Notes A department for short papers of immediate interest.

Reaction of β-Bromostyrene and Dinitrogen Tetroxide. A Radical Displacement

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Addition of free radical reagents to halogenated olefins has been known to lead to adducts that have lost a halogen atom.[1] For instance, various alkyl radicals and 1,2-dichloroethylene interacted to produce 1-chloro-2-alkylethylenes,[2] and the dinitrogen tetroxide–allyl iodide reaction yielded 3-nitropropene.[3]

The addition of dinitrogen tetroxide to β-bromostyrene now has been found to give β-nitrostyrene as the major product, apparently by a radical path as outlined.[4] Slow addition of dinitrogen tetroxide to an ether solution of the bromostyrene produced the nitrostyrene (67%) and

$$NO_2 + C_6H_5{-}CH{=}CHBr \longrightarrow$$
$$[C_6H_5{-}\underset{\cdot}{C}H{-}CHBrNO_2] \longrightarrow C_6H_5{-}CH{=}CHNO_2 + Br\cdot$$

even inverse addition of the styrene to the tetroxide in ether yielded β-nitrostyrene (47%). Formation of the relatively stable intermediate radical which may reversibly eliminate the NO_2 radical or which may eliminate a bromine atom to give the unreactive β-nitrostyrene makes this a favorable case for the observation of such a radical displacement reaction.

The other products of this β-bromostyrene reaction undoubtedly were the saturated compounds derived from the addition of bromine and dinitrogen tetroxide to β-bromostyrene. Only one of the possible adducts, a dibromonitrophenylethane, m.p. 73–74°, was isolated. The nitro group absorption at 1540 cm.$^{-1}$ in the infrared spectrum of this adduct indicated it was 1,1-dibromo-2-nitro-2-phenylethane; absorption at higher wave length would be expected for the isomeric 1,2-dibromo-1-nitro-2-phenylethane.[5]

EXPERIMENTAL

Addition of dinitrogen tetroxide to β-bromostyrene. A solution of 4.3 g. (23.5 mmoles) of β-bromostyrene in 100 ml. of ether was stirred at 10° while 25 mmoles of dinitrogen tetroxide[6] was swept into the ether solution in a nitrogen stream over a 1-hr. period. The mixture was stirred for an additional hour at 15°. Water (100 ml.) then was added, and the ether layer was separated and washed with water and 10% sodium bicarbonate solution. Evaporation of the ether left 4.72 g. of residue. The residue was dissolved in methylene chloride–pentane and chromatographed on a silica gel column as described previously.[4] The first fraction eluted, 1.60 g., contained almost no β-nitrostyrene as evidenced by infrared spectra of the cuts. A 0.83-g. portion of this, probably 1,1-dibromo-2-nitro-2-phenylethane, solidified, and was recrystallized from hexane, m.p. 73–74°.

Anal. Calcd. for $C_8H_7Br_2NO_2$: C, 31.10; H, 2.28; N, 4.53. Found: C, 31.31; H, 2.39; N, 4.38.

The next fraction eluted was β-nitrostyrene, 2.36 g., (67%), m.p. 56–57°; the mixed melting point with an authentic sample of the same melting point was not depressed. The infrared spectrum was identical with that of an authentic specimen.

The last fractions eluted from the column, a total of 0.71 g. of oily material showing hydroxyl absorption in the infrared spectrum, were not characterized.

Addition of β-bromostyrene to dinitrogen tetroxide. A solution of 28 mmoles of dinitrogen tetroxide in 100 ml. of ether was stirred at 10° while 23.5 mmoles of β-bromostyrene in 15 ml. of ether was added over 20 min. The reaction mixture was stirred in a nitrogen atmosphere during this addition and for an additional hour at 15°. The reaction mixture then was worked up as described above. From 4.40 g. of crude residue was obtained 1.55 g. of material eluted prior to β-nitrostyrene; a 0.73-g. portion of this solidified and melted at 74° after hexane recrystallization. The β-nitrostyrene fraction weighed 1.66 g. (47%), m.p. 56–57°, identified as described above.

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[1] Several examples are given in C. Walling, *Free Radicals in Solution*, Wiley and Sons, New York, 1957, pp. 268–271.

[2] L. P. Schmerling and J. P. West, *J. Am. Chem. Soc.*, **71**, 2015 (1949); **75**, 6216 (1953).

