

PREPARATION OF O-(METHYL, DIMETHYL AND ARYL-CARBAMOYL)-METHYL 5-NITROPHENYL-2-FURYL KETOXIMES*

A. KRUTOŠÍKOVÁ^a, V. KONEČNÝ^b and J. KOVÁČ^a

^a Department of Organic Chemistry,

Slovak Institute of Technology, 880 37 Bratislava and

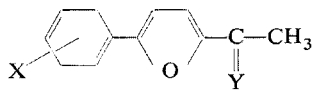
^b Research Institute of Agrochemical Technology, 810 04 Bratislava

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The preparation of methyl 5-nitrophenyl-2-furyl ketoximes is described. On their reaction with methyl and aryl isocyanates O-(methyl or arylcarbamoyl)methyl 5-nitrophenyl-2-furyl ketoximes have been prepared. Reaction of the sodium salt of methyl 5-nitrophenyl-2-furyl ketoximes with dimethylcarbamoyl chloride gave O-dimethylcarbamoyl methyl 5-nitrophenyl-2-furyl ketoximes.

In our preceding paper¹ the preparation of O-(methyl and arylcarbamoyl) 5-nitrophenyl-furaldehydoximes was described, among which some had a very good fungicide activity. We were interested in the investigation of this property in compounds of a similar type, prepared from newly synthesized methyl 5-nitrophenyl-2-furyl ketoximes.

The starting compounds, such as 5-(4-nitrophenyl)-2-acetylfuran (*III*), as well as the newly synthesized 5-(3- and 2-nitrophenyl)-2-acetylfurans (*I*, *II*), were prepared according to literature². Corresponding oximes *IV*–*VI* were prepared on reaction of 5-nitrophenyl-2-acetylfurans with hydroxylamine.



I, X = 2-NO₂, Y = O

II, X = 3-NO₂, Y = O

III, X = 4-NO₂, Y = O

IV, X = 2-NO, Y = N—OH

V, X = 3-NO₂, Y = N—OH

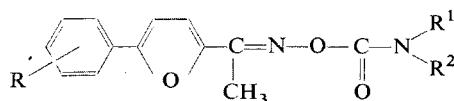
VI, X = 4-NO₂, Y = N—OH

Reaction of methyl 5-nitrophenyl-2-furyl ketoximes with methyl or aryl isocyanates gave O-(methyl and arylcarbamoyl)methyl 5-nitrophenyl-2-furyl ketoximes (Tables I and II). O-Dimethylcarbamoyl methyl 5-nitrophenyl-2-furyl ketoximes (*VIII*, *XXIV*, *XXX*) were prepared by reaction of the sodium salt of methyl 5-nitrophenyl-2-furyl ketoxime with dimethylcarbamoyl chloride.

* Part LVII in the series Furan Derivatives; Part LVI: This Journal 40, 1550 (1975).

When compounds *I* and *II* were prepared the formation of by-products was not observed, similarly as in the case of compound *III*, which is in agreement with literature². During the preparation of *O*-arylcarbamoyl methyl 5-nitrophenyl-2-furyl ketoximes under catalysis with triethylamine we did not observe the formation of the by-products which are mentioned in our preceding paper¹. The reason for this is evidently the impossibility of the formation of the nitrile of 5-nitrophenyl-2-furan-carboxylic acid from *O*-arylcarbamoyl methyl 5-nitrophenyl-2-furyl ketoxime.

In the IR spectra of compounds *I–III* the frequencies of the C=O vibration are in the 1676 cm^{-1} region. The effect of the position of the nitro group on the shift of the $\nu(\text{C}=\text{O})$ band was not observed. The frequencies of the C=O vibrations of *O*-methylcarbamoyl methyl 5-nitrophenyl-2-furyl ketoximes are observed in the 1743 to 1745 cm^{-1} region, in the case of compounds *VIII*, *XXIV* and *XXX* they are in the $1734–1737\text{ cm}^{-1}$ region and in the case of *O*-arylcarbamoyl methyl 5-nitrophenyl-2-furyl ketoximes in the $1752–1770\text{ cm}^{-1}$ region. The effect of the nitro group on the benzene nucleus of the phenylfuran skeleton has no influence on the position of the absorption bands of $\nu(\text{C}=\text{O})$. As is evident from the IR spectral data the position of the $\nu(\text{C}=\text{O})$ bands is affected by the substituent on the nitrogen atom of the carbamoyl group. In the case of *O*-arylcarbamoyl methyl 5-nitrophenyl-2-furyl ketoximes the substituent on the benzene nucleus of the arylcarbamoyl grouping did have an effect, the consequence of which is the broad range of the $\nu(\text{C}=\text{O})$ values, $1752–1770\text{ cm}^{-1}$. The frequencies of the NO_2 vibrations were the following: in the position 4 $\nu(\text{NO}_2)_{\text{as}} 1535$ and $\nu(\text{NO}_2)_{\text{s}} 1345\text{ cm}^{-1}$, in the position 3 the respec-



