

## PREPARATION AND REACTIONS OF METHYL 2-BROMOMETHYL-3-(5-NITRO-2-FURYL)PROPENOATE

Vladimír ŽVAK, Jaroslav KOVÁČ and Miroslav KRÍŽ

*Department of Organic Chemistry,  
Slovak Institute of Technology, 880 37 Bratislava*

Received January 4th, 1981

Methyl 2-bromomethyl-3-(5-nitro-2-furyl)propenoate was prepared by nitration of methyl 2-bromomethyl-3-(2-furyl)propenoate with nitric acid and acetic anhydride at  $-30^{\circ}\text{C}$ . 5-Nitrofuran derivatives of a new type were synthesized by nucleophilic substitutions at bromomethyl group.

Methyl 2-bromomethyl-3-(5-nitro-2-furyl)propenoate is a possible starting material for the synthesis of potentially biologically active preparations having the 5-nitro-furan grouping in a branched olefinic system. 2-Methyl-3-(2-furyl)propenoic acid (*I*) (ref.<sup>1</sup>) and its 5-nitro derivative<sup>2</sup> have already been described. The carboxyl group of the latter was used for synthetic purposes<sup>2,3</sup>. Goal of this paper was to find a suitable method to prepare 2-bromomethyl-3-(5-nitro-2-furyl)propenoic acid or its methyl ester and to study nucleophilic substitutions at the bromomethyl group.

Nitration of *I* with nitric acid-acetic anhydride furnished various products depending on the reaction temperature. Nitration at  $-30^{\circ}\text{C}$  afforded product *III* having the nitro group in position 5 of the furan ring<sup>4</sup>. At  $0^{\circ}\text{C}$  a concurrent decarboxylation occurred under formation of 2-nitro-1-(5-nitro-2-furyl)propene (*V*). Methyl 2-methyl-3-(5-nitro-2-furyl)propenoate (*IV*) was prepared in a high yield providing the temperature during nitration of methyl 2-methyl-3-(2-furyl)propenoate did not exceed  $-30^{\circ}\text{C}$ ; at  $0^{\circ}\text{C}$ , only polymeric substances could be isolated. Bromination of *III* and *IV* with N-bromosuccinimide in tetrachloromethane failed either with chemical initiation with  $\alpha, \alpha'$ -azobis (isobutyronitrile), or with photochemical initiation by a medium-pressure mercury lamp. 2-Bromomethyl-3-(5-nitro-2-furyl)propenoic acid (*VI*) or its methyl ester (*VII*) was obtained by bromination of *I* and *II* followed by nitration<sup>5</sup>. When using nitric acid-acetic anhydride no bases were necessary to decompose the 5-nitro-2-acetoxy-2,5-dihydrofuran adducts<sup>6,7</sup>; satisfactory results were achieved by decomposition with water.

The ester *VII* reacted with amines to give products of nucleophilic displacement at the bromomethyl group *VIII*–*XIV*. Similarly as with reactions of methyl 2-bromomethyl-3-(2-furyl)propenoate with amines no product of anomalous bimolecular mechanism could be isolated; it is characteristic of compounds having reactions of

TABLE I  
Methyl 2-X-methyl-3-(5-nitro-2-furyl)propenoates

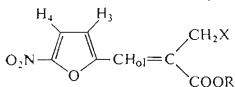
Compound	Formula (mol. weight)	M.p., °C (yield, %)	Calculated/Found			$\lambda_{\max}(\log \epsilon)$
			% C	% H	% N	
<i>VIII</i>	C <sub>14</sub> H <sub>18</sub> N <sub>2</sub> O <sub>5</sub> (294.3)	96 (73)	59.17 58.90	6.16 6.06	9.53 9.78	239 (4.11), 277 (3.83), 352 (4.23)
<i>IX</i>	C <sub>13</sub> H <sub>16</sub> N <sub>2</sub> O <sub>6</sub> (296.3)	92 (81)	52.70 52.65	5.44 5.49	9.45 9.40	239 (4.15), 276 (3.93), 351 (4.27)
<i>X</i>	C <sub>13</sub> H <sub>16</sub> N <sub>2</sub> O <sub>5</sub> (280.3)	54 (85)	55.71 55.62	5.75 5.60	10.00 9.94	240 (4.13), 278 (3.86), 355 (4.22)
<i>XI</i>	C <sub>14</sub> H <sub>19</sub> N <sub>3</sub> O <sub>5</sub> (309.3)	88 (61)	54.36 54.12	6.19 6.05	13.60 13.45	238 (4.05), 278 (3.82), 352 (4.17)
<i>XII</i>	C <sub>19</sub> H <sub>21</sub> N <sub>3</sub> O <sub>5</sub> (371.4)	93 (70)	61.44 60.95	5.69 5.55	11.30 11.28	245 (4.35), 351 (4.21)
<i>XIII</i>	C <sub>16</sub> H <sub>16</sub> N <sub>2</sub> O <sub>5</sub> (316.3)	105 (64)	60.75 60.68	5.09 5.05	8.86 8.86	250 (4.38), 353 (4.22)
<i>XIV</i>	C <sub>15</sub> H <sub>14</sub> N <sub>2</sub> O <sub>5</sub> (302.3)	79 (75)	59.60 58.15	4.66 4.10	9.26 8.90	249 (4.35), 354 (4.23)