[3] J. F. Brown, Jr., General Electric Company, personal communication.

[4] The homolytic nature of the dinitrogen tetroxide–olefin reaction appears to be well established; see H. Shechter, J. J. Gardikes, and A. H. Pagano, *J. Am. Chem. Soc.*, **81**, 5421 (1959) and T. E. Stevens, *J. Am. Chem. Soc.*, **81**, 3593 (1959).

[5] J. F. Brown, Jr., *J. Am. Chem. Soc.*, **77**, 6341 (1955).

[6] Obtained from the Matheson Co. and distilled before use.

The Hydrogenation of Nitriles to Primary Amines

Francis E. Gould, Grannis S. Johnson, and Arthur F. Ferris

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The catalytic hydrogenation of nitriles to primary amines is a reaction of considerable importance in organic synthesis and has been the subject of many investigations because good yields of primary amines are frequently difficult to obtain. The difficulty apparently arises because the re-

TABLE I

HYDROGENATION OF NITRILES IN ACETIC ANHYDRIDE OVER RANEY CATALYSTS

Nitrile	Raney Catalyst	Co-catalyst	Product	Yield, %
$C_6H_5CH_2CN$	Ni	NaOAc	$C_6H_5CH_2CH_2NHAc$	97
C_6H_5CN	Ni	None	$C_6H_5CH_2NH_2\cdot HCl$	91
$CH_3(CH_2)_{11}CN$	Ni	NaOAc	$CH_3(CH_2)_{12}NHAc$	100
$CH_3(CH_2)_{11}CN$	Ni—Cr	NaOAc	$CH_3(CH_2)_{12}NHAc$	89
$CH_3(CH_2)_{11}CN$	Co	NaOAc	$CH_3(CH_2)_{12}NHAc$	60
$CH_2{=}CHCN$	Ni	NaOAc	$CH_3CH_2CH_2NHBz$	92
$(CH_3)_2C(OH)CN$	Ni	NaOAc	$(CH_3)_2C(OH)CH_2NH_2\cdot HCl$	40
$NC(CH_2)_4CN$	Ni	NaOAc	$AcNH(CH_2)_6NHAc$	100
$NC(CH_2)_4CN$	Ni	NaOH	$AcNH(CH_2)_6NHAc$	80
$NC(CH_2)_4CN$	Ni—Cr	NaOAc	$AcNH(CH_2)_6NHAc$	77
$NC(CH_2)_4CN$	Co	NaOAc	$AcNH(CH_2)_6NHAc$	25

duction proceeds stepwise through the aldimine, some of which condenses with primary amine already formed and ultimately leads to secondary amines.[1,2]

Recent work in this laboratory has shown that hydrogenation of ethyl 5-cyano-2-oximinovalerate in acetic anhydride over a Raney nickel catalyst in the presence of a basic cocatalyst, followed by hydrolysis with hydrochloric acid, gives DL-lysine monohydrochloride in almost quantitative yield.[3] It has been found now that hydrogenation in acetic anhydride in the presence of a Raney metal catalyst and a basic cocatalyst, a technique which appears never to have been applied to simple nitriles, is very effective for the reduction of a variety of nitriles to primary amines. In fact, this technique frequently may be the method of choice for carrying out this conversion in the laboratory because it gives very high yields simply and rapidly at moderate temperatures and low pressures. As an example of the very mild conditions which may be employed, with Raney nickel catalyst and sodium acetate cocatalyst hydrogenation of most nitriles is complete in 45–60 minutes at 50° and 50 p.s.i. hydrogen pressure. Lower temperature may be used but requires longer reduction time. Raney nickel–chromium appears to be as effective as Raney nickel, but Raney cobalt is somewhat less effective. Sodium acetate is a very mild cocatalyst suitable for most purposes, but strong bases such as sodium hydroxide give more rapid reduction. Caution should be exercised when strong bases are used, as very rapid reduction become vigorously exothermic. Catalyst life is affected strongly by the nature of the cocatalyst. With sodium acetate the activity of the Raney catalyst diminishes markedly with each use and is too low to be of practical value after three or four cycles, whereas with strong base recovered catalyst is as active as fresh and can be re-used repeatedly. With some nitriles such as benzonitrile no cocatalyst is necessary, but in general its presence gives better yields and purer products. Unsaturated nitriles are reduced to saturated primary amines by the new technique and, although the point has not been studied, it is likely that any other easily reduced group would also be attacked.

