) von Auwers, K. *Chem. Ber.* **1896**, *29*, 1255. von Auwers, K.; Strödter, P. *Ibid.* **1926**, *59*, 529.
(5) (a) Dziewonski, K.; Sternbach, L. *Bull. Int. Acad. Pol. Sci. Lett., Cl. Sci. Math. Natl., Ser. A* **1935**, 333; *Chem. Abstr.* **1936**, *30*, 2972. (b) Kametani, T.; Sota, K.; Shio, M. *J. Heterocycl. Chem.* **1970**, *7*, 815.
(6) Boulton, A. J.; Khosrowshahi, J. S.; Thoe K.-W. *J. Chem. Soc., Chem. Commun.* **1978**, 1052.
(7) Adger, B. M.; Bradbury, S.; Keating, M.; Rees, C. W.; Storr, R. C.; Williams, M. T. *J. Chem. Soc., Perkin Trans. 1* **1975**, 31.
(8) Weil, T.; Stange, H. (FMC Corp.) South African Patent 6800916; *Chem. Abstr.* **1969**, *70*, 77 591w.
(9) Dr. H. Stange informs us that there are no spectra of the compound assigned structure **9** in the FMC archives, nor is there any mention in the records of these data having been obtained. We thank him for correspondence of this matter.
(10) Coffen, D. L.; Fryer, R. I.; Katonak, D. A.; Wong, F. *J. Org. Chem.* **1975**, *40*, 894.

benzophenone oximes is known to provide 4-aryl-1,2,3-benzotriazine 3-oxides,[11] and benzotriazines show diazonium reactivity under suitable conditions (usually acidic).[12] The oxime **18** of the amino ketone **15** was treated with nitrous acid, and the triazine oxide **19** formed was stirred with an excess of sodium azide in acetic acid to give an azido oxime (**20**), mp 170–175 °C dec, evidently different from that (**17**) formed from the azido ketone with hydroxylamine. The oxime **20** decomposed more readily than **17** in hot xylene, and from the thermolysate the hydroxyindazole could be isolated as a crystalline solid, mp 198–200 °C. Like the 3-methyl analogue **10**, this product showed a broad band in the IR spectrum, with a maximum at 2680 cm^{-1}: a second maximum in the 1600-cm^{-1} region was weak and obscured by overlapping bands. Its structure is undoubtedly **21** (or its 1*H* 2-oxide tautomer). A parallel set of reactions produced the chlorine-free analogue (**6**; Ar = Ph), mp 168–170 °C, from *o*-aminobenzophenone.



These "authentic" 3-aryl-2-hydroxyindazoles are stable crystalline solids, melting unchanged, and their mass spectra showing intense parent ions. Like the 3-methyl derivative **10**, they are acidic. Their properties contrast strongly with those of the compounds formerly assigned these structures, prepared by Auwers' method,[4] and for which we now propose the structures **8**.

The 5-chloro analogue of **8**, from **15** by successive treatment with nitrous acid and sodium sulfite,[5] was the stablest of the compounds of this type that we have investigated. Prominent in its IR spectrum was a broad, but rather pointed, ν_{OH} band, with its maximum at 3210 cm^{-1}. Auwers' compounds are weakly acidic; they dissolve in ca 1 N alkali (but not in 0.1 N), from which acetic acid precipitates them unchanged. The compounds can be recrystallized from, and their spectra measured in, alcohol or ether solvents, such as dioxane, but in nonpolar media, e.g., $CHCl_3$, they decompose very vigorously, probably via the chain tautomer, a monoaryl diazene. When heated in strong alkali they rearrange to the isomeric 2,3-dihydro-2-aryl-3-indazolones. This reaction was discovered by Auwers[4] and provides a useful route to the indazolones.[5b]

The 2-hydroxyindazoles (**6**) are soluble in aqueous sodium carbonate. With diazomethane they form both *N*- and *O*-methyl derivatives, while with methyl iodide and benzyl bromide they give just the *O*-substituted compounds, as with the 3-methyl analogue **10**. The *N*-methyl derivative of **21** has been prepared before, by a different route;[13] our melting point corresponds closely to that reported by the earlier group.

