Preparation of 4-Bromo-1-hydroxypyrazole 2-Oxides by Nitrosation of α-Bromo-α,β-unsaturated Ketoximes

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Nitrosation of the oximes of 3-bromo-3-penten-2-one, 3-bromo-4-phenyl-3-buten-2-one, and 2-bromo-1,3-diphenyl-2-propen-1-one using sodium nitrite in acetic acid gave low yields of 4-pyrazolone 1,2-dioxides. Nitrosation using butyl nitrite in the presence of copper(II) sulfate and pyridine in aqueous ethanol produced insoluble copper complexes from which 3,5-dimethyl-, 3-methyl-5-phenyl-, and 3,5-diphenyl-4-bromo-1-hydroxypyrazole 2-oxides could be liberated by treatment with dilute potassium hydroxide, filtration, and acidification of the filtrate. High yields were obtained with the first two oximes, but, presumably due to unfavorable stereochemistry of the oxime, the diphenyl derivative gave a lower yield of the complex, accompanied by 4-bromo- and 4-nitro-3,5-diphenylisoxazole and 4-oximino-3,5-diphenyl-4,5-dihydroisoxazole.

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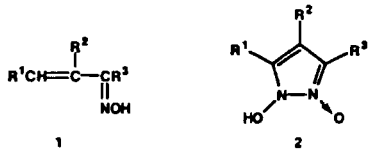
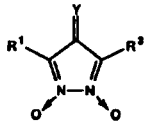
The nitrosation of α,β-unsaturated ketoximes **1** (R is alkyl or aryl except as specified) has been applied in the preparation of a variety of mono-, di-, and trisubstituted 1-hydroxypyrazole 2 oxides. Freeman and Gannon found that for oximes of type **1a**, nitrosation with sodium nitrite in acetic acid gave 3,4,5-trisubstituted-1-hydroxypyrazole 2-oxides **2a** [1]. Under similar conditions they reported that oximes of type **1b** were converted to 4-pyrazolone 1,2-dioxides **3** and the structurally related oximes **4**, which they suggested were formed through the intermediacy of 1-hydroxypyrazole 2-oxides of type **2b** [2]. Subsequently we described a nitrosation method using butyl nitrite in the presence of pyridine and a transition metal ion (*i.e.* Co^{+2} or Cu^{+2}) by which **2b** could be isolated as their insoluble metal complexes, from which the free pyrazoles could be liberated [3]. This method has been applied in the preparation of other examples of **2b** [4], and we recently prepared 1-hydroxypyrazole 2-oxides of types **2c** and **2d** in a similar fashion [5]. To date, however all reported examples have involved unsaturated oximes in which the only types of substituents attached to the olefinic carbons were alkyl or aryl groups. We now wish to report the extension of this method to the preparation of 4-bromo-1-hydroxypyrazole 2-oxides by the nitrosation of α-bromo-α,β-unsaturated ketoximes.

For purposes of this investigation the three α-bromo-α,β-unsaturated ketoximes **5a-c** were prepared by reaction of the appropriate α-bromoketones with hydroxylamine. The oximes **5b** and **5c** have been reported previously, but **5a** appears to be a new substance. Reaction of **5a** under conditions of the Beckmann rearrangement gave *N*-acetylpropanamide **6** (R^1 = Me), analogous to the reported formation of *N*-acetylphenylacetamide **6** (R' = Ph) from **5b** under similar conditions [6]. Accordingly, one may infer that **5a** and **5b** are the (E)-oximes. The oxime **5c** is reported to behave in an atypical fashion in the Beckmann rearrangement [7,8], but its behavior on nitrosation, *vide infra*, and the ease with which it undergoes conversion to 3,5-diphenylisoxazole [6,7,9] suggest that it possesses the (*Z*) geometry as shown.



