Oxidative Dehydrogenation of Pyrazolines with Cobalt(II) and Oxygen

Jayant N. Shah* and Chandrakant K. Shah

Research and Development Centre, Indian Petrochemicals Corporation Limited, Baroda 391 346, India

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Synthesis of pyrazoles can be accomplished in several ways, including the dehydrogenation of pyrazolines.[1-5] A number of dehydrogenating agents have been employed for this purpose. However, none except tetrachloro-1,2-benzoquinone qualifies as a truly general reagent. They either require too severe a reaction condition or their use is accompanied by products of decompositions and ring scission.

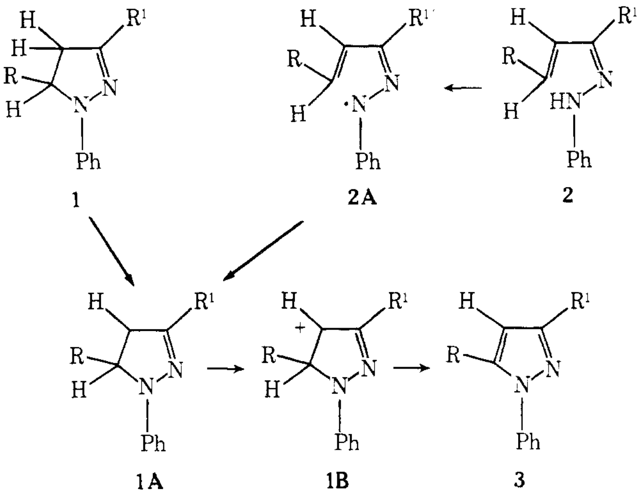
We now wish to report a mild general route for the oxidative dehydrogenation of *N*-phenyl-3,5-disubstituted-2-pyrazolines to the corresponding pyrazoles using catalytic amounts of cobalt soap of fatty acids (C_6–C_{10}). The reactions proceed smoothly and in high yields under fairly mild conditions compared to the methods reported previously. For example, 1,3,5-triphenylpyrazoline on treatment with catalytic amounts of cobalt soap and oxygen at 1 atm in refluxing benzene yielded 1,3,5-triphenylpyrazole (**3**, R, R′ = Ph) in quantitative yield in less than 30 min. The generality of the method is evident from the fact that a wide variety of substituted pyrazolines underwent smooth oxidation in good yields. The results are summarized in Table I.

We propose that Co(III) ions are responsible for the oxidative dehydrogenation reaction. The Co(III) ions may be formed by the interaction of the Co(II) soap with traces of peroxides present in solution under the conditions of reaction.[7-9]

The pyrazolines are converted to a cyclic radical intermediate (**1A**, see Scheme I) by a hydrogen abstraction by Co(III) followed by further oxidation of the radical to a carbenium ion (**1B**). Loss of a proton from the carbenium ion intermediate leads to the pyrazole **3**. The reduced Co(II) ions formed during this oxidation are reoxidized to Co(III) under the conditions of the reaction. Thus, only a catalytic amount (50–100 ppm) of Co(II) ions is required for the completion of the reaction. The proposed scheme is analogous to the mechanism of liquid-phase oxidation of hydrocarbons using Co(II) ions and oxygen as catalyst.[7-9]

It occurred to us that the cyclic radical intermediate **1A** could also be generated from chalcone phenylhydrazones (**2**) through the intermediary of a nitrogen radical (**2A**) (see Scheme I). Accordingly we oxidized benzalacetophenone phenylhydrazone (**2**, R, R′ = Ph) and *m*-nitrobenzalacetophenone phenylhydrazone (**2**, R = *m*-$NO_2C_6H_4$; R′ = Ph) using reaction conditions identical with those used previously for pyrazolines and could realize 90 and 60% yields of the corresponding pyrazoles.

Scheme I



Experimental Section

All melting points are uncorrected. IR spectra were determined on a Perkin-Elmer Infracord spectrometer in Nujol and UV spectra on a Perkin-Elmer Coleman Model 55 spectrophotometer in ethanol.

All pyrazolines were prepared by the reaction of the appropriate substituted chalcones with phenylhydrazine in refluxing acetic acid[4] and were fully characterized prior to use.

Preparation of Cobalt Soap. To a solution of sodium hydroxide (4.2 g) in water (100 mL) was added fatty acids with 6–10 carbons (23.5 mL) without allowing the temperature to rise above 25 °C. The pH of the solution was then set to 7 either by adding fatty acids or alkali. Benzene (350 mL) was added followed by a solution of $CoSO_4 \cdot 2H_2O$ (19 g) in water (75 mL). The organic layer was separated, washed, dried (Na_2SO_4), the concentration of cobalt in catalyst solution was estimated.

The experimental procedure can be simplified by a single dilution with benzene. The cobalt concentration is then estimated and the requisite volume to give 96 ppm of cobalt(II) is added to the reaction mixture. This change implies that 16 g/L of cobalt catalyst concentration as mentioned previously is not the only suitable catalyst concentration for this reaction.