| | R | R ¹ | R ² | | R | R ¹ | R ² |
|--------------|-------------------|-----------------|---|---------------|-------------------|-----------------|---|
| <i>VII</i> | 2-NO ₂ | H | CH ₃ | <i>XXI</i> | 2-NO ₂ | H | 3-NO ₂ -4-Cl-C ₆ H ₃ |
| <i>VIII</i> | 2-NO ₂ | CH ₃ | CH ₃ | <i>XXII</i> | 2-NO ₂ | H | 2,4,5-Cl ₃ -C ₆ H ₂ |
| <i>IX</i> | 2-NO ₂ | H | C ₆ H ₅ | <i>XXIII</i> | 3-NO ₂ | H | CH ₃ |
| <i>X</i> | 2-NO ₂ | H | 3-CH ₃ -C ₆ H ₄ | <i>XXIV</i> | 3-NO ₂ | CH ₃ | CH ₃ |
| <i>XI</i> | 2-NO ₂ | H | 3-Cl-C ₆ H ₄ | <i>XXV</i> | 3-NO ₂ | H | Ph |
| <i>XII</i> | 2-NO ₂ | H | 3-CF ₃ -C ₆ H ₄ | <i>XXVI</i> | 3-NO ₂ | H | 3-Cl-C ₆ H ₄ |
| <i>XIII</i> | 2-NO ₂ | H | 3-CH ₃ O-C ₆ H ₄ | <i>XXVII</i> | 3-NO ₂ | H | 3,4-Cl ₂ -C ₆ H ₃ |
| <i>XIV</i> | 2-NO ₂ | H | 4-F-C ₆ H ₄ | <i>XXVIII</i> | 3-NO ₂ | H | 3-CF ₃ -4-Cl-C ₆ H ₃ |
| <i>XV</i> | 2-NO ₂ | H | 4-Cl-C ₆ H ₄ | <i>XXIX</i> | 4-NO ₂ | H | CH ₃ |
| <i>XVI</i> | 2-NO ₂ | H | 4-CH ₃ -C ₆ H ₄ | <i>XXX</i> | 4-NO ₂ | CH ₃ | CH ₃ |
| <i>XVII</i> | 2-NO ₂ | H | 4-CH ₃ O-C ₆ H ₄ | <i>XXXI</i> | 4-NO ₂ | H | Ph |
| <i>XVIII</i> | 2-NO ₂ | H | 3-Cl-4-CH ₃ -C ₆ H ₃ | <i>XXXII</i> | 4-NO ₂ | H | 3-Cl-C ₆ H ₄ |
| <i>XIX</i> | 2-NO ₂ | H | 3,4-Cl ₂ -C ₆ H ₃ | <i>XXXIII</i> | 4-NO ₂ | H | 3,4-Cl ₂ -C ₆ H ₃ |
| <i>XX</i> | 2-NO ₂ | H | 3-CF ₃ -4-Cl-C ₆ H ₃ | <i>XXXIV</i> | 4-NO ₂ | H | 3-CF ₃ -4-Cl-C ₆ H ₃ |

tive frequencies were 1564 and 1361, and in the position 2 1542 and 1355 cm^{-1} . According to our expectations the frequencies of the NO_2 -vibrations in 3-substituted derivatives were observed at higher values than in the case of 4-substituted derivatives. The anomalous values for 2-substituted derivatives are due to the non-coplanar arrangement of the 5-(2-nitrophenyl)furan grouping, which we already discussed in preceding papers^{3,4}.

