# Alkyl *N*-Methylfuroxanylcarbamates. Synthesis and Structure. II.

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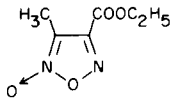
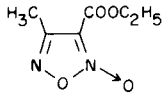
From 3-methyl-4-furoxancarboxylic acid hydrazide and 4-methyl-3-furoxancarboxylic acid hydrazide the corresponding azides have been synthesized. 3-Methyl-4-furoxancarboxylic acid azide normally underwent the Curtius reaction to give the expected carbamic acid derivative. The degradation of 4-methyl-3-furoxancarboxylic acid azide led to the *N*-(4-methylfuroxan-3-yl)-carbamic acid derivative at low temperatures and to *N*-(3-methylfuroxan-4-yl)carbamic acid derivative at higher temperatures.

## Introduction.

The mixture of isomeric esters Ia and Ib obtained heating 3-methyl-4-furoxancarboxylic acid ethyl ester Ia (1), is an excellent intermediate for the synthesis of a variety of variously substituted 3-methyl and 4-methyl-furoxan derivatives.



Ia



Ib

From the hydrazides IIa and IIb, prepared from the above mentioned mixture of esters, the 3-methyl-4-furoxan and 4-methyl-3-furoxancarboxylic acid azides IIIa and IIIb were synthesized. These azides, on Curtius degradation, lead to carbamic acid derivatives, the synthesis, structures and properties of which are described in the present paper.

## Structure Assignments.

The structure assignment criteria are identical with those used in the previous work (1); in this group of compounds, also, the 4-methyl proton resonance positions are almost identical with those of the corresponding furazans. (See Table I).

## Results and Discussion.

Treatment of IIa and IIb with nitrous acid gave the 3-methyl-4-furoxan and 4-methyl-3-furoxan carboxylic acid azides IIIa and IIIb. Unlike the corresponding furazan azide (2), these compounds are crystalline, white solids, stable at room temperature. They are easily hydrolysed by dilute alkali to give the corresponding acids IVa and IVb, identical to those obtained from basic hydrolysis of their amides (1). Curtius degradation of the 3-methyl-4-furoxancarboxylic acid azide in the presence of ethyl, *n*-propyl, isopropyl, isobutyl and benzyl alcohols gave

SCHEME 1

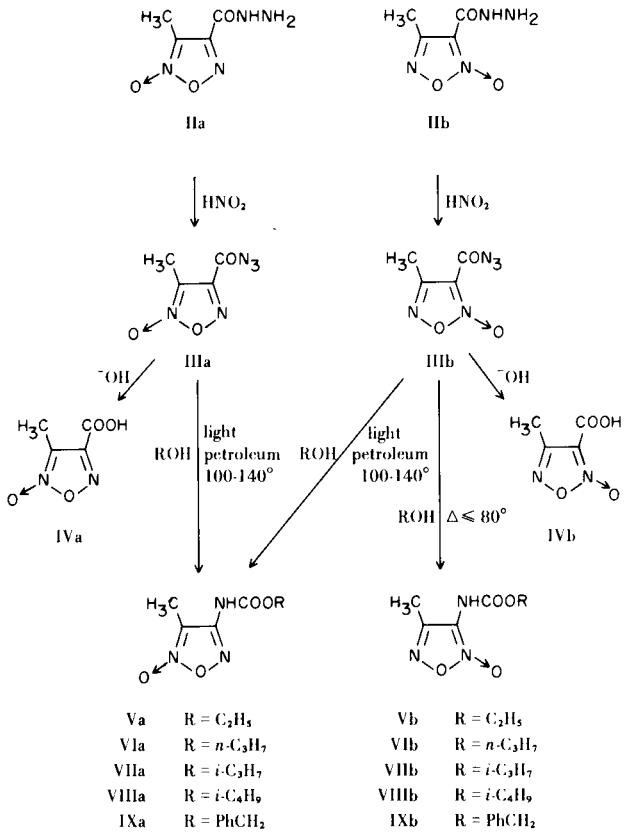
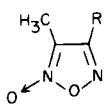
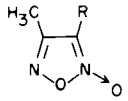