Experimental Section

Spectroscopic instruments were as described earlier.[1] For spectrophotometric p*K* measurements, acetate (pH 3.7–5.6) and phosphate (pH 5.8–8.0) buffers at ca. 0.01 M concentrations were used, the acidity of samples being checked by a Pye Model 290 pH meter and glass electrode. The weakly basic pK_a values of **12** and **13** were measured in sulfuric acid solutions of known concentration between 0.5% and 40%.[14] Estimated errors in the latter measurements are ±0.05 unit; the buffer solution data are more accurate (±0.02). Thermostatic control was not applied for these approximate measurements: the laboratory temperature was 18 ± 2 °C. Preparative layer chromatographic separations were on Kieselgel PF254 silica.

2-Azidoacetophenone. 2-Nitrobenzoic acid was converted into the acid chloride[15] ($SOCl_2$), and thence into 2-nitroacetophenone[16] (diethyl malonate), which was reduced (Sn/HCl) to the aminoacetophenone.[17] The amine was diazotized and treated with sodium azide to give the oily azidoacetophenone, which could be recrystallized at low temperature from EtOH/light petroleum. The product was not pure (mp ca. 12–15 °C; lit.[11] mp 22–22.5 °C), but the IR spectrum indicated that it was predominantly the azido ketone: ν_{max} 2125 (vs) and 2100 (s) (N_3), 1685 (s, C=O) cm^{-1} (liquid film). It could be purified also by passing through a short column of neutral alumina, eluting with light petroleum.

2-Azidoacetophenone Oxime (9). The azido ketone (1.0 g) was stirred for 12 h in methanol (20 mL) with hydroxylamine hydrochloride (0.49 g) and hydrated sodium acetate (0.42 g) in water (5 mL). White needles separated, and precipitation was complete with addition of a further 15 mL of water and cooling in ice. Filtration and recrystallization from methanol/water (9:1) or from toluene gave the oxime **9** as fine needles (0.49 g, 45%): mp 123–124 °C (lit.[8] mp 78–79 °C, see footnote 9); IR (Nujol mull) ν_{max} 3200 (m), 2125 (s), 2100 (s) cm^{-1}.

Anal. Calcd for $C_8H_8N_4O$: C, 54.5; H, 4.6; N, 31.8. Found: C, 54.3; H, 4.8; N, 31.6.

Attempts at azido dechlorination of 2-chloroacetophenone oxime (cf. ref 8), both in aqueous methanol and in dimethyl sulfoxide, gave products containing no azide group (IR) in the organic fraction, and which appeared to consist, in the main, of partly deoximated starting material.

2-Hydroxy-3-methylindazole (10). The azido oxime **9** (0.3 g) was refluxed in toluene (20 mL) for 17 h. The solution was cooled and extracted with 0.1 M aqueous sodium hydroxide (2 × 20 mL). The aqueous layer was acidified (HCl) and extracted with ether (3 × 20 mL). The ether was dried (Na_2SO_4) and evaporated, and the residue was recrystallized from ethyl acetate to give the hydroxyindazole **10** as fine needles (0.15 g, 60%): mp 173–175 °C; ^1H NMR δ 2.58 (s, 3 H), 7.0–7.6 (m, 4 H); IR (KBr) see text; the IR spectrum in ca. 0.02 M $CHCl_3$ was very similar to that of the solid phase; UV (at pH 2.0) λ_{max} 274 nm (ε 9800), 293 (5600), 304 (4700); UV (at pH 8.6) λ_{max} 295 nm (ε 8300).

Anal. Calcd for $C_8H_8N_2O$: C, 64.9; H, 5.4; N, 18.9. Found: C, 64.7; H, 5.5; N, 18.5.