Dehydrogenation of 2-Pyrazolines (General Procedure). The reaction assembly consisted of a flask fitted with a gas disperser and a reflux condenser connected to the flask through a Dean and Stark water separator. The top of the condenser was attached to a pressure gauge, and the pressure was regulated using an exit valve. Pyrazoline (0.01 mol) was dissolved in anhydrous benzene (150 mL), and the catalyst [96 ppm Co(II)] was added to this solution. The reaction vessel was pressurized to 1 atm at room temperature by bubbling oxygen into the reaction flask. The reactants were then brought to reflux and maintained for 30 min at an oxygen pressure of 1 atm.[10] The organic layer was then washed with 2% hydrochloric acid and water and dried, and the solvent was evaporated. The residue was purified by crystallization or by chromatography on silica gel, eluting with benzene–diethyl ether (98:2 v/v). When treated similarly for 3 h, chalcone phenylhydrazone gave pyrazole. The UV and IR spectra of all pyrazoles were in agreement with those reported in the literature.[3-6]

Table I. Yields of Products from the Oxidation of *N*-Phenyl-3,5-disubstituted-2-pyrazolines

Pyrazole	Registry no.	R	R¹	Yield, %	Mp, °C	Lit. mp, °C
3a	2183-27-9	Ph	Ph	100	139	140[4]
3b	16860-55-2	*m*-$NO_2C_6H_4$	Ph	60	130	130[5]
3c	16860-68-7	α-Furyl	Ph	88	71	64[5]
3d	16860-69-8	α-Thienyl	Ph	92	113	112[5]
3e	10252-53-6	Ph	PhCH═CH	95	141	141[4,5]
3f	16901-34-1	Ph	*p*-BrC_6H_4	92	157	159[5]
3g	21159-63-7	α-Furyl	*p*-ClC_6H_4	65	83	
3h	33045-42-0	α-Thienyl	*p*-ClC_6H_4	95	133	134[6]
3i	21159-60-4	α-Furyl	*p*-$OMeC_6H_4$	80	86	
3j	58950-01-9	α-Thienyl	*p*-$OMeC_6H_4$	94	91	
3k	1128-54-7	H	Me	89	33	33[4]

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Registry No.—**1A**, 742-01-8; **1B**, 6969-04-6; **1C**, 2755-71-7; **1D**, 2755-72-8; **1E**, 2515-62-0; **1F**, 19429-34-6; **1G**, 4035-38-5; **1H**, 5204-27-3; **1I**, 4035-37-4; **1J**, 20264-73-7; **1K**, 10252-46-7.

References and Notes

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(10) It was found that bubbling in oxygen through an open system was less efficient, requiring about 5 h to complete the reaction. Use of a slight positive pressure is expected to increase the dissolved oxygen content, thereby accelerating the oxidation reaction.

Deoxygenation of Amine *N*-Oxides or *C*-Nitroso Compounds by Dialkyl Sulfoxylates

Hiroaki Kagami and Shinichi Motoki*

Department of Chemistry, Faculty of Science, Science University of Tokyo, Kagurazaka, Shinjuku-ku, Tokyo, Japan

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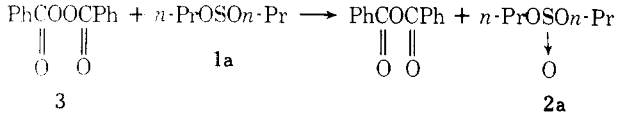
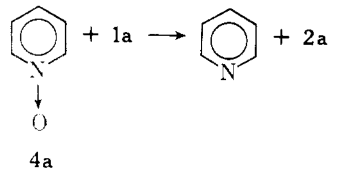
Deoxygenation reactions of a variety of organic compounds by trivalent phosphorus compounds are well known. For example, dibenzoyl peroxide,[1] pyridine *N*-oxide,[2] or nitrosobenzene[3] is deoxygenated by triphenyl phosphine or triethyl phosphite to give benzoic anhydride, pyridine, or azoxybenzene, respectively. Sulfoxylates (**1**) are readily oxidized,[4] yielding sulfites (**2**) upon exposure to air; nevertheless, little attention has been paid to the deoxygenation reactions by **1**. Thus it seemed reasonable that a similar deoxygenation reaction could be carried out by **1**. Di-*n*-propyl sulfoxylate (**1a**) and diethyl sulfoxylate (**1b**) were used in the present study; the former was more accessible and stable than the latter.

