tone as solvent. The data for individual runs could be fitted to the first-order rate law as is usually the case.[15] The data are summarized in Table I.

As would be expected from the small range of observed rates, attempts to fit the data by the method of Nozaki and Bartlett[15] led to trivial results. The rates are somewhat faster than the "true" unimolecular rates observed in other solvents in the presence of inhibitors[16,17] or at very high dilution.[14] This suggests that a first-order induced decomposition may be of some importance. This could be the consequence of the crossed termination of induced chains as is the case in ether solution.[16,18] However, the similarity of the rates in the two ketones suggests that no unusual reactivity toward the radicals from the peroxide can be attributed to the cyclopropyl group. It is entirely possible that interaction, if it does occur, involves the methyl group. The same conclusion is reached on the basis of coupling experiments with cyclopropyl methyl ketone. Kharasch and co-workers[19] have reported that acetone is converted to 2,5-hexandione by decomposing acetyl peroxide. A high-boiling fraction was obtained in a similar experiment with cyclopropyl methyl ketone. However, the product gave only a slight reaction with hypoiodite indicating that coupling was largely through the methyl groups. No yield of coupling product was obtained in a similar decomposition conducted in cyclopropyl cyanide. When gross amounts of benzoyl peroxide were decomposed in cyclopropyl methyl ketone a 20% yield of benzoic acid and a small yield of *p*-phenylbenzoic acid were produced. The significance of the latter product is to suggest that the ketone is not able to scavenge phenyl radicals well enough to prevent their reacting with either unreacted peroxide or benzoic acid.

Phenylcyclopropane proved to be entirely inert toward polymerization by benzoyl peroxide. Interestingly enough it was found that β-methylstyrene could be removed very selectively from the cyclopropane by decomposing benzoyl peroxide in a mixture of the two hydrocarbons.

The results of this study are consistent with the previous observations of Trotman-Dickenson and Steacie[4] and the predictions of Brown and Gerstein[20] in that they imply that the abstraction of hydrogen from the cyclopropane ring by free radicals is a relatively slow reaction. It is further shown that ring opening by free radicals is much more difficult than is the analogous addition reaction of olefins.

(15) K. Nozaki and P. D. Bartlett, THIS JOURNAL, **68**, 1686 (1946); P. D. Bartlett and K. Nozaki, *ibid.*, **69**, 2299 (1947).

(16) C. G. Swain, W. H. Stockmeyer and J. T. Clarke, *ibid.*, **72**, 5426 (1950).

(17) A. T. Blomquist and I. A. Berstein, *ibid.*, **73**, 5546 (1951).

(18) W. E. Cass, *ibid.*, **68**, 1976 (1946).

(19) M. S. Kharasch, H. C. McVay and W. H. Urry, *ibid.*, **70**, 1269 (1948).

(20) H. C. Brown and M. Gerstein, *ibid.*, **72**, 2926 (1950).

AMES, IOWA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, WEST VIRGINIA UNIVERSITY]

Preparation of Nitro Compounds from Oximes. III. The Synthesis of Nitroalkanes

BY DON C. IFFLAND AND TEH-FU YEN[1]

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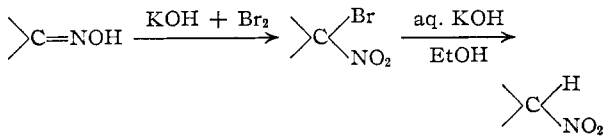
A synthesis of secondary nitroalkanes from aliphatic ketoximes *via* bromonitroso and bromonitro intermediates is described. The sequence is shown to be free of rearrangement. Ten nitroalkanes were prepared and characterized.

In 1900, Forster prepared nitrocamphane from camphor oxime by the steps[2]



Recently this sequence of reactions was examined in this Laboratory in order to determine its generality as an adjunct to existing preparations of nitro compounds.[3] With alicyclic ketoximes it was found that the alkaline solution of bromine produced a bromonitroso compound which, however, could be oxidized to a bromonitro compound with the aid of concentrated nitric acid. Although the sequence was completed with this additional step, the over-all yields of nitrocycloalkanes were poor. It was only after finding that the bromination and debromination steps could be considerably improved by the use of N-bromosuccinimide (NBS) and sodium borohydride, respectively, that a practical synthesis of nitrocycloalkanes resulted.