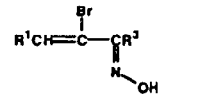
1 **2**

a (R^1, R^2, R^3 ≠ H)
b (R^2 = H)
c (R^1 = H)
d (R^1 = R^2 = H)

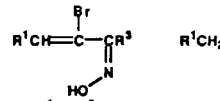


3 (Y = O)
4 (Y = NOH)

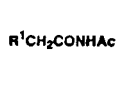
a (R^1 = R^3 = Me)
b (R^1 = Me; R^3 = Ph)
c (R^1 = R^3 = Ph)



5a (R^1 = R^3 = Me)
5b (R^1 = Ph, R^3 = Me)



5c (R^1 = R^3 = Ph)



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Nitrosations of **5a-c** were first examined using sodium nitrite in acetic acid, conditions similar to those used by Freeman [1] to prepare **2a**. Under these conditions no 4-bromo-1-hydroxypyrazole 2-oxides could be isolated. Instead, 4-pyrazolone 1,2-dioxides **3** were obtained which

were identical with the products reported by Freeman from the nitrosation of oximes of type **1b**. It is probable that the 4-bromo-1-hydroxypyrazole 2-oxides are formed as intermediates in these nitrosations of **5a-c**, but that they undergo conversion to **3** under the reaction conditions, much as the intermediate pyrazoles of types **2b** are converted to **3** during nitrosations of **1b** with sodium nitrite in acetic acid.

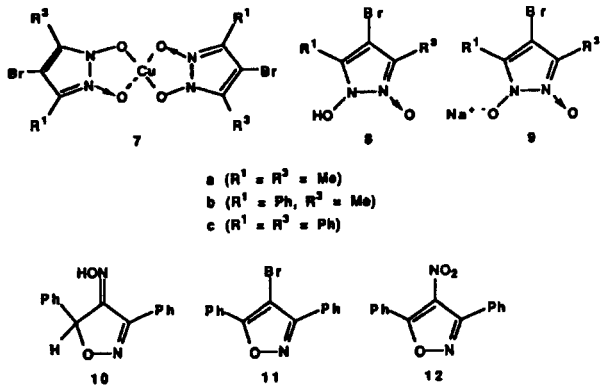
The nitrosation of **5a-c** using butyl nitrite in the presence of pyridine and copper(II) sulfate resulted in the formation of insoluble green to brown solids which were easily isolated and were identified as copper complexes **7** of the conjugate bases of the 4-bromo-1-hydroxypyrazole 2-oxides. The free 4-bromo-1-hydroxypyrazole 2-oxides were obtained by stirring the complexes with dilute potassium hydroxide in aqueous ethanol for several minutes, filtration to remove inorganic solids, and acidification of the filtrates, whereupon **8a-c** precipitated as colorless solids.

Compounds **8a-c** were identical with samples previously prepared during our investigation of the halogenation of *N*-oxygenated pyrazoles [10]. Both the free pyrazoles and the copper complexes were only sparingly soluble in common organic solvents, and decomposition of the pyrazoles occurred upon heating during attempted recrystallization. Crystalline sodium salts **9a-c** were obtained by treating **8a-c** with sodium hydroxide in aqueous ethanol. The salts were readily recrystallized, and samples of the free oxygenated pyrazoles could be obtained by acidification of aqueous solutions of the salts.

The very limited solubility of the free pyrazoles in common solvents also made their analysis by nmr spectroscopy impractical, but the sodium salts were readily examined in deuterium oxide. The ^{1}H nmr spectrum of **9a** consisted of only a single signal for the two methyl groups, which are equivalent in the resonance-hybridized anion. Likewise, the ^{13}C spectrum of **9a** consisted of only three signals, which were located at δ 124.1 ppm for the two equivalent carbons at C3 and C5 of the pyrazole ring of the anion, at 84.7 ppm for the C4 carbon, and at 11.4 ppm for the two equivalent methyl groups. The nmr spectra of **9b** and **9c** were also consistent with the assigned structures.

The ir spectra of **8a-c** included the envelope of strong, broad bands between 1000-2000 cm^{-1} which is the most distinctive feature of 1-hydroxypyrazole 2-oxides in the ir. The ir spectra of the vacuum-dried sodium salts indicated retention of water of hydration in the cases of **9a** and **9b**, and elemental analysis indicated that they were hemihydrates. Under similar conditions **9c** was free of water of hydration. The ir spectra of the sodium salts bore a strong resemblance to those of the corresponding copper complexes.

