1.4525. The 4-bromo-2,4-dinitro-2-methylpentane melted at 77–79° (lit.[11] 76°).

Use of sodium hydroxide as catalyst yielded 5.3 g. (50%) after two hours reflux, b.p. 104–107° (3 mm.), $n^{20}D$ 1.4542. Use of no catalyst at all (except the released diisopropylamine) yielded 4.5 g. (44%) of the dinitropentane in one hour. However, the reaction left considerable residue, and the product was more difficult to purify than when Triton B was used.

2,4-Dinitrohexane.—Excess 1-nitropropane, 11.2 g. (0.06 mole) of 1-diisopropylamino-2-nitropropane and Triton B catalyst yielded 3.5 g. (33%) of 2,4-dinitrohexane in 15 minutes, b.p. 100–103° (3 mm.), $n^{20}D$ 1.4531.

Anal. Calcd. for $C_6H_{12}N_2O_4$: N, 15.91. Found: N, 16.13.

LOUISVILLE, KENTUCKY

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[11] A. Lambert and H. A. Piggott, *J. Chem. Soc.*, 1489 (1947).

[CONTRIBUTION FROM THE WALKER LABORATORY, DEPARTMENT OF CHEMISTRY, RENSSELAER POLYTECHNIC INSTITUTE]

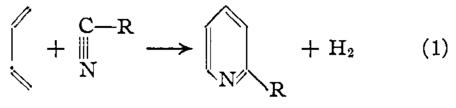
The Reaction of Cyanogen and Related Nitriles with 1,3-Dienes. VII. Acetonitrile

BY GEORGE J. JANZ AND SAMUEL C. WAIT, JR.

RECEIVED MAY 3, 1954

The reaction of acetonitrile with butadiene, isoprene and 2-methyl-1,3-pentadiene, at 400° yields 2-methylpyridine, 2,4-dimethylpyridine and 2,4,6-trimethylpyridine, respectively. The rate of reaction is appreciably enhanced by aluminum oxide as a catalyst. The relative reactivity of the dienes above was found to be 1:6:8, respectively, in the presence of the alumina surface. The preferential formation of one isomeric product, and the enhanced rate over the alumina are in accord with a semi-ionic Diels–Alder type reaction mechanism. Thermodynamic considerations show that the yield achieved over the alumina catalyst is approximately 8% of the value predicted for reaction equilibrium.

This communication reports the reaction of acetonitrile with butadiene, isoprene and 2-methylpentadiene-1,3 at 400°. Under comparable conditions it has been shown[1] that the (C≡N) group of organic nitriles adds to butadiene yielding 2-substituted pyridines as products. This reaction formulated as



(1)

has been demonstrated to be quite general for nitriles with R = H, CH_3, C_6H_5 and CN, respectively. With the exception of cyanogen which was more reactive, the relative reactivities of these nitriles were found to be of the same order of magnitude,[2] apparently little influenced by the internal electronic polarizability within these molecules. The present work extended these studies to determine the relative reactivities of substituted dienes in this reaction. Acetonitrile was selected as the nitrile since the reaction products, mono-, di- and trimethylpyridines are well known and can readily be characterized.

Experimental

Acetonitrile, isoprene and 2-methylpentadiene-1,3 (Eastman Organic Chemicals, Technical grade) were fractionally distilled before use. The physical constants for these were: b.p. 80–81° (1 atm.), $n^{25}D$ 1.3430; b.p. 32–33° (1 atm.), $n^{25}D$ 1.4187; b.p. 75–76° (1 atm.), $n^{25}D$ 1.4470, respectively. Butadiene was a C.P. grade (Matheson) and, after passing over anhydrous $CaCl_2$, was used without further purification. The aluminum oxide (Harshaw Chemical Co., Al-0501) had a composition of 99.5% Al_2O_3, and a surface area of 186 m.²/g. This alumina has been found[3] to have an activity almost as great as the Cr_2O_3–Al_2O_3 catalysts used in the previous investigations of this series. The continuous flow apparatus, the catalyst activation and procedure for an experiment have been described elsewhere in detail.[4] Nitrogen was used as an inert gas in the reactant feed in equimolal ratio to the diene and nitrile.