The amine products may be isolated in several ways, dependent in part on the nature of the particular amine. In many cases the *N*-acetyl derivative of the amine crystallizes from the reduction medium when it is cooled, and the solid may be obtained in a high state of purity by filtration and drying. In other instances it is convenient to subject the entire reduction mixture to acidic or basic hydrolysis and to isolate the amine as the hydrochloride or as the free base. Where a particular derivative is desired, it may be obtained frequently by treating the hydrolysis mixture with the appropriate derivatizing agent. Each of these methods has been used at least once to isolate the products reported in Table I, which lists the results obtained with six typical nitriles. The yield of 2-hydroxy-2-methylpropylamine hydrochloride from acetone cyanohydrin is not regarded as representative because the extremely hygroscopic nature of the product made isolation difficult.

EXPERIMENTAL[4]

Pretreatment of Raney catalyst. The Raney catalysts were purchased in active form under water from the Raney Catalyst Co., Chattanooga, Tenn. Immediately before use the 2–3 g. (wet weight) of catalyst needed for the 0.10 mole scale

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(1) H. Adkins and R. L. Shriner, *Organic Chemistry*, Vol. I, 2nd Ed., H. Gilman, ed., J. Wiley and Sons, New York, 1943, p. 809.

(2) R. B. Wagner and H. D. Zook, *Synthetic Organic Chemistry*, J. Wiley and Sons, New York, 1953, p. 658.

(3) A. F. Ferris, G. S. Johnson, F. E. Gould, and H. Stange, *J. Org. Chem.*, **25,** 1302 (1960). References to the previous use of the combination of Raney nickel and acetic anhydride are given in this paper.

(4) All melting points are uncorrected.

reductions reported below was filtered from the water and washed with two 20-ml. portions of absolute ethanol and two 20-ml. portions of acetic anhydride. Catalyst so treated lost activity rapidly if allowed to stand under acetic anhydride.

Reduction of tridecanenitrile. A 2–3 g. portion of Raney nickel treated as described above and 12.0 g. of anhydrous sodium acetate were added to a solution of 19.5 g. (0.10 mole) of tridecanenitrile in 120 ml. of acetic anhydride. The resulting mixture was heated to 50° and shaken under hydrogen at an initial pressure of 50 p.s.i. After about 1 hr. hydrogen uptake was complete, and the catalyst was filtered from the hot solution. When the filtrate was cooled in ice, a white solid precipitated. After recovery and drying, this amounted to 24.1 g. (100%) of *N*-acetyltridecylamine, m.p. 57–58°.

Anal. Calcd. for $C_{15}H_{31}ON$; C, 74.62; H, 12.94; N, 5.80. Found: C, 74.62; H, 13.04; N, 5.44.

Reduction of benzonitrile. A mixture of 2–3 g. of treated Raney nickel, 10.3 g. (0.10 mole) of benzonitrile, and 120 ml. of acetic anhydride was shaken at 50° under an initial hydrogen pressure of 50 ps.i. When the reaction was complete (1 hr.), the mixture was filtered hot and the filtrate was treated with 40 ml. of water. Then 180 ml. of concd. hydrochloric acid was added, and the mixture was heated under reflux for 16 hr. The resulting solution was cooled to 25°, made strongly basic with 5*N* sodium hydroxide solution, and extracted with two 100-ml. portions of ether. The ether solution was dried over anhydrous magnesium sulfate, filtered, and treated with gaseous hydrogen chloride until no further precipitate formed. After recovery and drying, there was obtained 13.0 g. (91%) of benzylamine hydrochloride, m.p. 248–249° (lit.,[5] m.p. 248°).