The yields of the copper complexes from nitrosation of the (*E*)-oximes **5a** and **5b** were both greater than 80%,

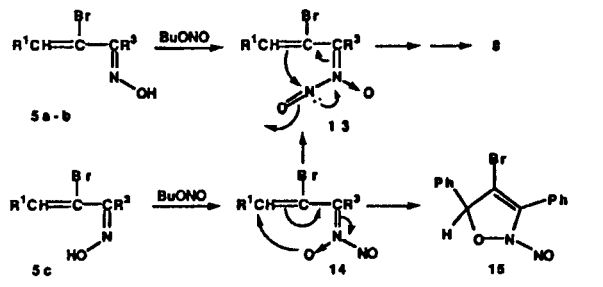


while nitrosation of **5c** gave only about 40% of the complex along with three other products identified as the isoxazole derivatives **10**,**11**, and **12**, Compounds **11** and **12** were identified by reference to reports of their previous preparation. In the case of **10**, we have previously observed its formation along with **2b** (R^1 = R^3 = Ph) in the nitrosation of **1b** [11], and a similar experiment has been reported by Fadda [4]. Although we do not doubt that Fadda has prepared **10**, there are several inaccuracies in that report, prompting us to include a description of our preparation of the compound herein.

The fact that a lower yield of the pyrazole is obtained from **5c** than from **5a** and **5b**, and the formation of isoxazole derivatives during the nitrosation of **5c** are consistent with the (*Z*) geometry about the carbon-nitrogen bond. We recently investigated the nitrosation of the stereoisomeric oximes of 3,4-dimethyl-3-penten-2-one and observed nearly quantitative yield of the oxygenated pyrazole, 3,3,4,5-tetramethyl-3*H*-pyrazole 1,2-dioxide, from the (*E*)-oxime. However, the (*Z*)-oxime, as in the case of **5c**, gave a lower yield of the pyrazole, along with several other products identified as isoxazole derivatives [12], suggesting a similarity with **5c**.

The formation of the 4-bromo-1-hydroxypyrazole 2-oxides from **5a** and **5b** may be explained by a straightforward extension of the mechanistic hypotheses of Freeman for the formation of other 1-hydroxypyrazole 2-oxides [1,13]. Nitrosation of the (*E*)-oximes produces the (*E*)-*N*-nitrosonitrones **13**, which cyclize by electrophilic attack of the *N*-nitroso group at the β position as shown in Scheme 1. If **5c** does, indeed, have the (*Z*) oxime configuration, then its nitrosation would produce the (*Z*)-*N*-nitrosonitrone **14** in which the nitroso group is unfavorably oriented for pyrazole formation. The formation of the pyrazole from **5c** would require a stereoisomerization of **14** to **13**, while the isoxazole derivatives could be formed through a competing cyclization of **14** to the 4-bromo-2-nitroso-3-isoxazoline **15**, a process involving bond formation between the β-carbon and the nitrone oxygen. The latter process is analogous to the formation of 3-isoxazo-

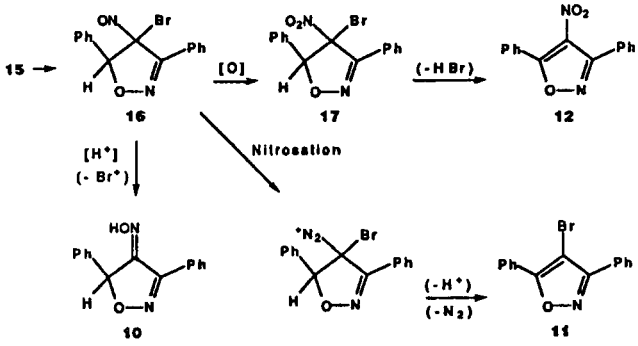
Scheme 1. Proposed Cyclization Mechanisms



lines from α,β-unsaturated nitrones reported by Ooi and Wilson [14]. We have suggested similar mechanisms in the nitrosation of the (*E*)- and (*Z*)-oximes of 3,4-dimethyl-3-penten-2-one [12].