From the UV spectra of compounds VII–XXXIV we determined that the substituent on the nitrogen atom of the carbamoyl group does not affect the λ_{max} position at longest wave-lengths. This value does not practically differ from those of the starting oximes, and it lies in the following regions: for compounds VII–XXII at 306.7 nm ($\log \epsilon \approx 4.4$), for compounds XXIII–XXVIII at 317 nm ($\log \epsilon \approx 4.4$), and for compounds XXIX–XXXIV at 362.3 nm ($\log \epsilon \approx 4.4$). The testing of the pesticide activity has not yet been completed.

TABLE I
Methyl 5-Nitrophenyl-2-furyl Ketones and Their Oximes

| Compound ^a | Composition (m.w.) | Calculated/Found | | | M.p., °C (yield, %) |
|-------------------------|---|------------------|------|-------|------------------------|
| | | % C | % H | % N | |
| <i>I</i> | $\text{C}_{12}\text{H}_9\text{NO}_4$ (231.2) | 62.34 | 3.92 | 6.06 | 108–108 |
| | | 62.28 | 3.90 | 6.02 | (86) |
| <i>II</i> | $\text{C}_{12}\text{H}_9\text{NO}_4$ (231.2) | 62.34 | 3.92 | 6.06 | 118 |
| | | 62.30 | 3.88 | 6.02 | (78) |
| <i>III</i> ^b | $\text{C}_{12}\text{H}_9\text{NO}_4$ (231.2) | 62.34 | 3.92 | 6.06 | 168–169 |
| | | 62.34 | 3.92 | 6.04 | (80) |
| <i>IV</i> | $\text{C}_{12}\text{H}_{10}\text{N}_2\text{O}_4$ (246.2) | 58.53 | 4.09 | 11.38 | 169 |
| | | 58.43 | 4.00 | 11.24 | (82) |
| <i>V</i> | $\text{C}_{12}\text{H}_{10}\text{N}_2\text{O}_4$ (246.2) | 58.53 | 4.09 | 11.38 | 203 |
| | | 58.48 | 4.07 | 11.30 | (86) |
| <i>VI</i> | $\text{C}_{12}\text{H}_{10}\text{N}_2\text{O}_4$ (246.2) | 58.53 | 4.09 | 11.38 | 194–195 |
| | | 58.50 | 4.06 | 11.32 | (85) |

^a Compounds I–VI were crystallized from ethanol; ^b m.p. according to lit.² 164.5–165.5°C (ethyl acetate).

EXPERIMENTAL

5-(4-, 3-, 2-Nitrophenyl)-2-acetylfurans (I–III) were prepared according to the procedure given in paper². Acetylfuran was prepared according to⁵.

TABLE II
O-(Methyl, Dimethyl and Arylcarbamoyl)methyl 5-Nitrophenyl-2-furyl Ketoximes