Production Separation and Identification.—The separation of 2-methylpyridine from the crude product of the butadiene–acetonitrile reaction, as well as the identification already has been described.[5] A similar procedure was followed for investigation of the crude product obtained from the isoprene–acetonitrile and methylpentadiene–acetonitrile reactions, respectively. In each case the reactants were passed over the catalyst bed at 400° using flow rates to give a 4-second contact time in the hot zone. The duration of an experiment was 2 hr. The short contact time was chosen to keep side reactions to a minimum, and the 2-hr. reaction period was selected to give results comparable with the earlier studies. It had been observed that the rate of reaction decreased rapidly if a catalyst bed was used for periods longer than 2 hr. After each 2-hr. period the catalyst was revivified by oxidation with a slow stream of oxygen at a temperature of 475° to remove the surface deposits. The experiment was then continued for another 2-hr. period. A series of such batch runs was made in each case until about 500 g. of crude product (sufficient for investigation) had been gained. The separation of the pyridinic product from the crude was as follows. The unreacted diene and nitrile were removed by distillation. The high-boiling residue in the pot was then extracted with 10% aqueous sulfuric acid to remove the pyridinic products. The latter were recovered from the aqueous acid layer by adding an excess of sodium hydroxide and steam distilling. The pyridinic products were isolated finally by ether extraction of the aqueous steam distillate, and recovered from the ether solution after drying over anhydrous sodium sulfate. For the quantitative determination of the amount of pyridinics, it was found that the non-aqueous potentiometric titration of bases[6,7] with perchloric acid in glacial acetic acid was applicable. An aliquot of the crude residue above after removal of the unreacted nitrile and diene was taken for this determination, thus avoiding the possible mechanical losses in the subsequent handling of the product during the separation of the actual pyridinic products. Picrate and picrolonate derivatives were prepared and purified by recrystallization according to Hackmann and Wibaut[8] for identification. The data are summarized in Table I. The mixed melting points were made with samples prepared from authentic samples of the 2,4- and 2,4,6-isomers. No appreciable depression was found. The composition of each product was confirmed by micro-analysis of the picrate derivatives.

Anal. of dimethylpyridine picrate. Calcd. for $C_{13}H_{12}N_4O_7$: C, 46.41; H, 3.60; N, 16.7. Found: C, 47.30;

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[1] G. J. Janz and P. J. Hawkins, *Nature*, **162**, 28 (1948).

[2] G. J. Janz and R. E. Myers, Pt. IV, THIS JOURNAL, **75**, 1910 (1953).

[3] G. J. Janz and W. J. G. McCulloch, unpublished work.

[4] G. J. Janz, W. J. G. McCulloch and E. F. Timpane, *Ind. Eng. Chem.*, **45**, 1343 (1953).

[5] P. J. Hawkins and G. J. Janz, Pt. I, *J. Chem. Soc.*, 1479 (1949).

[6] J. F. Fritz, *Anal. Chem.*, **22**, 1028 (1950).

[7] H. N. J. Wilson, *J. Soc. Chem. Ind.* (*London*), **67**, 237 (1948).

[8] J. Th. Hackmann and J. P. Wibaut, *Rec. trav. chim.*, **162**, 229 (1943).

H, 3.52; N, 16.7. *Anal.* of trimethylpyridine picrate. Calcd. for $C_{14}H_{14}N_4O_7$: C, 47.98; H, 4.03; N, 16.0. Found: C, 48.31; H, 4.09; N, 16.4.