(11) Meisenheimer, J.; Senn, O.; Zimmermann, P. *Chem. Ber.* **1927**, *60*, 1736. This cyclization, like others in the same area [see also Sternbach, L. H.; Kaiser, S.; Reeder, E. *J. Am. Chem. Soc.* **1960**, *82*, 475], is known to depend on the configuration of the oxime group. We did not, however, observe any indoxazenes, derived from the (*Z*)-oximes, in the product; probably they were eliminated during the workup.

(12) Kobylecki, R. J.; McKillop, A. *Adv. Heterocycl. Chem.* **1976**, *19*, 215.

(13) Zenchoff, G. S.; Walser, A.; Fryer, R. I. *J. Heterocycl. Chem.* **1976**, *13*, 33.

(14) Rochester, C. H. "Acidity Functions"; Academic Press: New York, 1970.

(15) The violent decomposition of *o*-nitrobenzoyl chloride on attempted distillation is a well-known hazard. Excess of thionyl chloride should be removed in vacuo, a little dry light petroleum added, and the vacuum reapplied to remove the solvent, at room temperature.

(16) Reynolds, G. A.; Hauser, C. R. "Organic Syntheses"; Wiley: New York, 1963; Collect. Vol. IV, p 708.

(17) Leonard, N. J.; Boyd, S. N. *J. Org. Chem.* **1946**, *11*, 405.

2-Methoxy-3-methylindazole (12). 2-Azidoacetophenone (1.0 g) was stirred for 12 h in methanol (20 mL) with methoxyamine hydrochloride (0.57 g) and hydrated sodium acetate (0.42 g) in water (5 mL). After standing for a further 24 h, the solution was poured into ice–water and the resultant precipitate was filtered off and recrystallized from aqueous methanol, giving needles (0.45 g, 40%) of the azidoacetophenone oxime *O*-methyl ether, mp 45 °C. This product was refluxed in toluene for 11 h. The solvent was removed and the residue was separated by preparative LC, eluting with toluene/ethanol (15:1). Two principal fractions were observed, the more mobile being the unchanged oxime ether, the less providing the methoxyindazole **12** (0.14 g, 37%) as a light-brown oil: ^{1}H NMR δ 2.51 (3 H, CMe), 4.18 (3 H, OMe), 6.75–7.85 (m, 4 H); MS, *m/e* 162 (100, P$^+$); UV (EtOH/H_2O, 1:3) λ_{max} 277 nm (ϵ 6500), 297 (7200).

Anal. Calcd for $C_9H_{10}N_2O$: C, 66.6; H, 6.2; N, 17.3. Found: C, 66.6; H, 7.0; N, 17.0.

Methylation of 2-Hydroxy-3-methylindazole with Diazomethane. The reagent gas was generated in carbitol and slowly swept through a solution of the hydroxyindazole (0.23 g) in dioxane (20 mL) by a stream of nitrogen until the yellow color persisted in the reaction mixture. Solvent and excess diazomethane were removed in vacuo, and the products were separated by preparative LC, eluting with chloroform/ethyl acetate (2:1). Two main bands were detected by UV, the faster yielding an oil identical with the methoxy derivative **12**, the slower giving needles (0.08 g) from ligroin of 1,3-dimethylindazole 2-oxide (**13**): mp 81–83 °C; ^{1}H NMR δ 2.47 (3 H, CMe), 3.80 (3 H, NMe), 7.0–7.6 (m, 4 H); UV (H_2O) λ_{max} 276 nm (ϵ 12000), 295* (6000), 310* (4700) (an asterisk denotes inflection).

Anal. Calcd for $C_9H_{10}N_2O$: C, 66.6; H, 6.2; N, 17.3. Found: C, 67.0; H, 6.5; N, 17.3.

From the ^{1}H NMR of the mixture before chromatography, the ratio of the *O*-methyl and *N*-methyl isomers **12** and **13** was found to be ca. 1.4. The chemical shifts of the methyl peaks proved to be rather variable with concentration and solvent/solute.