Processes which may account for the formation of **10**, **11**, and **12** are suggested in Scheme 2. The proposed rearrangement of **15** to the geminal bromonitroso compound **16** is directly analogous to a rearrangement which was proposed by Freeman as a key step in the thermal rearrangement of 3,3,5-trimethyl-3*H*-pyrazole 1,2-dioxide to 4-oximino-3,5,5-trimethyl-4,5-dihydroisoxazole [15]. Although we consider the details of the conversion of **16** to **10**, **11**, and **12** as open to speculation, there are some precedents for processes similar to those shown in Scheme 2 in the chemistry of other geminal halonitroso compounds. For example, it is reported that 1-chloro-1-nitrosocyclohexane is converted to cyclohexanone oxime by heating with ethanol [16], and this may provide a model for the conversion of **16** to **10**.

Scheme 2. Possible Routes to Isoxazole Derivatives



It has been shown by Ogloblin, *et al.*, that 2-chloro-2-nitrosopropane and 2-chloro-2-nitrosobutane react under nitrosating conditions (nitric oxide was used) to give a variety of products [17]. The formation of nitrogen gas in greater than 90% of the theoretical amount led them to suggest that diazonium salts are key intermediates in the transformations observed. The formation of **11** by elimination from the diazonium intermediate suggested in Scheme 2 is analogous to the mechanism suggested by Ogloblin, *et al.*, for the formation of 2-chloropropene and 2-chloro-2-butene in their reactions. The formation of **12** might involve an intermediate geminal bromonitro compound **17**, which might be formed by the oxidation of the nitroso group or through a somewhat more complicated process such as that proposed for the formation of geminal chloronitro compounds in the reference cited. Elimination of hydrogen bromide from **17** would seem to provide a plausible route to **12**.

One could also account for the formation of **11** by a process similar to that which has been reported for its formation from **5c** by reaction with electrophilic halogenating agents such as *N*-bromosuccinimide [18]. The species functioning as the halogenating agent in this case could be the geminal bromonitroso compound **16**, which would undergo conversion to **10** as bromine is displaced.

The results of this investigation show that the formation of 1-hydroxypyrazole 2-oxides by the nitrosation of a,β-unsaturated ketoximes is not limited to ketoximes having only alkyl or aryl substituents attached to the double bond. It also seems to suggest that, as we have previously observed, the stereochemistry about the carbon-nitrogen bond of the oxime has a significant influence on the distribution of products formed in the nitrosation reaction. We are pursuing further investigations into the influence of oxime stereochemistry on the reaction and the extension of the reaction to unsaturated ketoximes which have other heteroatomic substituents.

EXPERIMENTAL

The ir spectra were run as nujol mulls, using a Nicolet 5SXC FT-IR Spectrometer; nmr spectra were run on a Varian Gemini-300 Spectrometer in deuteriochloroform with tetramethylsilane as an internal standard, except for the sodium salts, which were examined in deuterium oxide with sodium 3-trimethylsilyl-1-propanesulfonate as an internal standard. Elemental analyses were performed by Micro-Analysis, Inc., Wilmington, DE, except for those of **10** and its acetate, which were done by Clark, Means, and Perkins Microanalytical Laboratory, Urbana, IL. Melting point values were obtained with a Thomas Hoover Unimelt apparatus and are uncorrected.

CAUTION: Although we have encountered no problems in working with the substances described, the violent decomposition observed for some of the oxygenated pyrazole derivatives upon melting indicates that a potential for serious explosion could exist. We would consider it unwise to work with large quantities of the compounds.

3-Bromo-3-penten-2-one Oxime (**5a**).