TABLE I

MELTING POINT DATA

Derivative	Melting points, °C. Observed (uncor.)	Literature[8]	
Dimethylpyridine		2,4-	2,5-
picrate	177 (sint. 174)	184–185	170
picrolonate	208 (sint. 205)	207–208	171
Trimethylpyridine		2,4,6-	2,3,5-
picrate	153 (sint. 150)	156	183
picrolonate	226 (sint. 223)	230	No ref.

It follows that the products from the isoprene–acetonitrile and the methylpentadiene–acetonitrile reactions are the 2,4-dimethyl- and the 2,4,6-trimethylpyridines, respectively.

Homogeneous Gas Phase Experiments.—Three runs were carried out using an unpacked reaction vessel. The conditions used, total material balance and space–time yields are listed in Table II. The crude product was investigated for the amount of pyridinic product by the non-aqueous titration technique. From the space–time yield, it is seen that in each instance the rate is very slow. The three dienes have the same order of reactivity (1.2 to 1.9 × 10^{-4} mole/hr./100 cc.) with acetonitrile in the homogeneous gas phase.

TABLE II

REACTION CONDITIONS, MATERIAL BALANCE AND SPACE–TIME YIELDS

Reactants	Temp., °C.	Contact time, sec.	Input Mole ratio RCN/diene	Input Total, g.	Crude (−80°), g.	Recovery Catalyst deposit, g.	Total wt., %	Space–time, yield moles pyridinic × 10^4/hr./100 cc.
			Homogeneous gas phase					
Acetonitrile and								
(i) Butadiene	395	4.3	2.8/1.0	46.9	46.5	..	99.0	1.88
(ii) Isoprene	400	7.8	2.2/1.0	33.8	33.1	..	98.0	1.18
(iii) 2-Methylpentadiene-1,3	400	4.5	2.1/1.0	145.2	144.8	..	99.6	1.65
			Activated alumina (Al-0501) catalyst					
(iv) Butadiene	408	3.6	0.84/1.0	58.7	53.3	3.40	98.5	23.7
(v) Isoprene	420	4.5	1.0/1.0	64.0	57.7	4.50	99.0	139
(vi) 2-Methylpentadiene-1,3	402	3.9	1.2/1.0	67.8	64.6	2.08	99.9	187

Reactions Over Aluminum Oxide.—The reaction conditions and space–time yields for the three catalyzed runs are also given in Table II. The temperature is the average catalyst bed temperature during the two-hour period of a run. Before each experiment the alumina had been freshly activated by treatment with oxygen at 475° (one hour) and a nitrogen flush. The gain in weight of the catalyst bed was measured by weighing the whole reactor immediately before and after each experiment. In addition to the pyridinic product formed, some ammonia (as ammonium carbonate) was found present in the crude products. This was removed by filtration, and heating before an aliquot of the crude product was taken for determination of the yield of pyridinic product. The formation of the ammonium carbonate may be attributed to side reactions of the acetonitrile with water vapor (from the alumina) at these temperatures. The following data and observations were noted specifically for each experiment. Run (iv): **Acetonitrile and Butadiene.**—The catalyst bed weighed 80.70 g. initially, having 49.5 cc. as free space. A maximum temperature increase of 17° was observed in the catalyst during the experiment. Analysis of the crude product showed that the diene and nitrile conversions per pass were 31 and 9.6 mole per cent., respectively. The yield of 2-methylpyridine (calculated on the nitrile converted) was 7.0 mole per cent. Run (v): **Acetonitrile and Isoprene.**—A catalyst bed of 99.80 g. and 65 cc. free space was used. The maximum temperature rise in the catalyst was 22°. The diene and nitrile conversions were 70 and 34 mole per cent., respectively. The yield of 2,4-dimethylpyridine was 14.7 mole per cent of the nitrile converted. Run (vi): **Acetonitrile and 2-Methylpentadiene-1,3.**—The catalyst charge and free space were the same as in run (iv). The maximum temperature rise was 20°. The diene and nitrile conversions were 26 and 22 mole per cent., and the yield of 2,4,6-trimethylpyridine was 5.6 mole per cent. of the nitrile converted.