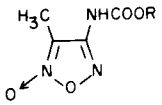
TABLE I

| R |  δ ($CH_3$) | Solvent |  δ ($CH_3$) | Solvent |  δ ($CH_3$) | Solvent |
|---|---|---|---|---|---|---|
| $CON_3$ (a) | 2.39 | $CD_3COCD_3$ | 2.59 | $CD_3COCD_3$ | 2.56 | $CD_3COCD_3$ |
| $NHCOOC_2H_5$ | 2.18 | $CDCl_3$ | 2.45 | $CDCl_3$ (b) | 2.43 | $CDCl_3$ |
| $NHCOOC_3H_7$-*n* | 2.21 | $CDCl_3$ | 2.46 | $CDCl_3$ (b) | 2.43 | $CDCl_3$ |
| $NHCOOC_3H_7$-*i* | 2.21 | $CDCl_3$ | 2.35 | $CDCl_3$ (b) | 2.38 | $CDCl_3$ |
| $NHCOOC_4H_9$-*i* | 2.22 | $CDCl_3$ | 2.40 | $CDCl_3$ (b) | 2.40 | $CDCl_3$ |
| $NHCOOCH_2Ph$ | 2.13 | $CDCl_3$ | 2.30 | $CDCl_3$ (b) | 2.33 | $CDCl_3$ |

(a) The furazan derivative has been prepared in accordance with reference (2). (b) From reference (2).

TABLE II

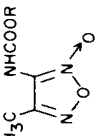
Alkyl *N*-(3-Methylfuroxan-4-yl)carbamates



| Comp. | R | M.P. °C | Formula | Calcd. % C | H | N | Found % C | H | N |
|---|---|---|---|---|---|---|---|---|---|
| Va | $C_2H_5$ | 100-102 | $C_6H_9N_3O_4$ | 38.51 | 4.85 | 22.45 | 38.45 | 4.91 | 22.45 |
| VIa | $C_3H_7$-*n* | 64-66 | $C_7H_{11}N_3O_4$ | 41.79 | 5.51 | 20.89 | 41.91 | 5.54 | 20.95 |
| VIIa | $C_3H_7$-*i* | 110-112 | $C_7H_{11}N_3O_4$ | 41.79 | 5.51 | 20.89 | 41.84 | 5.51 | 20.86 |
| VIIIa | $C_4H_9$-*i* | 84-86 | $C_8H_{13}N_3O_4$ | 44.65 | 6.09 | 19.53 | 44.77 | 6.20 | 19.50 |
| IXa | $CH_2Ph$ | 106-108 | $C_{11}H_{11}N_3O_4$ | 53.01 | 4.45 | 16.86 | 53.33 | 4.46 | 16.90 |

TABLE III

Alkyl *N*-(4-Methylfuroxan-3-yl)carbamates



| Comp. | R | Medium | Time Minutes | Reaction Temp. °C | M.P. °C | Formula | Calcd. % C | Calcd. % H | Calcd. % N | Found % C | Found % H | Found % N |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Vb | $C_2H_5$ | ethanol | 90 | 68-70 | 87-88 | $C_6H_9N_3O_4$ | 38.51 | 4.85 | 22.45 | 38.43 | 5.13 | 22.47 |
| VIb | $C_3H_7$-*n* | *n*-propanol | 90 | 70-73 | 63-65 | $C_7H_{11}N_3O_4$ | 41.79 | 5.51 | 20.89 | 41.74 | 5.52 | 20.86 |
| VIIb | $C_3H_7$-*i* | isopropanol | 40 | 83 | 105-107 | $C_7H_{11}N_3O_4$ | 41.79 | 5.51 | 20.89 | 42.08 | 5.56 | 20.63 |
| VIIIb | $C_4H_9$-*i* | benzene (a) | 30 | 80 | 50-52 | $C_8H_{13}N_3O_4$ | 44.65 | 6.09 | 19.53 | 44.36 | 6.14 | 19.65 |
| IXb | $CH_2Ph$ | benzene (b) | 40 | 80 | 116-118 | $C_{11}H_{11}N_3O_4$ | 53.01 | 4.45 | 16.86 | 52.82 | 4.46 | 17.13 |

(a) With 0.5 ml. of anhydrous isobutyl alcohol. (b) With 0.5 ml. of anhydrous benzyl alcohol.

predominantly compounds Va, VIa, VIIa, VIIIa, and IXa. Under the same conditions, the 4-methyl-3-furoxancarboxylic acid azide led to carbamates whose structures are strongly affected by the temperature of reaction. At higher temperatures the 3-methyl derivatives are mainly formed, while at lower temperatures the 4-methyl derivatives are mainly formed with retention of the original furoxan structure. Accordingly, the carbamates Vb, VIb, VIIb, VIIIb, and IXb, have been prepared. The experimental conditions were chosen so that the various *N*-(4-methylfuroxan-3-yl)carbamates obtained were only slightly contaminated by the corresponding isomers. This required incomplete decomposition of the azide (and therefore yields were lowered), but the purification of the compounds on silica gel was simplified. The general outline of synthesis and relations between the isomeric furoxan carbamates is given in Scheme I.