These improvements in the synthesis of nitrocycloalkanes from oximes now have been extended successfully to the preparation of ten secondary nitroalkanes from aliphatic ketoximes, in spite of the complete failure in this series by conditions originally used by Forster.[3a] In this series, the bromonitroso and bromonitro intermediates were not isolated or purified in order to simplify the laboratory procedure and, in particular, to minimize personal contact with these lachrymatory substances. Thus, the crude bromonitro compound was converted to the nitro compound by the action of sodium borohydride. As the crude bromonitro compounds were contaminated with the related ketone, the reduction mixtures contained small amounts of the corresponding alcohol. No difficulty was experienced, however, in the purification of the nitro compound in the procedure described in the Experimental part.

The reaction of the lower molecular weight ali-

(1) Taken in part from the M.S. Thesis of T.-F. Yen, West Virginia University, August, 1953.

(2) M. O. Forster, *J. Chem. Soc.*, **77**, 254 (1900).

(3) (a) D. C. Iffland, G. X. Criner, M. Koral, F. J. Lotspeich, Z. B. Papanastassiou and S. M. White, THIS JOURNAL, **75**, 4044 (1953); (b) D. C. Iffland and G. X. Criner, *ibid.*, **75**, 4047 (1953).

TABLE I

YIELDS, PROPERTIES AND ANALYSES OF NITROALKANES

Nitroalkane	Yield from oxime, %	B.p. °C.	B.p. Mm.	$n^{25}D$	d^{25}_4	Molar refraction Calcd.	Molar refraction Found	Nitrogen, % Calcd.	Nitrogen, % Found[a]
2-Nitropentane	38[b]	88[c]	100	1.4092	0.938	30.91	30.88	11.95	11.67
3-Nitropentane	29[b]	90[d]	100	1.4091	.939	30.91	30.84	11.95	11.82
3-Nitro-2-methylbutane	48[b]	88[e]	100	1.4122	.943	30.91	30.89	11.95	11.91
2-Nitrohexane	19	95[f]	50	1.4168	.920	35.53	35.44	10.68	10.38
3-Nitrohexane	25	91	50	1.4152	.932	35.53	35.27	10.68	10.39
3-Nitro-2,2-dimethylbutane[g]	30[b]	96[h]	100	1.4251	.936	35.53	35.84	10.68	10.71
2-Nitroheptane	16	95[i]	25	1.4219	.912	40.15	40.26	9.65	9.38
3-Nitroheptane	29[j]	91	25	1.4210	.917	40.15	40.16	9.65	9.68
4-Nitroheptane	28	90	25	1.4200	.920	40.15	36.96	9.65	9.46
2-Nitroöctane	10	106[k]	20	1.4263[l]					