It was noted that high-boiling residues were present in each of the crude reaction products. These were not investigated further since the interest in the present work was in the pyridinic product.

Discussion

Comparison of the space–time yields (Table II) in the catalyzed systems shows that isoprene and methylpentadiene are 6 and 8 times more reactive than butadiene in this nitriles–dienes cyclization reaction. In the case of isoprene and butadiene some kinetic data exist for a related reaction in the homogeneous gas phase. Wassermann[9] has reported the energies of activation to be 18.7 and 19.7 kcal., respectively, for the additions to acrolein at 333° in the gas phase. From this it is estimated that the reactivity of isoprene is 2.3 times greater than butadiene. The enhanced reactivity and increased rate of reaction may be attributed to the importance of polar structures in the electronic description of the transition state in the Diels–Alder reaction.[10,11] Thus for isoprene the two ends of the diene skeleton are non-equivalent, the methyl group contributing to a polar structure through the +E and +I electron displacement effects. The much greater increase in rate observed over the alumina surface suggests that the mode of action is to promote the electron displacements in the diene leading to the polar structures important in the transition state of the reaction. A first premise thus is the assumption that there is chemisorption at the center of highest electron density in the diene, *i.e.*, the nucleophilic center on the 1-carbon position. The slightly acidic nature of the catalyst surfaces (alumina and chromia-on-alumina) act as centers of electrophilic attraction. A decreased activity was observed with a surface when sodium oxide was present.[4] With isoprene and acetonitrile the processes would be

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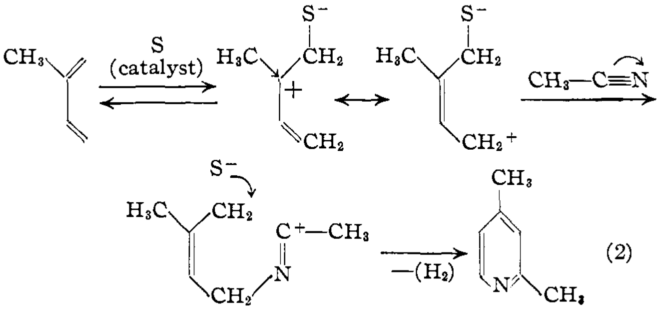
(9) A. Wassermann, *Trans. Faraday Soc.*, 34, 128 (1938).

(10) A. E. Remick, "Electronic Interpretation of Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1946.

(11) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953.



(2)

The point of attack by the dienophilic group is at the 4-carbon position in the diene skeleton. Desorption from the catalyst with subsequent ring closure would lead through a cyclic transition state, and with the spontaneous loss of hydrogen, to the final pyridinic product. The preferential formation of 2,4-dimethyl- and 2,4,6-trimethyl- pyridines when isoprene and methylpentadiene were used with acetonitrile can be understood from this viewpoint.

The influence of substituents on the structure and reactivity of nitriles in this reaction with butadiene has been considered.[2] It was found that the rate was increased in the presence of the catalyst, but that the enhancement was approximately the same for R = H, CH_3, C_2H_5 and C_6H_5 in RCN, and of the same order of magnitude as found for acetonitrile and butadiene in the present work. In view of the much greater effects observed with variation in diene structure, this suggests that the catalyst surface has little influence on the polarizability of the nitrile and acts almost preferentially for the activation of the diene. The effect on the rate when −E substituents are introduced into the nitrile is under investigation.

The thermodynamics of these reactions using benzonitrile and butadiene as a specific example, have been discussed in detail elsewhere.[4] In the present work an estimate of the free energy change was made for the acetonitrile–methylpentadiene reaction. The method of group increments,[12,13] taking cognizance where necessary of differences in the symmetry numbers and in the potential barriers restricting internal rotation, was used to calculate the data for methylpentadiene and trimethylpyridine. At 400°, the free energy change for the reaction was found to be −4.1 kcal. The equilibrium space–time yield predicted from this result is 0.24 mole/hr./100 cc. catalyst. The experimental space–time yield (Table II) was 1.9 × 10^{-2} mole/hr./100 cc., *i.e.*, about 8% of the predicted value for reaction equilibrium.