In each case, the presence of a single isomer was confirmed by nmr spectroscopy (a single peak in the furoxan-$CH_3$ region) and by means of tlc. In addition the Rf of the 4-methylcarbamates was always higher than that of the 3-methylcarbamates. This means that tlc also may be a simple and useful method to distinguish between such compounds when both isomers are available.

## EXPERIMENTAL

Melting points are uncorrected. Mass measurements were carried out on a Varian CH7 MAT mass spectrometer. Ir spectra were recorded in potassium bromide pellets using a Perkin Elmer 257 spectrophotometer. Nmr were recorded on a Varian A-60 spectrometer using TMS as internal standard. The purity of analytical samples was checked by tlc (silica gel).

3-Methyl-4-furoxancarboxylic Acid Azide (IIIa).

Compound IIa (2.0 g.) was added to a solution of 6 *N* hydrochloric acid (2.5 ml.) in water (40 ml.).

To the resulting solution, sodium nitrite (0.86 g.) dissolved in water (6 ml.) was added dropwise with stirring at 0°. The mixture was stirred for another 15 minutes at 0°.

The solid which separated was collected, dried (1.7 g.) and recrystallized from acetone-water to give IIIa, m.p. 94-95° dec.; nmr (deuterioacetone): δ 2.39 (s, $CH_3$-Furox); ir: $cm^{-1}$ 2180 ($N_3$), 1705 (C=O); $M^+$ m/e 169.

*Anal.* Calcd. for $C_4H_3N_5O_3$: C, 28.41; H, 1.78; N, 41.41. Found: C, 28.23; H, 1.84; N, 41.45.

4-Methyl-3-furoxancarboxylic Acid Azide (IIIb).

Compound IIb (2.0 g.) was treated as described above. The solid was collected by filtration, dried (1.7 g.), and recrystallized from acetone-water to give IIIb, m.p. 83-84° dec.; nmr (deuterioacetone): δ 2.56 (s, $CH_3$-Furox); ir: $cm^{-1}$ 2200, 2175 ($N_3$), 1680 (C=O); $M^+$ m/e 169.

*Anal.* Calcd. for $C_4H_3N_5O_3$: C, 28.41; H, 1.78; N, 41.41. Found: C, 28.38; H, 1.86; N, 41.40.

3-Methyl-4-furoxancarboxylic Acid (IVa).

A mixture of IIIa (1.7 g.) and sodium hydroxide (0.85 g.) in water (25 ml.) was shaken vigorously at room temperature until

