NUCLEOPHILIC SUBSTITUTION REACTION OF METHYL 2-BROMOMETHYL-3-(2-FURYL)PROPENOATE WITH AMINES

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Nucleophilic replacement of bromine in methyl 2-bromomethyl-3-(2-furyl)propenoate by amines (piperidine, morpholine, N-methylaniline, diethylamine and tert-butylamine) was studied. In all cases only products of direct substitution of bromine were obtained; this shows that a 2-furyl group in γ-position of an allylic system plays a decisive role in the change of mechanism, characteristic for keto allylic mobile systems.

Nucleophilic substitutions with amines in keto allylic mobile systems are characterized by S'_N2 mechanism, in which the C_γ—N bond is formed under simultaneous fission, of the C_α—halogen bond. In the transition state electron delocalisation in the whole system takes place, the carbonyl oxygen accepting a certain amount of the formed negative charge, carried by the departing halide ion. Previous studies on keto allylic mobile systems[1-4] did not investigate the effect of substituents in the γ-position of the allyl system; in all cases this substituent was phenyl or a substituted phenyl group.

In order to study how a furan nucleus in the γ-position of an allylic system affects nucleophilic substitution reaction with amines we prepared methyl 2-bromomethyl-3-(2-furyl)propenoate.

2-Methyl-3-(2-furyl)propenoic acid (*I*) was prepared by Perkin reaction in the presence of small amount of pyridine which suppressed the polymerisation, increasing thus the yield. Extractive esterification of the acid afforded methyl 2-methyl-3-(3-furyl) propenoate (*II*) which was selectively brominated with N-bromosuccinimide using α,α'-azobisisobutyronitrile as catalyst. Since the yield was decreased by the arising molecular bromine, the reaction mixture was irradiated with UV light: this decomposed homolytically the bromine and resulted in practically quantitative yields. According to chromatography, the bromination took place only at the methyl group, affording methyl 2-bromomethyl-3-(2-furyl)propenoate (*III*) as the sole product (Scheme 1).

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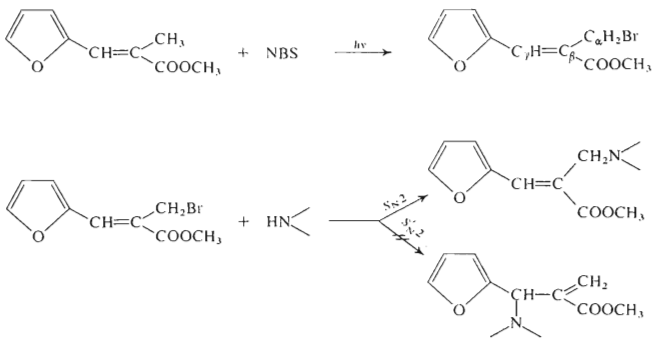


HN : *IV* – piperidine, *V* – morpholine, *VI* – diethylamine, *VII* – N-methylaniline, *VIII* – tert-butylamine

SCHEME 1

Amines, shown[1] to react with methyl 2-bromomethyl-3-phenylpropenoate by the S_N2 and S'_N2 mechanisms (in the case of tert-butylamine only by the S'_N2 mechanism), reacted with the ester *III* under analogous conditions to give solely products of direct substitution of bromine. Such reaction course can be explained by electrostatic repulsion between lone electron pairs of the furan oxygen and the electron pair of nitrogen in the nucleophilic reagent. This interaction hinders the attack of the allylic γ-carbon by the nucleophile suppressing thus formation of anomalous substitution products. On the basis of products and reaction conditions one can assume that methyl 2-bromomethyl-3-(2-furyl)propenoate reacts with amines by a bimolecular mechanism. Contrary to the previous investigations we have shown that also the nature of γ-substituents affects significantly the reaction of keto allylic mobile systems with amines.

Structure of all the prepared compounds was proved by ^{1}H-NMR, UV and IR spectroscopy (Table I and II). Comparison of experimental chemical shifts of H_{o1} with the values, calculated according to the Pascual–Matter relationship[5], shows that in all our compounds the methoxycarbonyl group has *trans*-configuration with respect to the furan nucleus.