| Compound | Composition (m.w.) | Calculated/Found | | | M.p., °C (yield, %) |
|----------|---|------------------|------|-------|------------------------|
| | | % C | % H | % N | |
| VII | C ₁₄ H ₁₃ N ₃ O ₅ (303·3) | 55·45 | 4·32 | 13·85 | 98—100 |
| | | 55·65 | 4·38 | 13·63 | (96·3) |
| VIII | C ₁₅ H ₁₅ N ₃ O ₅ (317·3) | 56·78 | 4·76 | 13·24 | 146 |
| | | 56·72 | 4·63 | 13·05 | (70·8) |
| IX | C ₁₉ H ₁₅ N ₃ O ₅ (365·35) | 62·46 | 4·14 | 11·50 | 129—131 |
| | | 62·32 | 4·20 | 11·61 | (74·4) |
| X | C ₂₀ H ₁₇ N ₃ O ₅ (379·4) | 63·32 | 4·52 | 11·08 | 114—117 |
| | | 63·48 | 4·48 | 10·93 | (77·6) |
| XI | C ₁₉ H ₁₄ ClN ₃ O ₅ (399·8) | 57·08 | 3·53 | 10·51 | 135—137 |
| | | 57·22 | 3·48 | 10·63 | (81·7) |
| XII | C ₂₀ H ₁₄ F ₃ N ₃ O ₅ (433·3) | 55·43 | 3·26 | 9·70 | 155—156 |
| | | 55·40 | 3·16 | 9·56 | (75·8) |
| XIII | C ₂₀ H ₁₇ N ₃ O ₆ (395·4) | 60·76 | 4·33 | 10·63 | 45—46 |
| | | 60·58 | 4·30 | 10·42 | (78·2) |
| XIV | C ₁₉ H ₁₄ FN ₃ O ₅ (383·3) | 59·53 | 3·68 | 10·96 | 143—147 |
| | | 59·50 | 3·60 | 10·68 | (99·0) |
| XV | C ₁₉ H ₁₄ ClN ₃ O ₅ (399·8) | 57·08 | 3·53 | 10·51 | 150—151 |
| | | 57·00 | 3·48 | 11·42 | (91·6) |
| XVI | C ₂₀ H ₁₇ N ₃ O ₅ (379·4) | 63·32 | 4·52 | 11·08 | 141 |
| | | 63·30 | 4·48 | 11·01 | (70·2) |
| XVII | C ₂₀ H ₁₇ N ₃ O ₆ (395·4) | 60·76 | 4·33 | 10·63 | 106 |
| | | 60·54 | 4·30 | 10·34 | (66·2) |
| XVIII | C ₂₀ H ₁₆ ClN ₃ O ₅ (413·8) | 58·05 | 3·90 | 10·15 | 128—131 |
| | | 58·26 | 3·96 | 10·20 | (92·0) |
| XIX | C ₁₉ H ₁₃ Cl ₂ N ₃ O ₅ (434·2) | 52·55 | 3·02 | 9·68 | 180—182 |
| | | 52·50 | 2·98 | 9·48 | (96·1) |
| XX | C ₂₀ H ₁₃ ClF ₃ N ₃ O ₅ (467·8) | 51·35 | 2·80 | 8·98 | 134—136 |
| | | 51·30 | 2·72 | 9·17 | (74·3) |
| XXI | C ₁₉ H ₁₃ ClN ₄ O ₇ (444·8) | 51·31 | 2·95 | 12·60 | 159—161 |
| | | 51·38 | 2·85 | 12·78 | (63·5) |
| XXII | C ₁₉ H ₁₂ Cl ₃ N ₃ O ₅ (468·7) | 48·69 | 2·58 | 8·97 | 186—188 |
| | | 48·65 | 2·62 | 9·09 | (96·8) |
| XXIII | C ₁₄ H ₁₃ N ₃ O ₅ (303·3) | 55·45 | 4·32 | 13·85 | 163—165 |
| | | 55·65 | 4·42 | 13·61 | (84·2) |
| XXIV | C ₁₅ H ₁₅ N ₃ O ₄ (317·3) | 56·78 | 4·76 | 13·24 | 140—141 |
| | | 56·86 | 4·80 | 13·02 | (82·2) |

TABLE II
(Continued)

| Compound | Composition (m.w.) | Calculated/Found | | | M.p., °C (yield, %) |
|----------|---|------------------|------|-------|------------------------|
| | | % C | % H | % N | |
| XXV | C ₁₉ H ₁₅ N ₃ O ₅ (365.3) | 62.46 | 4.14 | 11.50 | 156 |
| | | 62.00 | 4.20 | 11.46 | (89.3) |
| XXVI | C ₁₉ H ₁₄ ClN ₃ O ₅ (399.8) | 57.08 | 3.53 | 10.51 | 156—157 |
| | | 57.00 | 3.48 | 10.20 | (98.1) |
| XXVII | C ₁₉ H ₁₃ Cl ₂ N ₃ O ₅ (434.2) | 52.55 | 3.02 | 9.68 | 197—199 |
| | | 52.42 | 3.00 | 9.72 | (94.7) |
| XXVIII | C ₂₀ H ₁₃ ClF ₃ N ₃ O ₅ (467.8) | 51.35 | 2.80 | 8.98 | 168—170 |
| | | 51.38 | 2.64 | 8.78 | (81.2) |
| XXIX | C ₁₄ H ₁₃ N ₃ O ₅ (303.3) | 55.45 | 4.32 | 13.85 | 161 |
| | | 55.48 | 4.40 | 13.99 | (98.0) |
| XXX | C ₁₅ H ₁₅ N ₃ O ₅ (317.3) | 56.78 | 4.76 | 13.24 | 187—191 |
| | | 56.62 | 4.60 | 13.15 | (46.9) |
| XXXI | C ₁₉ H ₁₅ N ₃ O ₅ (365.3) | 62.46 | 4.14 | 11.50 | 193—195 |
| | | 62.58 | 4.12 | 11.37 | (96.8) |
| XXXII | C ₁₉ H ₁₄ ClN ₃ O ₅ (399.8) | 57.08 | 3.53 | 10.51 | 212—214 |
| | | 57.30 | 3.60 | 10.54 | (94.3) |
| XXXIII | C ₁₉ H ₁₃ Cl ₂ N ₃ O ₅ (434.2) | 52.55 | 3.02 | 9.68 | 219—223 |
| | | 52.70 | 3.12 | 9.70 | (94.3) |
| XXXIV | C ₂₀ H ₁₃ ClF ₃ N ₃ O ₅ (467.8) | 51.35 | 2.80 | 8.98 | 217—218 |
| | | 51.14 | 2.68 | 9.15 | (81.3) |