TABLE II  
<sup>1</sup>H NMR Spectra of methyl 2-X-methyl-3-(5-nitro-2-furyl)propenoates

Compound	H <sub>olef</sub> <sup>a</sup>	H <sub>3</sub>	H <sub>4</sub>	CH <sub>2</sub>	OCH <sub>3</sub>	Others
<i>VIII</i>	7.53 s	7.03 d	7.37 d	3.65 s	3.87 s	N(CH <sub>2</sub> ) <sub>2</sub> = 2.46 m, (CH <sub>2</sub> ) <sub>3</sub> = 1.47 s
<i>IX</i>	7.55 s	7.01 d	7.38 d	3.63 s	3.86 s	O(CH <sub>2</sub> ) <sub>2</sub> = 3.69 t, N(CH <sub>2</sub> ) <sub>2</sub> = 2.56 t
<i>X</i>	7.51 s	7.04 d	7.39 d	3.70 s	3.84 s	N(CH <sub>2</sub> ) <sub>2</sub> = 2.63 q, (CH <sub>2</sub> ) <sub>2</sub> = 1.77 m
<i>XI</i> <sup>b</sup>	7.53 s	7.00 d	7.39 d	3.59 s	3.84 s	N—CH <sub>3</sub> = 2.03 s, H <sub>A</sub> = 3.15 t, H <sub>B</sub> = 2.69 t
<i>XII</i> <sup>b</sup>	7.52 s	6.98 d	7.31 d	3.64 s	3.84 s	C <sub>6</sub> H <sub>5</sub> = 6.78—7.31 m, H <sub>A</sub> = 3.15 t, H <sub>B</sub> = 2.69 t
<i>XIII</i>	7.46 s	6.78 d	7.28 d	4.52 s	3.77 s	N—CH <sub>3</sub> = 2.56 s, C <sub>6</sub> H <sub>5</sub> = 6.75—7.28 m
<i>XIV</i>	7.47 s	6.80 d	7.30 d	4.50 s	3.77 s	C <sub>6</sub> H <sub>5</sub> = 6.70—7.29 m

<sup>a</sup> Values calculated for  $\delta(\text{H}_{\text{olef}})$ : *E*-isomer 7.56 ppm, *Z*-isomer 6.99 ppm; <sup>b</sup> H<sub>A</sub>, H<sub>B</sub> protons of the piperazine ring.

a keto-allyl grouping<sup>8</sup>. Azido and thiocyanato derivatives *XV* and *XVI* were prepared by reacting *VII* with either sodium azide, or potassium thiocyanate in a water-benzene biphasic system. An attempt to isomerize thermally *XV* and *XVI* at 200°C failed; only starting material could be isolated from the mixture.

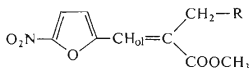


*III*, X = H, R = H

*IV*, X = H, R = CH<sub>3</sub>

*VI*, X = Br, R = H

*VII*, X = Br, R = CH<sub>3</sub>



*VIII*, R =

*X*, R =

*XII*, R =

*XIV*, R = -NH-C<sub>6</sub>H<sub>5</sub>

*XVI*, R = SCN

*IX*, R =

*XI*, R =

*XIII*, R =

*XV*, R = -N<sub>3</sub>

The structure of the synthesized compounds was proved by IR, UV and <sup>1</sup>H NMR spectra. The carboxyl, or the methoxycarbonyl and the furan ring are in an *E*-configuration, as it follows from comparison of the experimentally determined chemical shift of the olefinic proton with those calculated according to Pascual-Matter relationship<sup>9</sup>. Coupling constant <sup>5</sup>J<sub>H<sub>4</sub>,H<sub>olef</sub> = 0.6 Hz indicated the *s-cis* conformation of the double bond and the furan ring. Protons *H*<sub>4</sub> and *H*<sub>olef</sub> are in a *W* arrangement in this conformation, what is advantageous for long-range interactions<sup>10,11</sup>.</sub>