EXPERIMENTAL

IR spectra (700—3 800 cm^{-1}) were taken in 10^{-2}M chloroform solutions on double-beam UR-20 spectrophotometer (Zeiss, Jena) in 0·26 mm cells. UV spectra were measured in ethanol ($5 . 10^{-5}$M) on a UV VIS (Zeiss, Jena) instrument in 10 mm cells. ^{1}H-NMR spectra were taken

in deuteriochloroform on an 80 MHz spectrometer BS 4876 (Tesla), internal standard tetramethylsilane.

2-Methyl-3-(2-furyl)propenoic Acid (*I*)

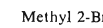
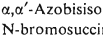
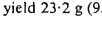
A mixture of 2-furaldehyde (192·g; 2 mol), propionic anhydride (393 g; 3 mol) and potassium propionate (253 g; 2·5 mol) was heated to 110°C. After the exothermic reaction had ceased, the mixture was heated to 120°C for 2 h and to 140°C for 6 h, poured into water (3 l) and allowed to stand overnight. The separated *I* was crystallized from acetic acid–water (1 : 2), m.p. 107°C; yield 205 g (67%).

Methyl 2-Bromomethyl-3-(2-furyl)propenoate (*III*)

α,α′-Azobisisobutyronitrile (200 mg) was added to a boiling mixture of *II* (17·6 g; 0·1 mol), N-bromosuccinimide (17·9 g; 0·1 mol) and tetrachloromethane (250 ml) and the mixture was irradiated with UV light. After the reaction had ended, the succinimide was filtered, the filtrate evaporated *in vacuo* and the crude product crystallized from light petroleum, m.p. 50·5—52°C; yield 23·2 g (95%).

TABLE I

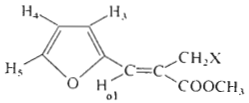
Ultraviolet (nm) and Infrared (cm^{-1}) Spectra of 2-Substituted Methyl 3-(2-Furyl)propenoates

Compound	λ_{max}, nm log ε	ν(C=O)	ν(C=C)	ν(C—O)	Furan[a]
III —Br	304 4·28	1 716	1 634	1 295	1 022
IV 	299 4·35	1 703	1 635	1 291	1 019
V 	308 4·34	1 708	1 631	1 270	1 023
VI —$N(C_2H_5)_2$	303 4·40	1 714	1 634	1 281	1 022
VII 	300 4·24 252 4·42	1 716	1 635	1 275	1 021
VIII —N—$C(CH_3)_3$	305 4·20	1 715	1 635	1 280	1 021

[a] Skeletal vibrations of the furan ring.

TABLE II

^{1}H-NMR Data (δ, ppm) of 2-Substituted Methyl 3-(2-Furyl)propenoates



Compound	H_3	H_4	H_5	$COOCH_3$	CH_2	H_{o1}[a]
III	6·84 d	6·55 q	7·65 d	3·85 s	4·71 s	7·49 s
IV	6·82 d	6·39 q	7·48 d	3·75 s	3·49 s	7·55 s
V	6·78 d	6·47 q	7·53 d	3·77 s	3·58 s	7·54 s
VI	6·73 d	6·41 d	7·45 d	3·72 s	3·57 s	7·35 s
VII	6·61 d	6·41 q	7·46 d	3·68 s	4·50 s	7·51 s
VIII	6·95 d	6·47 q	7·52 d	3·76 s	3·80 s	7·43 s

[a] Calculated values for $\delta_{C=C-Ho1}$: compound *III*: *E*-isomer 7·20, *Z*-isomer 7·60; compounds *IV*—*VIII*: *E*-isomer 7·56, *Z*-isomer 6·99.

Methyl 2-X-Methyl-3-(2-furyl)propenoates

Piperidine, morpholine, N-methylaniline, diethylamine or tert-butylamine (0·2 mol) was added to methyl 2-bromomethyl-3-(2-furyl)propenoate (0·1 mol) in pentane (75 ml). After standing at room temperature for 10 h, the precipitated amine hydrobromide was filtered. The filtrate was taken down *in vacuo* and the residue immediately analysed by ^{1}H-NMR spectroscopy. The products were crystallized from light petroleum: *IV* (86·5%), m.p. 34—36°C; *V* (80%), m.p. 48·5—50°C; *VI* (71·5%), oil; *VII* (70%), m.p. 37·5—39°C; *VIII* (82%), oil.

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