Reduction of acrylonitrile. A mixture of 2–3 g. of treated Raney nickel, 5.3 g. (0.10 mole) of acrylonitrile, 12.0 g. of anhydrous sodium acetate, and 120 ml. of acetic anhydride was shaken at 25° under hydrogen at an initial pressure of 50 p.s.i. Hydrogen uptake was complete after 16 hr., and the catalyst was removed by filtration. The filtrate was treated with 40 ml. of water and the mixture was allowed to stand with occasional stirring for 3 hr. Then 180 ml. of concd. hydrochloric acid was added, and the mixture was heated under reflux for 16 hr. After cooling to 25° the solution was made strongly basic with 5*N* sodium hydroxide solution and was stirred for 2 hr. with 16.8 g. (0.12 mole) of benzoyl chloride. The solid which separated was recovered by filtration and dried. There was thus obtained 15.0 g. (92%) of *N*-propylbenzamide, m.p. 84–85° (lit.,[6] m.p. 84–85°).

Reduction of adiponitrile. A mixture of 10.8 g. (0.10 mole) of adiponitrile, 2–3 g. of treated Raney nickel, 4.4 g. of solid sodium hydroxide, and 120 ml. of acetic anhydride was shaken with hydrogen under 50 p.s.i. pressure, and the temperature was raised cautiously to 50°. At this point a vigorously exothermic reaction set in, and, although the heater was cut off, the temperature rose rapidly to 75° and then dropped slowly. Hydrogen uptake was complete in 15 min. The reaction mixture was filtered hot and the filtrate was cooled in ice to precipitate the product. After recovery and drying there was obtained 16.0 g. (80%) of *N,N'*-diacetylhexamethylenediamine, m.p. 125–126°. (lit.,[7] m.p. 125–126°).

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(5) I. Heibron and H. M. Bunbury, *Dictionary of Organic Compounds*, Vol. I, Oxford Univ. Press, N. Y., 1953, p. 270.

(6) I. Heibron and H. M. Bunbury, *Dictionary of Organic Compounds*, Vol. IV, Oxford Univ. Press, N. Y., 1953, p. 243.

(7) T. Curtius and H. Clemm, *J. prakt. Chem.*, **62**, 210 (1900).

Selective Reactions of the Butadiene-Methoxybenzoquinone Adduct

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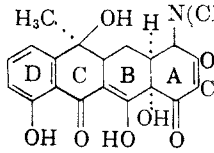
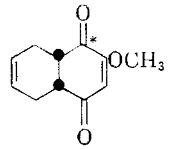
A recent publication by Barltrop and Burstall[2] prompts us to report our work with potential intermediates in a synthesis of tetracycline (I). We prepared 2-methoxy-4a,5,8,8a-tetrahydronaphthoquinone (II) in 85% yield. Further utilization of molecules of this type to elaborate rings A and B of tetracycline requires the introduction of the *N,N*-dimethylamino group in the place of the starred carbonyl. Selective reactions of this carbonyl were expected to be feasible since the other carbonyl group is deactivated by being conjugated with a free pair of electrons on the oxygen of the methoxy group. We were indeed successful in certain selective reactions. Compound II can be reduced selectively by sodium borohydride to give in 44% yield the keto alcohol IIIa. Its *p*-toluenesulfonate (IIIb) was prepared, but an attempt to prepare compound IVa by a displacement of the *p*-toluenesulfonate group was not successful as no reaction took place upon refluxing IIIb with diethylamine.

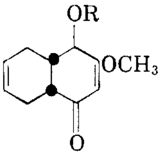
The monoxime of II, compound V, was also prepared in good yield. Catalytic hydrogenation of V with palladium-charcoal did not, however, yield the desired amine IVb.



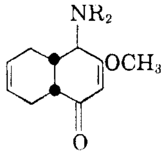
I



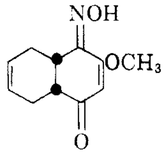
II



IIIa, R = H
b, R = p-$CH_3C_6H_4SO_2$



IVa, R = C_2H_5
b, R = H



V

EXPERIMENTAL[3]

2-Methoxy-4a,5,8,8a-tetrahydronaphthoquinone (II). Methoxybenzoquinone[4] (8.50 g.) and 15 ml. of dry benzene were placed in a heavy-walled glass tube cooled by Dry Ice. To

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(1) Present address: Department of Biochemistry, College of Physicians and Surgeons, Columbia University, New York, N. Y.

(2) J. A. Barltrop and M. L. Burstall, *J. Chem. Soc.*, 2183 (1959).

(3) Melting points are uncorrected. Analyses by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

(4) Prepared by the procedure of Ioffe and Sukhina, *J. Gen. Chem.*, **23**, 295 (1953), [*Chem. Abstr.* **48**, 2640d].