## EXPERIMENTAL

The IR spectra of chloroform solutions were measured with a UR-20 (Zeiss, Jena) spectrophotometer in 0.26 mm-cells at a 10 mmol concentration. The UV spectra of ethanol solutions (0.05 mmol) were recorded with a UV-VIS (Zeiss, Jena) apparatus in 10 mm-cells. The <sup>1</sup>H NMR spectra of deuteriochloroform solutions containing tetramethylsilane as internal reference were taken with a Tesla BS 487 B spectrometer operating at 80 MHz.

### Nitration with Nitric Acid-Acetic Anhydride

A solution of the furan derivative (0.1 mol) in acetic anhydride (0.4 mol) was added into a mixture of acetic anhydride (0.6 mol), fuming nitric acid (0.2 mol) and sulfuric acid (2 ml) at -30°C (compound *V* at 0°C). The mixture was stirred at the given temperature for 1 h, poured on crushed ice (500 ml) and allowed to stand overnight. The crude products were crystallized from *n*-heptane.

*2-Bromomethyl-3-(5-nitro-2-furyl)propenoic acid* (*VI*): m.p. 182°C, yield 51%. UV spectrum λ<sub>max</sub> nm, (log ε), 241 (4.07), 281 (3.83), 359 (4.27); IR spectrum  $\tilde{\nu}$ , cm<sup>-1</sup>: 1 025, 1 277, 1 345, 1 539, 1 630, 1 713; <sup>1</sup>H NMR spectrum δ, ppm: 7.52 (s, H<sub>olef</sub>), 7.36 (d, H<sub>3</sub>), 7.79 (d, H<sub>4</sub>), 4.27 (s, CH<sub>2</sub>), J<sub>3,4</sub> = 3.5 Hz. Calculated values for δ(H)<sub>olef</sub>: *Z*-isomer 7.57 ppm; *E*-isomer 6.97 ppm.

*Methyl 2-bromomethyl-3-(5-nitro-2-furyl)propenoate* (VII): m.p. 99°C, yield 89%. UV spectrum  $\lambda_{\max}$  nm, (log  $\epsilon$ ): 243 (4.07), 281 (3.83), 354 (4.29); IR spectrum  $\tilde{\nu}$ ,  $\text{cm}^{-1}$ : 1 028, 1 285, 1 353, 1 538, 1 635, 1 725.  $^1\text{H}$  NMR spectrum  $\delta$ , ppm: 7.49 (s,  $\text{H}_{\text{olef}}$ ), 7.03 (d,  $\text{H}_3$ ), 7.43 (d,  $\text{H}_4$ ), 4.69 (s,  $\text{CH}_2$ ), 3.94 (s,  $\text{OCH}_3$ ),  $J_{3,4} = 3.9$  Hz. Calculated values for  $\delta(\text{H})_{\text{olef}}$ : Z-isomer 7.60 ppm; E-isomer 7.20 ppm.

*2-Nitro-1-(5-nitro-2-furyl)propene* (V): m.p. 101°C, yield 46%. UV spectrum  $\lambda_{\max}$  nm, (log  $\epsilon$ ): 248 (3.68), 361 (4.14); IR spectrum  $\tilde{\nu}$ ,  $\text{cm}^{-1}$ : 1 354, 1 540, 1 708;  $^1\text{H}$  NMR spectrum  $\delta$ , ppm: 7.8 (s,  $\text{H}_{\text{olef}}$ ), 6.96 (d,  $\text{H}_3$ ), 7.41 (d,  $\text{H}_4$ ), 2.69 (s,  $\text{CH}_3$ ),  $J_{3,4} = 3.4$  Hz.