[a] Microanalysis by Galbraith Laboratories, Knoxville, Tenn. [b] This yield obtained *via* the NBS procedure—all others *via* NBA procedure. [c] G. D. Buckley and E. Ellery, *J. Chem. Soc.*, 1497 (1947), reported b.p. 148–150° (atm.). [d] J. Bewad, *J. prakt. Chem.*, [2] **48**, 380 (1893), reported b.p. 152–155 at 746 mm., d^0 0.9575. [e] M. H. Danzig and H. B. Hass, THIS JOURNAL, **66**, 2017 (1944), and L. W. Seigle and H. B. Hass, *Ind. Eng. Chem.*, **31**, 648 (1939), reported the formation of this nitroalkane in nitration mixtures obtained from 2,3-dimethylbutane and isopentane, respectively. However, neither paper reported physical properties. [f] M. Konowalow, *Zhur. Russ. Fiz.-Khim. Obshchestwa*, **25**, 488 (1883), reported the formation of this nitroalkane from nitration of *n*-hexane; b.p. 176°, d^{20}_0 0.9357, n^{24} 1.4162. The reduction of this nitroalkane to 2-aminohexane also was reported. [g] Dioxane was added in the NBS procedure as a solvent for the solid pinacolone oxime. The bromonitroso and bromonitro intermediates solidified at room temperature. Glacial acetic acid was added as solvent in H_2O_2–HNO_3 oxidation. [h] W. Markownikoff, *Ber.*, **32**, 1445 (1899), reported this nitroalkane formed *via* vapor phase nitration of the corresponding alkane; b.p. 167–169° at 748 mm. [i] M. Konowalow (footnote *f*) reported the formation of 2-nitroheptane from *n*-heptane similar to the formation of 2-nitrohexane; b.p. 194–196°, n^{22} 1.4242, d^{20}_0 0.9306. This nitroalkane also was reduced to the related amine. [j] NBS procedure gave 18% yield of crude 3-nitroheptane (b.p. 70–89° at 25 mm.). [k] N. Kornblum, *et al.*, THIS JOURNAL, **69**, 310 (1947), reported 2-nitroöctane produced *via* the Victor Meyer reaction: b.p. 102–104° (20 mm.), $n^{20}D$ 1.4280, d^{20}_4 0.9166. [l] $n^{20}D$ 1.4282.

phatic ketoximes with NBS proceeded satisfactorily following explicitly the method described for alicyclic ketoximes.[3b] However, with the normal hexanone to octanone oximes, which have lower solubility in the aqueous bicarbonate reaction mixture, the yields of bromonitroso compounds were poor. Considerable improvement was attained in the latter cases by the substitution of water-soluble N-bromoacetamide (NBA) for NBS and reversing the order of mixing materials, *i.e.*, adding an NBA solution to a stirred water suspension of the oxime and base.

Furthermore, zinc oxide was preferred over sodium bicarbonate as a base in this NBA procedure. It is believed that the superiority of this NBA procedure is a consequence of the more intimate contact possible between the oxime and brominating agent than that possible in the NBS procedure.

The reaction of an aqueous solution of NBA with the oxime in the absence of any base was found to be entirely unsatisfactory. Bromination of the oxime rapidly produced an acidic reaction mixture which in turn led to decomposition of the NBA, forming bromine, hydrolysis of the oxime and possible formation of bromoketones.

The bromonitroso intermediates in this series were oxidized to the bromonitro compounds with a 30% hydrogen peroxide–concentrated nitric acid mixture. At 50–70° this step proceeded very smoothly and was much faster than concentrated nitric acid alone, which was used in the alicyclic series. Considerable care was required in this oxidation to avoid temperatures above 75° as the reaction then often became uncontrollable.

Except for 2-nitrohexane, 2-nitroheptane and 2-nitroöctane the nitroalkanes reported in this paper have not been adequately characterized previously. In addition to the usual physical properties, molecular refractivity and nitrogen analyses reported in Table I, each nitroalkane was further characterized by hydrogenation to the related amine according to the procedure of Iffland and Cassis.[4] Alkylphenylthiourea or N-alkyl benzamide derivatives of the amines were prepared and found identical to the corresponding derivatives obtained from authentic samples of the amines prepared from ketoximes.[5]

In this way it has been established that structural rearrangement is absent in this sequence of preparation. This is particularly noteworthy in the formation of 3-nitro-2-methylbutane and 3-nitro-2,2-dimethylbutane. It is unlikely that existing methods of preparation of nitroalkanes would be practical routes to such compounds.[6]

Experimental

The preparations of 2-nitropentane and 2-nitrohexane are described and are representative of the methods used.

Preparation of 2-Nitropentane (NBS Procedure).—A brominating suspension was prepared by adding 16.8 g. of sodium bicarbonate to a mixture of 26.7 g. (0.23 mole) of N-bromosuccinimide in 250 ml. of water and cooled to 5°. Over a period of *ca.* 20 min., 10.1 g. (0.15 mole) of 2-pentanone oxime was added to the vigorously stirred suspension. The reaction temperature was maintained at 5–10° using an ice-bath. After the oxime addition was completed, stirring was continued *ca.* 45 min. The blue oil was collected by extracting the reaction mixture with 35–37° petroleum ether and the extract was concentrated to about 25 ml. by distillation on a steam-bath.

