Kline and French Laboratories. Results of these tests will be reported elsewhere.

Summary

Three new sulfanilamide derivatives of substituted ethylenediamines have been prepared and characterized. As intermediates for these compounds, the corresponding acetyl derivatives, one new aliphatic nitroamine, and one new substituted ethylenediamine were prepared and characterized.

An improvement in the preparation of nitroamines from secondary amines, formaldehyde and 2-nitropropane is reported. A satisfactory method for reduction of aliphatic nitro compounds is reported.

GAINESVILLE, FLORIDA RECEIVED SEPTEMBER 16, 1949

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF HOPE COLLEGE]

1-Nitro-1-methylethyl Alkyl Malonic Esters

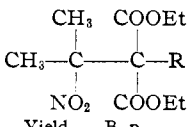
BY EUGENE E. VAN TAMELEN[1] AND GERRIT VAN ZYL

We have previously shown that, whereas 2-*bromo*-2-nitropropane reacts with sodium ethyl malonic ester to give sodium 2-nitropropane and ethyl bromomalonic ester, 2-*chloro*-2-nitropropane yields the normal alkylation product, 1-nitro-1-methylethyl ethyl malonic ester.[2] The present communication is concerned with the preparation of a series of 1-nitro-1-methylethyl alkyl malonic esters and an investigation of some of their properties.

The nitromalonic esters were obtained in fair yields by the condensation of the appropriate mono-substituted malonic esters with 2-chloro-2-nitropropane. Their properties are listed in Table I. The products are light yellow liquids, difficult to purify by the usual fractionation methods.

During the course of the initial distillation of several of these esters, white crystals identified as 2,3-dimethyl-2,3-dinitrobutane, were found to sublime. This product is also found in varying amounts while carrying out the reaction of 2-bromo-2-nitropropane and sodium ethyl malonic ester; it has its origin in the condensation of 2-bromo-2-nitropropane with the sodium 2-nitropropane formed initially.[2] The halogen interchange exhibited therein must, therefore, also be operative to some extent in the reaction of 2-chloro-2-nitropropane with mono-substituted malonic esters.

TABLE I



R	Formula	Yield, %[a]	B. p., °C.	Mm.	$n^{20}D$	Nitrogen, % Calcd.	Found
Methyl	$C_{11}H_{19}O_6N$	45	167	18	1.4483	5.36	5.20
Allyl	$C_{13}H_{21}O_6N$	46	155	6	1.4604	4.87	4.82
n-Butyl	$C_{14}H_{25}O_6N$	39	159	6	1.4511	4.62	4.86
i-Butyl	$C_{14}H_{25}O_6N$	45	151	4	1.4541	4.62	4.83
i-Amyl	$C_{15}H_{27}O_6N$	48	164	5	1.4510	4.41	4.05

[a] The yields are based on a fraction collected over a range boiling from 5° below to 5° above the b. p. of material used for analysis (adjacent column).

Catalytic reduction with Raney nickel of a typical nitro ester, 1-nitro-1-methylethyl ethyl malonic ester,[2] did not lead to the corresponding amine, but rather to a product of cleavage, ethylmalonic ester. The expected product, 1-amino-1-methylethyl ethylmalonic ester, may be considered to be the Mannich condensation product of ethylmalonic ester, ammonia and acetone; since the latter is not known to replace formaldehyde in the Mannich reaction,[3] the instability of the reduction product is not surprising. This "reverse Mannich" reaction must occur extremely readily, since considerable amounts of ammonia were evolved immediately after the completion of the hydrogenation, which was run at room temperature and at an initial pressure of 50 lb.

The nitro esters in Table I appear to be suitable for the preparation of the corresponding barbituric acids, since a typical member of the series (Table I, R = Methyl) gave the desired product, 5-(α-nitro-α-methylethyl)-5-methylbarbituric acid, upon condensation with urea in the usual manner.

Experimental[4]

1-Nitro-1-methylethyl Alkyl Malonic Esters.—The following experimental procedure was used for the preparation of the esters listed in Table I. The reactions were carried out in a 500-cc. three-necked flask equipped with a sealed stirrer and a reflux condenser (calcium chloride tube attached).

A solution of the sodium salt of the alkyl malonic ester (0.25 mole) was made ready by the addition of clean strips of sodium metal (5.7 g., 0.25 mole) to a solution of the dry ester in 225 cc. of absolute ether. The sodium reacted vigorously at first, but heating and stirring were eventually necessary to effect complete solution. The clear solution was cooled and the 2-chloro-2-nitropropane (49.2 g., 0.4 mole) added in one lot. A slight exothermic reaction usually took place, after which the contents were refluxed for seventy hours. A slight excess of glacial acetic acid was added, and then the ether solution was washed three times with 100-cc. portions of water and finally dried over sodium sulfate. Distillation from a Claisen flask yielded, after a forerun of unchanged alkyl malonic ester and other products, the desired nitro ester boiling over a 10° range. A middle cut was taken for analysis.

(1) Harvard University, Cambridge, Massachusetts.

(2) van Tamelen and Van Zyl, THIS JOURNAL, **71**, 835 (1949).

(3) Blicke, "Organic Reactions," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1942, p. 303.

(4) All melting points are corrected.

During distillation, a small amount of crystals was often observed to condense in the receiver just prior to the collection of the nitro ester fraction. The crystals were removed, washed with ether and dried. The melting point (214–215°) was undepressed when mixed with an authentic sample of 2,3-dimethyl-2,3-dinitrobutane[5] (m. p. 215.5–216.0°).