A solution of 3-bromo-3-penten-2-one [19], 8.15 g (0.05 mole), in 50 ml of ethanol (95%) was cooled in ice and treated

with 5.2 g (0.075 mole) of hydroxylamine hydrochloride in 20 ml of water and 2 drops of concentrated hydrochloric acid. Additional ethanol was added to give a homogeneous solution, which was kept at 5°. After 15 hours, a colorless solid, 7.79 g, mp 101-103°, was collected by suction filtration. The filtrate was warmed, diluted with water, and cooled to give a second crop of 0.88 g, mp 100-103°. The total yield was 8.67 g (97%) of **5a**, shown by nmr analysis to consist of a single stereoisomer. A sample sublimed at 80° and 15 torr had mp 101-103°; ir: 3259 cm^{-1} (brd), 1623 (mod), 1030, 942, 700; ^1H nmr: δ 10.3 ppm (brd, 1H), 6.49 (q, J = 6.7 Hz, 1H), 2.14 (s, 3H), 1.96 (d, J = 6.7 Hz, 3H); ^{13}C nmr: δ 152.8 ppm, 130.9, 123.4, 17.7, 11.7.

Anal. Calcd. for C_5H_8BrNO: C, 33.73; H, 4.53; N, 7.87. Found: C, 33.91; H, 4.29; N, 7.81.

Beckmann Rearrangement of **5a**.

A suspension of 0.26 g (1.2 mmoles) of phosphorous pentachloride in 10 ml of ether (anhydrous) was stirred in ice while 0.18 g (1 mmole) of **5a** was added over 10 minutes. After stirring in ice for 2 hours, and then at room temperature for 30 minutes the mixture was treated with 5 ml of water and stirred overnight. The ether layer was separated and the aqueous layer extracted with 10 ml of ether. The ether solutions were combined, washed with 5 ml of 5% sodium bicarbonate and 5 ml of saturated sodium chloride, dried (sodium sulfate) and evaporated to give 0.044 g of brown, oily solid, which was sublimed at 60° and 0.2 torr to give a colorless solid whose mp and nmr spectrum agreed with those reported for *N*-acetylpropanamide [20].

3,5-Dimethyl-4-pyrazolone 1,2-Dioxide (**3a**).

A solution of 0.53 g (3 mmoles) of **5a** in 8 ml of acetic acid and 20 ml of water was cooled in an ice bath and stirred while a solution of 0.48 g (7 mmoles) of sodium nitrite in 2 ml of water was added over 60 minutes. The yellow solution was stirred in ice for 30 minutes, then at room temperature for 60 minutes, followed by removal of the solvent under reduced pressure without heating. The residue was treated with 25 ml of ether and 5 ml of water, the ether layer was separated, and the aqueous layer was extracted with 25 ml of ether. The ether solutions were combined. washed with three 5 ml portions of 5% sodium bicarbonate and with 10 ml of saturated sodium chloride, dried (sodium sulfate), and evaporated. Flash chromatography of the residue on 20 g of silica gel (Davisil, grade 633, 200-425 mesh) was carried out with 5% acetone in hexane, collecting 25 ml fractions. Fractions 12-16 gave 0.073 g (17%) of **3a** as a yellow solid, mp 108-109° (reported mp 109-110° [2]).

3-Methyl-5-phenyl-4-pyrazolone 1,2-Dioxide (**3b**).

A suspension of 2.40 g (10 mmoles) of **5b** [6] in 20 ml of acetic acid and 5 ml of water was cooled in an ice bath and stirred while a solution of 1.54 g (22 mmoles) of sodium nitrite in 10 ml of water was added over 150 minutes. The mixture was stirred at room temperature for 180 minutes, diluted to 100 ml with water, cooled, filtered, and the gummy orange solid washed with water and with cold ethanol (95%). The solid was dissolved in 50 ml of dichloromethane washed, with 20 ml of saturated sodium chloride solution, dried (sodium sulfate) and evaporated. Recrystallization from ethanol gave 0.80 g (39%) of **3b**, mp 163-165° (reported mp 164-65° [2]), which was identical with an authentic sample.

3,5-Diphenyl-4-pyrazolone 1,2-Dioxide (**3c**).