Alkylation of 2-Hydroxy-3-methylindazole with Alkyl Halides. The hydroxyindazole was stirred at 20 °C in dimethylformamide with sodium carbonate (1.2 mol) and methyl iodide (1.2 mol) or benzyl bromide (1.2 mol) for 4 h. Removal of the solvent in vacuo, extraction, and washing with water of the residue gave the methyl (**12**) and benzyl ether (**14**), respectively, in 50–60% yields. No *N*-alkyl derivative was found (^{1}H NMR) in the products. The benzyl ether was an oil, not isolated pure; ^{1}H NMR δ 2.07 (3 H), 5.36 (2 H), 7.19 (5 H, s), 6.65–7.85 (4 H, m).

2-Azido-5-chlorobenzophenone (*Z*)-Oxime (17). The (*Z*)-oxime **17** was prepared from 2-amino-5-chlorobenzophenone (**15**) by conversion into the azide **16**, mp 80–83 °C (lit.[10] mp 83–84 °C), and treatment with hydroxylamine hydrochloride in pyridine, as described by Coffen et al.;[10] mp 144–146 °C dec (lit.[10] mp 140–142 °C dec).

2-Azido-5-chlorobenzophenone (*E*)-Oxime (20). 2-Amino-5-chlorobenzophenone (**15**) was converted into its oxime—probably a mixture of α-*Z* and β-*E* forms, as described by Sternbach et al.[11] This product was treated with nitrous acid by the method of Meisenheimer et al.,[11] to give 6-chloro-4-phenyl-1,2,3-benzotriazine 3-oxide (**19**), mp 184–186 °C dec, as orange plates (80%). The benzotriazine oxide **19** (10 g) was stirred for 48 h with sodium azide (12 g) in acetic acid (100 mL). Most of the acetic acid was removed in vacuo, and the residue was partitioned between water and ether. The ether layer was shaken with dilute aqueous sodium bicarbonate and then evaporated to dryness. The residue was crystallized from toluene, giving pale-brown crystals, turning red in light, of the (*E*)-oxime **20** (9.15 g, 86%), mp 170–175 °C dec.

Anal. Calcd for $C_{13}H_9ClN_4O$: C, 57.3; H, 3.3; N, 20.5. Found: C, 57.3; H, 3.25; N, 20.7.

When the benzotriazine oxide was stirred with sodium azide in dimethyl sulfoxide, containing a drop of 10 N HCl, for 48 h at 20 °C, followed by pouring into water and filtration, a pale yellow-brown, very light sensitive product, mp 163–165 °C dec, was produced (55%). The IR spectrum (ν_{max} 2120 (N_3) cm^{-1}, no ν_{OH} or ν_{NH} bands, no $\nu_{C=O}$) suggested the structure 6-azido-4-phenyl-1,2,3-benzotriazine 3-oxide, but satisfactory analytical data were not obtained.

2-Azidobenzophenone (*E*)-Oxime. 4-Phenyl-1,2,3-benzotriazine 3-oxide[11] (2.0 g) was treated with sodium azide in acetic acid, as described for the 6-chloro analogue **19**, above. The azido ketoxime (2.1 g, 98%) formed prisms, mp 148–152 °C dec from toluene.

2-Azidobenzophenone (*Z*)-Oxime. The isomeric oxime (2.4 g, 75%) was produced from 2-azidobenzophenone[18] (3.0 g) and hydroxylamine hydrochloride in pyridine.[10] It formed pale-yellow crystals from toluene, mp 135 °C dec.

2-Hydroxy-3-phenylindazoles. 2-Azidobenzophenone (*E*)-oxime (0.7 g) was refluxed for 1 h in xylene (10 mL). Nitrogen was evolved fairly vigorously in the early stages of the heating. The acidic product was isolated as described for the 3-methyl analogue **10**. Brown needles of **6** (Ar = Ph; 0.13 g, 20%) were obtained, after recrystallization from ethyl acetate, having mp 168–170 °C; IR ν_{max} ca. 2500 (v br) cm^{-1}; pK_a = 5.18.