The crude bromonitroso compound was cooled and transferred to a 500-ml. round-bottom flask fitted with an air condenser. In separate portions, 50 ml. of 30% hydrogen peroxide and 20 ml. of concentrated nitric acid were added and the mixture shaken vigorously. The reaction proceeded slowly until the temperature reached 50–55° and then

(4) D. C. Iffland and F. A. Cassis, THIS JOURNAL, **74**, 6284 (1952).

(5) D. C. Iffland and T.-F. Yen, *ibid.*, **76**, 4180 (1954).

(6) In a recent study, N. Kornblum, B. Taub and H. E. Ungnade, *ibid.*, **76**, 3209 (1954), have found that the Victor Meyer reaction is really useful only in the preparation of primary nitroalkanes and, even with primary alkyl halides, branching α to the carbon holding the halogen has a deleterious effect.

became rapid and strongly exothermic. External cooling was used as required in order to avoid a temperature above 75°. After the organic layer became pale yellow or colorless, the reaction mixture was diluted with 150 ml. of water, cooled and the crude 2-bromo-2-nitropentane was extracted with 35–37° petroleum ether. The extract was washed successively with 2% aqueous sodium hydroxide solution and with water, dried and concentrated by distillation of the solvent. The crude bromonitro compound—after evacuating to about 50 mm. to flash out the final traces of solvent—weighed 23 g. (about 0.115 mole).

The 2-bromo-2-nitropentane was debrominated using 22.0 g. (0.58 mole) of sodium borohydride (5 moles per mole of crude bromonitro compound) employing the procedure described by Iffland and Criner.[3b] After completion of the reaction, the mixture was made alkaline with 25% aqueous sodium hydroxide solution and thoroughly extracted with petroleum ether. The nitro compound was isolated from the alkaline solution by acidification with hydroxylamine hydrochloride and extraction in the usual manner.[3b] There was obtained 6.7 g. of 2-nitropentane having the properties listed in Table I.

Preparation of 2-Nitrohexane (NBA Procedure).—A suspension of 17.25 g. (0.15 mole) of 2-hexanone oxime and 9.1 g. (0.11 mole) of zinc oxide was prepared in 150 ml. of water and contained in a 500-ml. three-necked flask. A solution was prepared by dissolving 25 g. (0.18 mole) of N-bromoacetamide in 100 ml. of water and was added to the cooled (5°) and stirred oxime suspension. This addition required *ca.* 30 min. The reaction mixture was stirred an additional 30 min. while warming nearly to room temperature and then filtered. The excess zinc oxide was thoroughly washed with petroleum ether and the blue oil in the filtrate finally collected by extraction with 35–37° petroleum ether. This extract was processed exactly as described for the corresponding extract in the preparation of 2-nitropentane. There was obtained 3.85 g. of 2-nitrohexane having the properties indicated in Table I.

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[CONTRIBUTION FROM THE SAMUEL C. HOOKER LABORATORY OF THE DEPARTMENT OF CHEMISTRY OF WAYNE UNIVERSITY]

Terpenoids. VII.[1] Experiments in the Glycyrrhetic Acid Series

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The decarboxylation product of 18-dehydroglycyrrhetic acid acetate (IIc) is shown to be $\Delta^{13(18),19}$-30-noroleadien-3β-ol-11-one acetate (III), both double bonds moving out of conjugation with the carbonyl group. Chromium trioxide oxidation of this substance leads to opening of ring E with formation of an unsaturated triketone VI, the structure of which is substantiated by reduction and cyclization experiments. These results confirm the location of the carboxyl group of glycyrrhetic acid as proposed by Ruzicka and Jeger.

