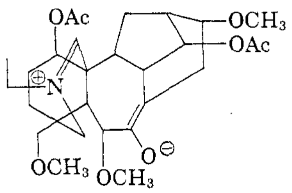
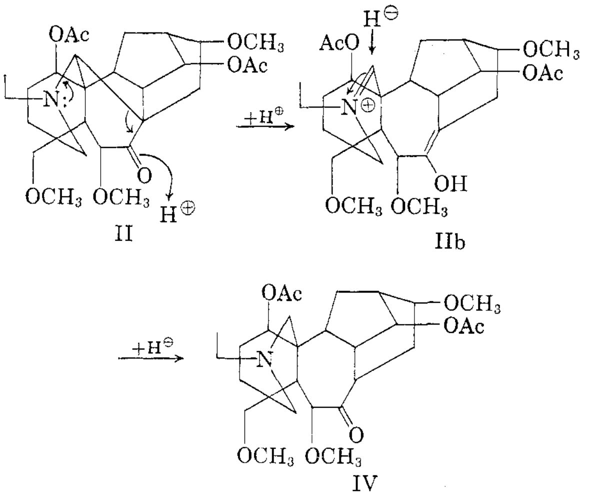


IIa

Furthermore, the formation of anhydrodihydrodiacetyllucaconine (IV) ($C_{28}H_{43}O_8N$)[5] from compound II by hydrogenation, may be expressed in the following way (II → IIb → IV) (Scheme A). The ultraviolet absorption spectrum of compound IV shows only end absorption. Compound III was recovered unchanged after being subjected to the conditions leading to the hydrogenation of compound II.



Scheme A

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Preparation of α-Diazo Ketones

Sir:

The preparation of α-diazo ketones by the oxidation of the monohydrazones of α-keto aldehydes or α-diketones has long been known.[1] The oxidizing agent most frequently used has been mercuric oxide,[1] often in the presence of bases[2]; silver oxide,[3] "mercuric acetamide,"[4] and mercuric trifluoroacetate[5] have also been used. An excellent variant of this method has been developed by Cava, Litle and Napier,[6] who prepared α-diazo ketones by the action of sodium hydroxide on the monotosylhydrazones of α-diketones. We now report on two new methods for the oxidation of the monohydrazones of α-diones which appear to have considerable general utility.

(i) "Activated" manganese dioxide[7] rapidly oxidizes the hydrazones in chloform solution to the corresponding α-diazo ketones in high yield. In a typical experiment 1.00 g. of 1-mesitylglyoxal 2-hydrazone[8] was dissolved in 15 ml. of chloroform (reagent grade) and to the solution was added 1.5 g. of "activated" manganese dioxide; the mixture was stirred for 1 hr. at room temperature, with initial cooling to abate the exothermic reaction. It was then filtered and the solvent was evaporated to give a quantitative yield of 2-diazo-2′,4′,6′-trimethylacetophenone, m.p. 59–61° dec. The infrared spectrum of this product was indistinguishable from that of a recrystallized sample, m.p. 59–61° dec., of the authentic diazo ketone prepared by oxidation of the hydrazone with mercuric oxide.[8] The latter method gives a less pure crude product in 75% yield. Manganese dioxide has also been used for the preparation of 2-diazopropiophenone, 2-diazo-2′,4′,6′-trimethylpropiophenone, 2-diazo-2-phenylacetophenone (azibenzil), 3-diazo-2-butanone, 3-diazo-D-camphor, and 2-diazo-1,5,5-trimethylbicyclo[2.2.1]heptan-3-one from the corresponding hydrazones; the scale varied from 0.060 g. to 10 g. of hydrazone and the weight of manganese dioxide used was *ca.* 1.5 times that of the hydrazone. In every case the diazo ketone was obtained directly from the reaction mixture in 90–100% yield and was free from significant amounts of impurities as vouchsafed by its infrared spectrum.[9]

(ii) α-Diazo ketones may also be prepared by oxidation of the corresponding hydrazones in methanolic solution containing sodium hydroxide with calcium hypochlorite. In a typical experiment, 0.100 g. of D-camphorquinone monohydrazone[4] was dissolved in 5 ml. of methanol and 1 ml. of 0.05*M* aqueous sodium hydroxide was added, the solution was stirred with 0.250 g. of calcium hypo-

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chlorite (Baker, 30–35% available chlorine) for 2 hr. The mixture was added to 10 ml. of ice water and then extracted with chloroform. The extract was washed with saturated brine, dried, and evaporated to give 0.079 g. (80%) of 3-diazo-D-camphor with an infrared spectrum indistinguishable from that of an authentic sample, m.p. 74–75°.[10] A single recrystallization of the crude product from pentane gave an 80% recovery of material, m.p. 73–75°. This method has also been applied successfully to the preparation of 2-diazo-1,5,5-trimethylbicyclo[2.2.1]heptan-3-one, 2-diazo-2′,4′,6′-trimethylacetophenone, 2-diazo-2′,4′,6′-trimethylpropiophenone, and azibenzil from the corresponding hydrazones. In every case the diazo ketone was obtained directly from the reaction mixture in 75–85% yield and was free from significant amounts of impurities.

In those cases where comparisons have been made, the use of manganese dioxide or calcium hypochlorite has been found to be preferable to that of mercuric oxide. In general, manganese dioxide appears to be the reagent of choice, although the use of calcium hypochlorite may be advantageous on occasion because of the concomitant solvent system.

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(9) Earlier mention has been made in the literature of the oxidation of simple hydrazones with manganese dioxide. M. Z. Barakat, M. F. Abdel-Wahab, and M. M. El-Sadr [*J. Chem. Soc.*, 4685 (1956)] observed the formation of a violet color during the oxidation of benzophenone hydrazone with manganese dioxide ("precipitated") which they attributed to the formation of diphenyldiazomethane. W. Schroeder, U.S. Patent **2,710,862** [*Chem. Abstr.*, **50**, 6510 (1956)], has reported that manganese dioxide is "much less effective" than silver oxide for the oxidation of substituted benzophenone hydrazones to the corresponding diazo compounds. Subsequently, "activated" manganese dioxide has been used successfully for the oxidation of this type of compound: E. J. Corey and L. H. Haefele, private communication.

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