A suspension of 0.45 g (1.5 mmoles) of **5c** [7] in 10 ml of acetic acid and 1 ml of water was cooled in ice and stirred while a solution of 0.23 g (3.3 mmoles) of sodium nitrite in 0.5 ml of water was added over 60 minutes. The mixture was stirred at room temperature for 150 minutes, another 0.14 g (2 mmoles) of sodium nitrite in 0.5 ml of water was added, and stirring at room temperature was continued for 120 minutes. The mixture was cooled in ice, and the red solid collected by suction filtration. The solid was dissolved in 25 ml of dichloromethane, filtered, and the dichloromethane solution washed with 10 ml of saturated sodium chloride solution, dried (sodium sulfate), and evaporated. The magenta solid was stirred with warm ethanol, cooled, and filtered to give 0.17 g (42%) of **3c**, mp 191-192° (reported mp 191-192° [2]), which was identical with an authentic sample.

4-Bromo-3,5-dimethyl-1-hydroxypyrazole 2-Oxide (**8a**).

Ethanol (95%) and water were deoxygenated by heating under reflux under a slow stream of nitrogen for 90 minutes. A solution of 3.56 g (20 mmoles) of **5a** in 50 ml of ethanol was treated under nitrogen in rapid succession with 3.16 g (40 mmoles) of pyridine, a solution of 5.0 g (20 mmoles) of copper(II) sulfate pentahydrate in 20 ml of water, and 3.1 g (30 mmoles) of butyl nitrite. The flask was swirled for a few minutes until the thick suspension became thin enough for magnetic stirring, then the mixture was stirred overnight under nitrogen at room temperature. A green solid was collected, washed with water until free of copper sulfate, then with ethanol and acetone and dried to give 3.93 g (84%) of the copper complex **7a** which detonated with a sharp report upon melting, mp 145° (the melting point values observed for different samples varied greatly, being sensitive to heating rate and to purity of sample). Further purification by recrystallization was impractical for the the copper complexes due to limited solubility in common solvents.

Anal. Calcd. for $C_{10}H_{12}Br_2N_4O_4Cu$: C, 25.25; H, 2.54; N, 11.78. Found: C, 25.73; H, 2.37; N, 11.97.

A suspension of 3.00 g (6.3 mmoles) of the copper complex **7a** in 30 ml of 5% aqueous potassium hydroxide and 10 ml of ethanol (95%) was stirred at room temperature. After 30 minutes the mixture was filtered through diatomaceous earth to remove inorganic solids. The filtrate was cooled in ice and acidified with concentrated hydrochloric acid to Congo red, and the finely divided colorless solid was collected by suction filtration, washed with cold water and ethanol, and dried under reduced pressure to give 2.50 g (96%) of 8a, mp 134° violent dec (reported mp 137° dec [10]), which was identical with an authentic sample.

The sodium salt **9a** was prepared by suspending 0.50 g of **8a** in 2 ml of ethanol and adding a slight excess of 50% aqueous sodium hydroxide. After warming gently until homogeneous, the yellow solution was treated with ether and cooled, and the pale yellow, crystalline salt was collected, washed with ether, recrystallized from ethanol-ether, and dried for several hours at room temperature and 0.1 torr. With slow heating the salt decomposed above 140°, never entirely liquifying up to 260°; a sample which was introduced at 220° detonated at 227° [21]; ir: 3276 cm^{-1} (str brd, water of hydration), 1707 (m), 1465, 1281, 1178, 1031, 823, 619; ^1H nmr: δ 2.14 ppm (s); ^{13}C nmr: δ 124.1 ppm, 84.7, 11.4.

Anal. Calcd. for $C_5H_6BrN_2O_2Na \cdot 1/2H_2O$: C, 25.23; H, 2.97; N, 11.77. Found: C, 25.05; H, 2.90; N, 11.57.

4-Bromo-3(5)-methyl-5(3)-phenyl-1-hydroxypyrazole 2-Oxide (**8b**).

The reaction of 4.80 g (20 mmoles) of **5b** with butyl nitrite in the presence of pyridine and copper(II) sulfate was carried out as described for **5a**, giving 5.08 g (85%) of the copper complex **7b** as an olive-green solid, mp 165° violent dec.

Anal. Calcd. for $C_{20}H_{16}Br_2N_4O_4Cu$: C, 40.05; H, 2.69; N, 9.34. Found: C, 40.17; H, 2.76; N, 9.50.