Glycyrrhetic acid (Ia)[3] is a pentacyclic triterpene of unusual interest. It occurs in licorice root as the disaccharide glycoside glycyrrhizic acid[4] and it is one of the few triterpenes with pronounced physiological effects.[3a] Particularly noteworthy is the observation of Groen and co-workers[5] that glycyrrhizic acid exhibits qualitatively the same effect on the electrolyte balance in Addison's disease as does the adrenal hormone desoxycorticosterone. From a chemical standpoint, the aglycone glycyrrhetic acid (Ia) is unusual in that it is the only known triterpene with an 11-oxygen function and, furthermore, by virtue of certain decarboxylation reactions described below, it offers a ready means to the opening of ring E and a potentially attractive synthetic entrance into the taraxasterol and α-amyrin series.[6]

The presently accepted structure of glycyrrhetic acid (Ia) is due principally to the outstanding researches of Ruzicka, Jeger and their collaborators and briefly is based on the following facts: The presence of the 11-keto group is demonstrated by the typical ultraviolet absorption maximum at 250 mμ[7] and the catalytic hydrogenolysis[8] of the unreactive keto group to desoxoglycyrrhetic acid. Conversion of the latter's carboxyl function to methyl[9] furnished β-amyrin, thus establishing the entire structure of glycyrrhetic acid with the exception of the position of the carboxyl group. The placement of the carboxyl group at C-20 was based to a large extent on two important experiments by Ruzicka and Jeger.[10,11] The first involved selenium dioxide oxidation of 11-desoxoglycyrrhetic acid to the corresponding $\Delta^{9(11),13(18)}$-dien-12,19-dione and the demonstration of a β-ketoester function in this compound, while the second approach dealt with an examination of the decarboxylation of dehydroglycyrrhetic acid (II). Since we were not completely satisfied with the correctness of the structure assignments in this instance and since these intermediates are of crucial importance for any subsequent conversion to taraxasterol derivatives, we have undertaken a reinvestigation of the decarboxylation of dehydroglycyrrhetic acid. The experiments described below represent additional evidence for the correctness of the Ruzicka–Jeger[10] formulation (Ia) for glycyrrhetic acid.

The glycyrrhetic acid was obtained directly as the methyl ester Ib by methanolic hydrochloric acid hydrolysis[12] of commercially available ammoniated glycyrrhizin rather than *via* the purified po-

(1) Paper VI, C. Djerassi, E. Farkas, A. J. Lemin, J. C. Collins and F. Walls, THIS JOURNAL, **76**, 2969 (1954).

(2) Organon Research Fellow, 1952–1954.

(3) The extensive literature has been reviewed by (a) C. Niemann, *Chem. Weekblad*, **48**, 213 (1952); (b) O. Jeger in L. Zechmeister's "Progress in the Chemistry of Organic Natural Products," **6**, 1 (1950); (c) Elsevier's "Encyclopedia of Organic Chemistry," **14** (Supplement), 1057 (1952).

(4) The structure of the disaccharide moiety has been elucidated by B. Lythgoe and S. Trippett, *J. Chem. Soc.*, 1983 (1950).

(5) J. Groen, H. Pelser, M. Frenke, C. E. Kamminga and A. F. Willebrands, *J. Clin. Invest.*, **31**, 87 (1952), and earlier references.

(6) If the α-amyrins are indeed epimeric at C-17 with the β-amyrins (*cf.* O. Jeger, *Angew. Chem.*, **63**, 196 (1951)) then glycyrrhetic acid would lead to the wrong stereochemical series.

(7) L. Ruzicka and S. L. Cohen, *Helv. Chim. Acta*, **20**, 804 (1937).

(8) L. Ruzicka, H. Leuenberger and H. Schellenberg, *ibid.*, **20**, 1271 (1937).

(9) L. Ruzicka and A. Marxer, *ibid.*, **22**, 195 (1939).

(10) L. Ruzicka and O. Jeger, *ibid.*, **25**, 775 (1942).

(11) L. Ruzicka, O. Jeger and M. Winter, *ibid.*, **26**, 265 (1943).

(12) *Cf.* P. Bilham, G. A. R. Kon and W. C. J. Ross, *J. Chem. Soc.*, 535 (1942).