#### Methyl 2-X-Methyl-3-(5-nitro-2-furyl)propenoates (VIII—XIV)

The respective piperidine, morpholine, pyrrolidine, N-methylpiperazine, N-phenylpiperazine, and aniline (10 mmol) was added to compound VII (5 mmol) dissolved in ether and left to stand at room temperature for 10 h. The separated hydrobromide was filtered off with suction, the ethereal solution evaporated and the residue immediately analyzed by  $^1\text{H}$  NMR spectrometry. The respective products VIII—XIV were recrystallized from heptane-toluene.

#### Substitution in a Biphasic System

Sodium azide (20 ml of a 30% aqueous solution), or potassium thiocyanate (20 ml of a 30% aqueous solution) and tetra-n-butylammonium hydroxide (2 ml of a 10% aqueous solution) were added to VII (5 mmol) dissolved in benzene (15 ml). The mixture was stirred at ambient temperature for 2 h, organic layer was separated and the aqueous one extracted with benzene. The combined benzene solution was evaporated and the product crystallized from n-heptane.

*Methyl 1-azidomethyl-3-(5-nitro-2-furyl)propenoate* (XV): m.p. 72°C, yield 90%. For  $\text{C}_9\text{H}_8\text{N}_4\text{O}_5$  (252.2) calculated: 42.86% C, 3.18% H, 22.22% N; found: 42.70% C, 3.10% H, 22.00% N. UV spectrum  $\lambda_{\max}$  nm, (log  $\epsilon$ ): 240 (4.05), 276 (3.81), 350 (4.23); IR spectrum  $\tilde{\nu}$ ,  $\text{cm}^{-1}$ : 1 718, 1 642, 1 538, 1 353, 1 282, 2 118;  $^1\text{H}$  NMR spectrum  $\delta$ , ppm: 7.59 (s,  $\text{H}_{\text{olef}}$ ), 6.92 (d,  $\text{H}_3$ ), 7.38 (d,  $\text{H}_4$ ), 4.54 (s,  $\text{CH}_2$ ), 3.93 (s,  $\text{OCH}_3$ ),  $J_{3,4} = 3.9$  Hz.

*Methyl 2-thiocyanatomethyl-3-(5-nitro-2-furyl)propenoate* (XVI): m.p. 59°C, yield 82%. For  $\text{C}_{10}\text{H}_8\text{N}_2\text{O}_4\text{S}$  (268.2) calculated: 44.77% C, 3.00% H, 10.44% N; found: 44.35% C, 3.12% H, 10.36% N. UV spectrum  $\lambda_{\max}$  nm, (log  $\epsilon$ ): 242 (4.07), 281 (3.78), 355 (4.18); IR spectrum  $\tilde{\nu}$ ,  $\text{cm}^{-1}$ : 1 725, 1 629, 1 538, 1 352, 1 280, 2 159;  $^1\text{H}$  NMR spectrum  $\delta$ , ppm: 7.59 (s,  $\text{H}_{\text{olef}}$ ), 6.93 (d,  $\text{H}_3$ ), 7.39 (d,  $\text{H}_4$ ), 4.46 (s,  $\text{CH}_2$ ), 3.92 (s,  $\text{OCH}_3$ ),  $J_{3,4} = 3.8$  Hz.

#### REFERENCES

1. Žvak V., Kováč J., Kříž M.: This Journal 45, 906 (1980).
2. Saikachi H., Suzuki K.: Chem. Pharm. Bull. 7, 584 (1959).
3. Kato Y., Hara Y., Hirao I.: Nippon Kagaku Zasshi 86, 957 (1966).
4. Venter K. K., Hiller A. A.: Dokl. Akad. Nauk SSR 137, 8385 (1961).
5. Žvak V., Kováč J.: Czech. 196 929 (1978).
6. Kováč J., Komanová E., Považanec F.: Chem. Zvesti 25, 63 (1971).
7. Lukevich E. J.: *Uspekhi Khimii Furana*, p. 146. Zinatne, Riga 1978.
8. Eagen M. C., Cromwell N. H.: J. Org. Chem. 39, 3863 (1974).
9. Matter N. E., Pascual C., Pretsch E., Simon V., Sternhell S.: Tetrahedron 25, 691 (1969).
10. Arcoria A., Bottino F. A., Sciotto D.: J. Heterocycl. Chem. 14, 1353 (1977).
11. Bottino F. A., Mineri G.: Tetrahedron 25, 2023 (1969).

Translated by Z. Votický.