TABLE IV

Spectrophotometric data

| Comp. | NMR (a) δ (b) | J | IR ν max (C=O) $cm^{-1}$ |
|---|---|---|---|
| Va | 1.31t, 3H, $CH_3CH_2$; 2.18s, 3H, $CH_3$-Furox; 4.23qu, 2H, $CH_3CH_2$; 7.51b, 1H, *NH*. | 7.0 | 1710 |
| Vb | 1.31t, 3H, $CH_3CH_2$; 2.43s, 3H, $CH_3$-Furox; 4.30qu, 2H, $CH_3CH_2$; 7.21b, 1H, *NH*. | 7.0 | 1710 |
| VIa | 0.95t, 3H, $CH_3CH_2$; 1.70sex, 2H, $CH_3CH_2CH_2$; 2.21s, 3H, $CH_3$-furox; 4.17t, 2H, $CH_2CH_2$; 7.95b, 1H, *NH*. | 7.5 | 1720 |
| VIb | 0.96t, 3H, $CH_3CH_2$; 1.73sex, 1H, $CH_3CH_2CH_2$; 2.43s, 3H, $CH_3$-Furox; 4.18t, 2H, $CH_2CH_2$; 7.00b, 1H, *NH*. | 7.0 | 1710 |
| VIIa | 1.28d, 6H, $CH(CH_3)_2$; 2.21s, 3H, $CH_3$-Furox; 5.01sp, 1H, $CH(CH_3)_2$; 7.53b, 1H, *NH*. | 6.5 | 1710 |
| VIIb | 1.28d, 6H, $CH(CH_3)_2$; 2.38s, 3H, $CH_3$-Furox; 4.91sp, 1H, $CH(CH_3)_2$; 6.76b, 1H, *NH*. | 6.5 | 1705 |
| VIIIa | 0.95d, 6H, $CH(CH_3)_2$; 2.00m, 1H, $CH_2CH(CH_3)_2$; 2.22s, 3H, $CH_3$-Furox; 3.98d, 2H, $CH_2CH$; 8.00b, 1H, *NH*. | 7.0 | 1710 |
| VIIIb | 0.95d, 6H, $CH(CH_3)_2$; 1.99m, 1H, $CH_2CH(CH_3)_2$; 2.40s, 3H, $CH_3$-Furox; 3.98d, 2H, $CH_2CH$; 7.03b, 1H, *NH*. | 6.5 | 1705 |
| Xa | 2.13s, 3H, $CH_3$-Furox; 5.20s, 2H, $CH_2Ph$; 7.33s, 5H, *Ph*; 7.76b, 1H, *NH*. | --- | 1720 |
| Xb | 2.33s, 3H, $CH_3$-Furox; 5.13s, 2H, $CH_2Ph$; 7.25s, 5H, *Ph*; 6.78b, 1H, *NH*. | --- | 1710 |

(a) Spectra recorded in deuteriochloroform solution. (b) Abbreviation: a = singlet; d = doublet; t = triplet; qu = quartet; sex = sextet; sp = septet; m = multiplet; b = broad.

the solid had dissolved. The solution was acidified with sulfuric acid 1:1 (2.0ml.), and sodium nitrite (0.69 g.) dissolved in a little amount of water added dropwise to decompose the hydrazoic acid. The solution was extracted several times with ether and the combined ether layers were dried over anhydrous magnesium sulfate and evaporated under vacuum. The solid residue (1.4 g.), recrystallized from benzene and dried *in vacuo*, melted at 92° and was identical (m.p., mixed m.p., ir spectra) with an authentic sample of 3-methyl-4-furoxancarboxylic acid prepared by the literature method (3).

4-Methyl-3-furoxancarboxylic Acid (IVb).

Compound IIIb (1.7 g.) was treated as described above for the preparation of IVa. The solid residue (1.4 g.) obtained from evaporation of the ether phase was recrystallized from water and dried *in vacuo* over phosphorus pentoxide m.p. 87-89°. This compound was identical (m.p., mixed m.p. ir spectra) with an authentic sample of 4-methyl-3-furoxancarboxylic acid prepared by hydrolysis of the corresponding amide (1).

General Method of Preparation of *N*-(3-Methylfuroxan-4-yl)carbamates from 3-Methyl-4-furoxancarboxylic Acid Azide.

Compound IIIa (0.5 g.) was refluxed for 1 hour with anhydrous alcohol (0.5 ml.) in light petroleum 100-140° (30 ml.). After the addition of chloroform, the hot solution was filtered with charcoal and partly evaporated under vacuum, to leave an oil which solidified on cooling. The solid material was collected and recrystallized from chloroform-light petroleum or ether-ligroin. Compound VIa was purified on a silica gel column using chloroform as eluent, (yield 60-80%). M.p.s and analytical data are reported in Table II; spectrophotometric data are reported in Table IV.

General Method of Preparation of Alkyl *N*-(3-Methylfuroxan-4-yl)-carbamates from 4-Methyl-3-furoxancarboxylic Acid Azide.

Compound IIIb (0.5 g.) was treated as described above. The product was identical (m.p., mixed m.p., ir spectra) to the product obtained from 3-methyl-4-furoxancarboxylic acid azide.

General Method of Preparation of Alkyl *N*-(4-Methylfuroxan-3-yl)-carbamates from 4-Methyl-3-furoxancarboxylic Acid Azide.

Compound IIIb (0.5 g.) was treated as reported in Table III. The reaction mixture was evaporated under vacuum at room temperature and the solid residue was purified on a silica gel column using chloroform as eluent. M.p.s and analytical data are reported in Table III; spectrophotometric data are reported in Table IV.

Acknowledgement.

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