Anal. Calcd for $C_{13}H_{10}N_2O$: C, 74.3; H, 4.8; N, 13.3. Found: C, 74.5; H, 4.9; N, 13.4.

In the same way, the 5-chloro analogue **21** was formed in 35% yield from the azide **20**. It formed brownish needles, mp 198–200 °C, from ethyl acetate: ν_{max} 2680 (v br) cm^{-1}; pK_a = 4.68.

Anal. Calcd for $C_{13}H_9ClN_2O$: C, 63.8; H, 3.7; N, 11.4. Found: C, 63.6; H, 3.65; N, 11.6.

Alkylation of 5-Chloro-2-hydroxy-3-phenylindazole. (a) With Methyl Iodide. The hydroxyindazole **21** was methylated as described above for the 3-methyl analogue **10**. The product, 5-chloro-2-methoxy-3-phenylindazole, formed crystals from ethyl acetate, mp 82–83 °C (45%), after chromatography on a short silica gel column. No N-methylated derivative was detected (NMR, TLC). ^{1}H NMR δ 4.09 (s, 3 H), 7.1–7.8 (m, 8 H).

Anal. Calcd for $C_{14}H_{11}ClN_2O$: C, 65.0; H, 4.3; N, 10.8. Found: C, 65.2; H, 4.4; N, 10.6.

(b) With Benzyl Bromide. In a similar way, benzyl bromide in DMF gave only the *O*-benzyl derivative, as an oil: ^{1}H NMR δ 5.27 (s, 2 H), 7.05 (s, 5 H), 6.9–7.65 (m, 8 H).

(c) With Diazomethane. The hydroxyindazole (0.4 g) in dioxane (30 mL) was reacted with diazomethane as described above for the 3-methyl compound. The products were separated by preparative LC, eluting with chloroform/ethyl acetate (3:1). The faster band (R_f 0.8) yielded the 2-methoxy compound (0.22 g); the slower (R_f 0.3) gave 5-chloro-1-methyl-3-phenylindazole 2-oxide (0.18 g) as white needles, mp 160–163 °C, from ethyl acetate (lit.[13] mp 158–163 °C): ^{1}H NMR δ 3.83 (s, 3 H), 7.0–8.2 (m, 8 H).

Registry No. **6** (Ar = Ph), 82980-01-6; **9**, 82979-90-6; **9** methyl ether, 82979-92-8; **10**, 82979-91-7; **12**, 82979-93-9; **13**, 82979-94-0; **14**, 82979-95-1; **15**, 719-59-5; **15** oxime, 18097-52-4; **16**, 53878-93-6; (*Z*)-**17**, 82979-96-2; **19**, 41608-99-5; (*E*)-**20**, 82979-97-3; **21**, 28561-52-6; **21** methyl ether, 82980-02-7; **21** benzyl ether, 82980-03-8; 2′-aminoacetophenone, 551-93-9; 2′-azidoacetophenone, 16714-26-4; hydroxylamine hydrochloride, 5470-11-1; methoxyamine hydrochloride, 593-56-6; 6-azido-4-phenyl-1,2,3-benzotriazine 3-oxide, 82979-98-4; 4-phenyl-1,2,3-benzotriazole 3-oxide, 41572-12-7; 2′-azidobenzophenone (*E*)-oxime, 82979-99-5; 2′-azidobenzophenone, 16714-27-5; 2′-azidobenzophenone (*Z*)-oxime, 82980-00-5; 5-chloro-1-methyl-3-phenylindazole 2-oxide, 59341-19-4.

(18) Smith, P. A. S.; Brown, B. B.; Putney, R. K.; Reinisch, R. K. *J. Am. Chem. Soc.* **1953**, *75*, 6335.