Catalytic Reduction of 1-Nitro-1-methylethyl Ethyl Malonic Ester.—Twenty-seven and a half grams (0.10 mole) of 1-nitro-1-methylethyl ethyl malonic ester was reduced in a Parr hydrogenator using 3 g. of freshly prepared Raney nickel catalyst[6] and absolute ethanol (100 cc.) as a medium. The initial pressure was 50 lb.; 0.30 mole of hydrogen was taken up within forty-five minutes. After the hydrogenation was complete, considerable amounts of ammonia were evolved upon opening the pressure bottle. The catalyst was removed by filtration and most of the ethanol taken off on the steam-bath. Distillation of the liquid residue gave 13.0 g. (69%) of a nitrogen-free ester boiling at 206–210°. The b. p.'s recorded for ethyl malonic ester are 211°[7] and 207°.[8] Saponification gave the diacid, m. p. 111.0–111.5°; the m. p. of ethyl malonic acid is 111.5.[9]

5-(α-Nitro-α-methylethyl)-5-methylbarbituric Acid.—The barbituric acid was obtained by refluxing sodium ethoxide, nitro ester and urea (molar proportions 2:2:3) in absolute ethanol for three days. The solid salt which had precipitated was removed from the ethanol by filtration and dissolved in water. The aqueous solution was extracted with ether, filtered and finally acidified with concentrated hydrochloric acid. After standing in the cold overnight, the barbituric acid was removed by filtration, washed with water and recrystallized from 95% ethanol. The m. p. was 246.0–246.5°.

Anal. Calcd. for $C_8H_{11}O_5N_3$: N, 18.03. Found: N, 18.39.

(5) Seigle and Hass, *J. Org. Chem.*, **5**, 100 (1940).
(6) Pavlic and Adkins, THIS JOURNAL, **68**, 1471 (1946).
(7) Michael, *J. prakt. Chem.*, [2] **72**, 550 (1905).
(8) Conrad, *Ann.*, **204**, 134 (1880).
(9) Markownikow, *ibid.*, **182**, 332 (1876).

Acknowledgment.—The authors wish to express their gratitude to the Commercial Solvents Corporation, who supplied the 2-chloro-2-nitropropane used in this investigation.

Summary

A series of 1-nitro-1-methylethyl alkyl malonic esters has been prepared by condensing 2-chloro-2-nitropropane with the sodium salt of the appropriate monoalkyl malonic ester.

Catalytic hydrogenation of a representative of the series, 1-nitro-1-methylethyl ethyl malonic ester, resulted in cleavage to ethyl malonic ester.

A typical member of the series, 1-nitro-1-methylethyl methyl malonic ester, has been converted to the corresponding barbituric acid.

HOLLAND, MICHIGAN RECEIVED NOVEMBER 7, 1949

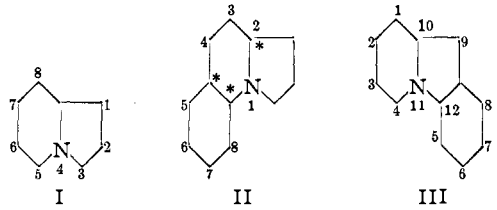
[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Reductive Cyclization of Amino α-Keto Esters. A General Method for the Synthesis of Nitrogen-Heterocyclics Having Fused Five- and Six-Membered Rings

BY NELSON J. LEONARD AND JOSEPH H. BOYER[1]

A new general method has been devised for the synthesis of fully-saturated nitrogen-heterocyclics having fused five- and six-membered rings. The method makes possible especially the facile synthesis of certain polycyclic compounds containing the octahydropyrrocoline moiety (I). The octahydropyrrocoline nucleus (1-azabicyclo-[4.3.0]nonane) is of particular interest since it is common to a number of different alkaloids: a substituted octahydropyrrocoline constitutes the heterocyclic portion of the molecule in the tertiary bases of the *Solanum* and *Veratrum* alkaloid series[2]; 3-hydroxyoctahydropyrrocoline is a likely cyclic form of the alkaloid pelletierine[3]; a methyloctahydropyrrocoline portion has been suggested to be present in certain structural isomers of the lupin alkaloid, sparteine[4]; finally, the octahydropyrrocoline nucleus itself (also called δ-coniceine) has been obtained from the hemlock alkaloid, coniine.[5] Efficient methods for the synthesis of octahydropyrrocoline have not been lacking, but the present method is applicable also to the preparation of compounds of the type in which additional rings are fused through vicinal carbons of I, such as compounds II and VI.

Isomeric with II and VI, a compound with structure III (11-azaperhydrofluorene) was re-



I II III

cently synthesized by Prelog, Frenkiel and Szpilfogel,[6] but by other means. The essential feature of the presently described method is the reductive cyclization of amino α-keto esters, which are available from the condensation of ethyl oxalate with compounds containing a methyl group activated by the imino linkage of a pyridinoid ring. The general method can be illustrated by the particular case of the synthesis of compound II, 1,2-trimethylenedecahydroquino-

(1) Department of Chemistry, University of Michigan, Ann Arbor, Michigan.
(2) Uhle and Jacobs, *J. Biol. Chem.*, **160**, 243 (1945).
(3) Beets, *Rec. trav. chim.*, **62**, 553 (1943).
(4) Winterfeld and Nitzche, *Arch. Pharm.*, **278**, 393 (1940).
(5) Henry, "The Plant Alkaloids," Churchill Ltd., London, England, 4th edition, 1949, p. 20.
(6) Prelog, Frenkiel and Szpilfogel, *Helv. Chim. Acta*, **29**, 484 (1946).