Methyl 5-(4-, 3-, 2-Nitrophenyl)-2-furyl Ketoximes (IV—VI)

A mixture of hydroxylamine hydrochloride (2.1 g, 0.03 mol) and sodium acetate (4.1 g) in water (30 ml) was added to 5-nitrophenyl-2-acetylfuran (6.9 g, 0.03 mol) dissolved in the necessary amount of ethanol and the mixture refluxed for 30 minutes. After concentration of the mixture to a half of its original volume and cooling the precipitate formed was filtered off and crystallized from ethanol.

O-Methylcarbamoyl Methyl 5-Nitrophenyl-2-furyl Ketoximes (VII, XXIII, XXIX)

Methyl isocyanate (1.43 g, 0.025 mol) and triethylamine (0.1 ml) were added to a solution of methyl 5-nitrophenyl-2-furyl ketoxime (6.1 g, 0.025 mol) in benzene (80 ml) and the mixture was stirred at room temperature for 2 hours and refluxed for 3 hours. After cooling the separated product was filtered off and crystallized.

O-Dimethylcarbamoyl Methyl 5-Nitrophenyl-2-furyl Ketoximes (VIII, XXIV, XXX)

Sodium methoxide solution (0.6 g, 0.025 mol of sodium in 20 ml of methanol) was added under stirring to a solution of methyl 5-nitrophenyl-2-furyl ketoxime (6.1 g, 0.025 mol) in benzene (100 ml) and methanol was distilled off as a binary mixture with benzene. 2-Butanone (80 ml) was added to the suspension of the sodium salt of methyl 5-nitrophenyl-2-furyl ketoxime in benzene formed after distillation off of methanol. The mixture was cooled to 10°C and dimethylcarbamoyl chloride (2.7 g, 0.025 mol) was added to it over 15 minutes. The temperature of the reaction mixture rose to 30°C. The stirring was continued for another hour at room temperature and the mixture refluxed for 4 hours. After cooling the mixture was washed 3 times with water, dried over sodium sulfate, benzene was distilled off *in vacuo* and the product purified by crystallization.

O-Arylcarbamoyl Methyl 5-Nitrophenyl-2-furyl Ketoximes (IX—XXII, XXV, XXVIII, XXXI—XXXIV)

The corresponding isocyanate (0.025 mol) and triethylamine (0.1 ml) were added to a solution of methyl 5-nitrophenyl-2-furyl ketoxime (6.1 g, 0.025 mol) in toluene (80 ml) and the mixture stirred at boiling temperature for two hours. After cooling the reaction product separated which was purified by crystallization.

Spectral Measurements

The infrared spectra ($800-3650\text{ cm}^{-1}$) were measured on a two-beam spectrophotometer UR-20 (Zeiss, Jena) in chloroform at a 0.02M concentration. The ultraviolet spectra were recorded with a Specord UV VIS (Zeiss, Jena) spectrophotometer in the 200—480 nm region. The measurements were carried out at room temperature in a 1 cm cell, in spectral dioxan and at $4 \cdot 10^{-5}$ mol/l concentration.

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