The free pyrazole was obtained as above by treating **7b** with aqueous ethanolic potassium hydroxide for 30 minutes, filtration, and acidification of the filtrate to give 94% of **8b**, mp 154° dec (reported mp 156° dec [10]).

The sodium salt **9b** was generated with 50% aqueous sodium hydroxide in ethanol as described for **9a**. Recrystallization from ethanol-ether gave the salt as a pale yellow solid, which became brighter yellow in color upon drying at room temperature at 0.1 torr. The decomposition temperature was determined as described [21]; a sample introduced into the melting point apparatus at 210° detonated at 217°; ir: 3229 cm^{-1} (brd) (water of hydration), 1603 (wk), 865, 856, 762, 656, 607; ^1H nmr: δ 7.4-7.7 ppm (m, 5H), 2.24 (s, 3H); ^{13}C nmr: δ 132.0 ppm, 131.5, 131.2, 130.1, 126.2, 124.9, 84.7, 11.6.

Anal. Calcd. for $C_{10}H_8BrN_2O_2Na \cdot 1/2H_2O$: C, 40.02; H, 3.02; N, 9.34. Found: C, 40.19; H, 2.97; N, 9.39.

Nitrosation of 2-Bromo-1,3-diphenyl-2-propen-1-one Oxime (**5c**).

A sample of 6.04 g (20 mmoles) of **5c** was nitrosated in oxygen-free ethanol-water with butyl nitrite as described for the other α-bromoketoximes. After stirring under nitrogen overnight the solid was collected by suction filtration. The copper complex in this case required repeated washing with acetone to remove solid contaminants such as had not been encountered in the other cases. The yield of pale brown copper complex **7c** was 2.91 g (40%), mp 167° dec.

Anal. Calcd. for $C_{30}H_{20}Br_2N_4O_4Cu$: C, 49.78; H, 2.79; N, 7.74. Found: C, 49.72; H, 2.79; N, 7.63.

The copper complex, 3.00 g, was treated with aqueous ethanolic potassium hydroxide in the usual way, and after filtration the free pyrazole **8c** was precipitated from the filtrate with hydrochloric acid, collected, washed, and dried to give 1.84 g (79%) of colorless solid, mp 155° dec (reported for **8c**, mp 157° dec [10]).

The sodium salt was prepared in the usual way and recrystallized from ethanol. In contrast to the other sodium salts, which were yellow in color, **9c** was a colorless, crystalline solid, which was free of water of hydration. Upon slow heating **9c** gradually decomposed above 235° without complete liquification up to 260°; a sample introduced at 250° [21] detonated at 255°; ir: 1602 cm^{-1} (m), 1383, 881, 760, 695; ^1H nmr: δ 7.63 ppm (d, J = 6.8 Hz, 2H), 7.35-7.50 (m, 3H); ^{13}C nmr: δ 132.3 ppm, 131.6, 131.2, 130.0, 127.0, 84.8.

Anal. Calcd. for $C_{15}H_{10}BrN_2O_2Na$: C, 51.01; H, 2.85; N, 7.93. Found: C, 50.90; H, 2.70; N, 7.60.

The wash solutions from the isolation of **7c** above were combined, treated with 100 ml of water, acidified with 20 ml of 3*M* hydrochloric acid, and extracted with three 200 ml portions of ether. The ether extract was washed with 50 ml portions of water, 5% sodium carbonate, and saturated sodium chloride, dried (sodium sulfate), and evaporated. The residue was applied to a column of 100 g of silica gel (Davisil, grade 633, 200-425 mesh). Flash chromatography was carried out, collecting 100 ml fractions. Elution was begun with 2000 ml of 5% acetone in hexane, then continued with 15% acetone in hexane. Fractions 4-8 gave 0.68 g (11%) of colorless solid, mp 134-135° (from ethanol) identified as 4-bromo-3,5-diphenylisoxazole **11** by comparison with an authentic sample (reported mp 133-135° [18]).