First, dibenzoyl peroxide (**3**) was allowed to react with **1a**. The reaction took place violently even at room temperature and benzoic anhydride and di-*n*-propyl sulfite (**2a**) were obtained in almost quantitative yields (eq 1). The result is in contrast to the reaction of dioxetane, a cyclic peroxide, and **1** which affords tetraalkoxysulfurane instead of oxirane.[5]

Pyridine *N*-oxide (**4a**) also reacted with **1a** at room temperature to give pyridine and **2a** in yields of 96 and 85%, respectively (eq 2). Similarly, 2-picoline *N*-oxide (**4b**), 3-picoline *N*-oxide (**4c**), or 4-picoline *N*-oxide (**4d**) reacts with **1a** at room temperature or in refluxing benzene to give amine and **2a** as shown in Table I. 4-Nitropyridine *N*-oxide (**4e**) did not react with **1a** under similar conditions, but, upon heating in the absence of solvent a vigorous exothermic reaction occurred with the evolution of nitric oxide. The only product isolated from the reaction mixture was di-*n*-propyl sulfite (**2a**). The deoxygenation of pyridine *N*-oxide (**4a**) or its homologues by triphenyl phosphine must be carried out under drastic conditions (heating above 200 °C).[2]



$$\underset{\mathbf{3}}{\mathrm{Ph\underset{O}{\overset{}{C}}OO\underset{O}{C}Ph}} + \underset{\mathbf{1a}}{n\text{-}\mathrm{PrOSO}n\text{-}\mathrm{Pr}} \longrightarrow \mathrm{Ph\underset{O}{C}O\underset{O}{C}Ph} + \underset{\mathbf{2a}}{n\text{-}\mathrm{Pr}\underset{O}{\underset{\downarrow}{\mathrm{O}S}}\mathrm{O}n\text{-}\mathrm{Pr}} \qquad (1)$$

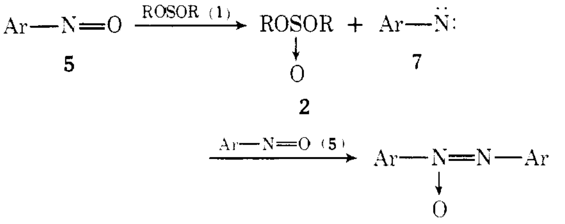


4a

(2)

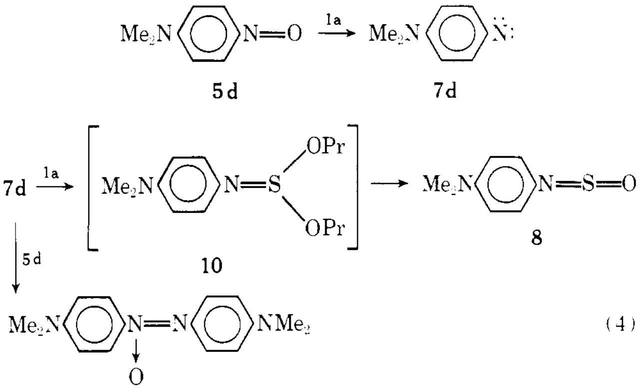
Reactions of *C*-nitroso compounds with sulfoxylates (**1**) gave a variety of products. When equimolar quantities of nitrosobenzene (**5a**) and **1a** or **1b** were refluxed in benzene or CCl_4, the solution gradually turned from green to reddish brown and azoxybenzene (**6a**) was obtained in 61–76% yields (eq 3). *p*-Nitrosotoluene (**5b**) or *o*-nitrosotoluene (**5c**) similarly reacted with **1a** to give 4,4′-dimethylazoxybenzene (**6b**) or 2,2′-dimethylazoxybenzene (**6c**). The sulfite (**2**) was not isolated in these cases but its formation was confirmed by an infrared spectrum.

In addition, we examined the reaction of **1a** and *p*-dimethylaminonitrosobenzene (**5d**) and found that *p*-dimethylamino-*N*-sulfinylaniline (**8**) was formed together with 4,4′-bis(dimethylamino)azoxybenzene (**6d**) and 4,4′-bis(dimethylamino)azobenzene (**9**). The mechanism of the formation of **8** is not obvious. Bunyan and Cadogan[3] proposed the mechanism of formation of **6** by assuming arylnitrene (**7**) to be a transient intermediate. Accordingly, the reaction presumably proceeds through the intermediate **10** generated by the attack of nitrene **7d** on **1a**.[6]



6

(3)

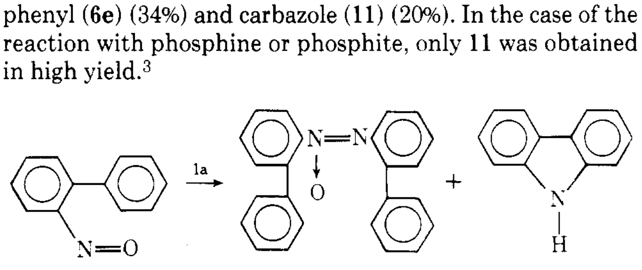


6d

(4)

The path of the formation of **9** also cannot be elucidated. However, the dimerization of **7d** to give **9** is excluded as has been pointed out by Bunyan and Cadogan,[3] and our separate experiment confirmed that both the deoxygenation of **6d** to **9** by **1a** and the reaction of **8** with **5d** to form **9** did not occur under similar conditions.

o-Nitrosobiphenyl (**5e**) reacted with **1a** to give *o*-azoxybiphenyl (**6e**) (34%) and carbazole (**11**) (20%). In the case of the reaction with phosphine or phosphite, only **11** was obtained in high yield.[3]



5e 6e 11

(5)

Finally, reactions of sulfoxylates and other compounds such as sulfoxides, sulfones, aromatic nitro compounds, or *N*-nitroso compounds were examined. However, deoxygenation

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