Acknowledgment.—The support of this work in part by a grant-in-aid from Research Corporation (New York) is gratefully acknowledged. The authors wish to thank Dr. H. F. Herbrandson for stimulating discussions.

[12] D. D. Wagman, J. E. Kilpatrick, K. S. Pitzer and F. D. Rossini, *J. Research Natl. Bur. Standards*, **35**, 468 (1945).

[13] J. E. Kilpatrick, E. J. Prosen, K. S. Pitzer and F. D. Rossini, *ibid.*, **36**, 559 (1946).

TROY, NEW YORK

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

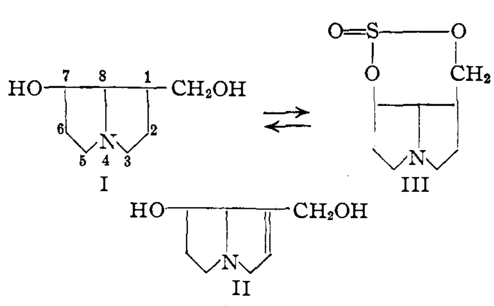
Stereochemistry of the Pyrrolizidine Bases

BY ROGER ADAMS AND BENJAMIN L. VAN DUUREN

RECEIVED JULY 16, 1954

Platynecine on treatment with thionyl chloride gives a new three-ring structure containing the sulfite ester group. This substance can be hydrolyzed readily to platynecine. From this and other evidence it may be deduced that the hydroxyl and hydroxymethyl groups in platynecine are both *trans* to the 8-hydrogen atom, that is, *cis* to each other. The diastereoisomer of platynecine, dihydroxyheliotridane, does not form a sulfite ester. Platynecine can be dehydrated with phosphorus oxychloride in benzene to anhydroplatynecine whereas dihydroxyheliotridane does not give the anhydro compound under identical conditions. It is deduced that in dihydroxyheliotridane the C_1–CH_2OH is *trans* to the 8-hydrogen atom, whereas the C_7–OH is *cis* to the 8-hydrogen atom. Since retronecine and heliotridine are reduced to platynecine and dihydroxyheliotridane, respectively, the stereoconfigurations of the former two bases are clarified. The stereochemistry of the necines is discussed on the basis of their relation to retronecine, platynecine, heliotridine and dihydroxyheliotridane.

The alkaloids of the Senecio group are mono- or diesters of the pyrrolizidine bases or necines. The three most common bases are platynecine (I), retronecine and its diastereoisomer heliotridine (II). The structures of these bases have been established beyond doubt.[1]



I

III

II

Recently Menshikov and Kuzovkov[2] reported the preparation of the diastereoisomer of platynecine by the catalytic reduction of heliotridine with Raney nickel and hydrogen as used previously by Adams and Rogers[3] for the reduction of retronecine to platynecine. The name dihydroxyheliotridane was suggested for this base.[2] This report deals with the stereochemistry of these four bases and of the necines related to them.

Konovalova and co-workers[4,5] found that when

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[1] N. J. Leonard, "The Alkaloids" (Editors R. H. F. Manske and H. L. Holmes), Vol. I, Academic Press, Inc., New York, N. Y., 1950, p. 108.

[2] G. P. Menshikov and A. D. Kuzovkov, *J. Gen. Chem., U.S.S.R.*, **14**, 1702 (1949).

[3] R. Adams and E. F. Rogers, THIS JOURNAL, **63**, 537 (1941).

[4] A. Orechov, R. Konovalova and W. Tiedebel, *Ber.*, **68**, 1886 (1935).

[5] R. Konovalova and A. Orechov, *ibid.*, **69**, 1908 (1936).