Fractions 10-15 gave, after washing with cold ethanol, 0.31 g (6%) of **12**. Recrystallization from ethanol gave colorless needles, mp 173-174° (reported for **12** mp 170.5-171° [22]); ir: 1615 cm^{-1}, 1587, 1520 and 1366 (str, ν asym and ν sym for NO_2 group), 1158, 827, 752, 693; ^1H nmr: δ 7.93 ppm (d, J = 6.5 Hz), 7.45-7.70 (mult, 8H); ^{13}C: δ 168.3 ppm, 158.4, 132.7, 130.8, 129.0, 128.9, 128.8, 128.7, 125.9, 124.6.

Fractions 23-25 gave 1.32 g (26%) of material identified as 4-oximino-3,5-diphenyl-4,5-dihydroisoxazole **10**. Recrystallization from methanol-water gave two distinct crystalline modifications, faintly yellow prisms, mp 122-124°, and colorless needles, mp 124-126°; The material was identical with a sample prepared as described below.

Nitrosation of 1,3-Diphenyl-2-propen-1-one Oxime.

A solution of 1.12 g (5 mmoles) of 1,3-diphenyl-2-propen-1-one (*E*)-oxime [14] in 25 ml of ethanol (95%) was stirred at room temperature and treated in rapid succession with 0.8 g (10 mmoles) of pyridine, 1.25 g of copper(II) sulfate pentahydrate in 5 ml of water, and 0.76 g (7.5 mmoles) of butyl nitrite. After stirring overnight the mixture was filtered and the solid washed with water, ethanol, and ether and dried to give 0.59 g (42%) of the pale brown copper complex of the conjugate base of 3,5-diphenyl-1-hydroxypyrazole 2-oxide, mp 227° dec. The free pyrazole **2b** ($R^1 = R^3 = Ph$), which was identical with an authentic sample [3], was obtained by stirring the complex with dilute aqueous, ethanolic potassium hydroxide followed by filtration and acidification as described above.

The filtrate and wash solutions after isolation of the copper complex were combined, acidified with 5 ml of 3*M* hydrochloric acid, and treated with 50 ml of water and 100 ml of ether. The ether layer was separated and washed with 25 ml portions of water, 5% sodium carbonate, and saturated sodium chloride, dried (sodium sulfate) and evaporated to give a yellow syrup which was triturated with hexane to give 0.68 g (54%) of cream-colored solid, which was identical with **10** isolated above. Recrystallization from methanol-water gave colorless needles, mp 121-123° [23]; ir: 3224 cm^{-1} (brd), 1456 (v str), 970, 923, 689; ^1H nmr: δ 8.47 ppm (brd s, 1 H), 8.02 (dd, J = 1.5, 6.5 Hz, 2H), 7.3-7.5 (m, 8H), 6.29 (s, 1H); ^{13}C nmr: δ 160.3 ppm, 152.0, 134.7, 130.6, 128.9, 128.6, 128.3, 127.9, 127.5, 126.8, 83.6.

Anal. Calcd. for $C_{15}H_{12}N_2O_2$: C, 71.41; H, 4.80; N, 11.11. Found: C, 71.35; H, 4.64; N, 11.44.

The *O*-acetyl derivative was prepared by treating a sample of 0.50 of (2 mmoles) of **10** in 2 ml of acetic acid with 0.5 ml of acetic anhydride and heating on a steam bath for 30 minutes. The solution was poured into 10 ml of ice water and stirred. The solid was collected, washed with water, and recrystallized from ethanol to give 0.33 g of colorless crystals, mp 118-120°; ir: 1778 cm^{-1}, 1637 (wk), 1206, 1190, 1165, 937, 907; ^1H nmr: δ 8.19 ppm (m, 2H), 7.49 (m, 3H), 7.3-7.45 (m, 5H), 6.30 (s, 1H), 2.03 (s, 3H); ^{13}C nmr: δ 166.8 ppm, 166.0, 151.5, 1 33.9, 130.9, 129.4, 128.9, 128.8, 127.9, 127.5, 126.2, 84.9, 18.8.

Anal. Calcd. for $C_{17}H_{14}N_2O_3$: C, 69.37; H, 4.79; N, 9.52. Found: C, 68.96; H, 4.99; N, 9.49.

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