Chemistry

K. K. VENTER, Academician of the Academy of Sciences of the Latvian SSR, S. A. GILLER, V. F. KUCHEROV,

1961

SovietRxiv

Abstract

Full Text

Chemistry

K. K. VENTER, Academician of the Academy of Sciences of the Latvian SSR, S. A. GILLER, V. F. KUCHEROV, V. V. TSIRULE, and A. M. KARKLINYA

SYNTHESES IN THE FIELD OF 5-NITROFURYL-2-POLYALKENALS

AND 5-NITROFURYL-2-POLYALKENONES

THE REACTION OF CARBETHOXYMETHYLENETRIPHENYLPHOSPHORANE

AND ACETYLMETHYLENETRIPHENYLPHOSPHORANE WITH α,β-UNSATURATED

AND POLYENE ALDEHYDES OF THE 5-NITROFURAN SERIES

In previous communications ([1–3]), routes of synthesis and the properties of unsaturated aldehydes and ketones of the general structure I were shown ($n = 1$; $R' = H$, alkyl, isoalkyl, alkoxymethyl; $R'' = H$, CH_3, $C(CH_3)_3$)

$$O_2N\text{-}\underset{O}{\text{furyl}}\text{-}(CH = CR')_n\text{-}C(= O)\text{-}R'' \qquad (I)$$

Ketones of type I with $n > 1$ have hitherto been unknown. Polyene carboxylic acids containing the 5-nitrofuran group are also unknown.

Meanwhile, S. S. Novikov and G. A. Shvekhgeimer ([4,5]) have recently obtained polyene nitroketones and nitrocarboxylic acids of the aromatic series, using for this purpose the well-known Wittig reaction ([6]), which, owing to its universality, simplicity of execution, and unambiguous course, is of great interest for the synthesis of polyene carboxylic acids (IIa) and polyene ketones (IIb) of the nitrofuran series; these compounds, as well as the non-nitrated (IIIa) and nitrated (IIIb) aldehydes serving as starting materials for their synthesis, are, as is known, very sensitive to acidic and alkaline agents, and therefore the preparation of II, $n > 1$, by use of other reactions (Perkin condensation, Claisen condensation, nitration, etc.) has until now proved impossible.

$$O_2N\text{-}\underset{O}{\text{furyl}}\text{-}(CH = CH)_n\text{-}C(= O)\text{-}R \qquad (II)$$

$$R\text{-}\underset{O}{\text{furyl}}\text{-}(CH = CH)_n\text{-}CHO \qquad (III)$$

$n = 1,\ 2,\ 3,\ 4$	$n = 0,\ 1,\ 2,\ 3$
IIa ($R = CH_3$)	IIIa ($R = H$)
IIb ($R = OH,\ OC_2H_5$)	IIIb ($R = NO_2$).

Thus, for example, our attempt to use the nitration method for the synthesis of 5-(5′-nitrofuryl-2′)-pentadiene-2,4-carboxylic acid by carrying out the reaction under the optimum nitration conditions for α,β-unsaturated furan aldehydes and ketones (temperature −25°, catalyst—sulfuric acid) ([2,3]) was unsuccessful, despite the fact that under the stated parameters the yield of β-(5-nitrofuryl-2)-acrylic acid, obtained by nitration of β-(furyl-2)-acrylic acid, reaches 75%.

On the other hand, by the interaction of unsaturated aldehydes of the 5-nitrofuran series (IIIb, $n = 0, 1, 2, 3$) with acetylmethylenetriphenylphosphorane (IV) and

Table 1

Esters of 5-nitrofurylpolyene carboxylic acids and 5-nitrofurylpolyenketones obtained by the Wittig reaction

Structural formula R = O_2N— ⟨furan ring⟩	Yield, %	M.p., °C	Solvent for recrystallization	Empirical formula	C, % calc.	C, % found	H, % calc.	H, % found	N, % calc.	N, % found	Ultraviolet absorption spectra (in ethanol)** λ_{max} ($\varepsilon \cdot 10^{-3}$)	Source
R — $CH{=}CH{-}CH{=}CH{-}COOH$ (VI)	77	214	Alcohol	$C_{11}H_9NO_4$	60.27	–	4.14	–	6.39	–	242 (2) (10.06), 345 (16.80)	
R — $CH{=}CH{-}C(CH_3){=}CH{-}COOH$ (VII)	74	240 (decomp.)	Alcohol	$C_{10}H_9NO_4$	57.97	–	4.38	–	6.76	–		
R — $(CH_3{-}CH{=})_2{-}CO$ (VIII)	36	136	Alcohol	$C_{10}H_9NO_4$	57.97	58.06	4.38	4.40	6.76	7.00	217 (2) (6.03), 274 (18.95), 380 (33.75)	

Structural formula R = O_2N–⟨furan ring	Yield, %	M.p., °C	Solvent for recrystallization	Empirical formula	Cl, % calc.	Cl, % found	H, % calc.	H, % found	N, % calc.	N, % found	Ultraviolet absorption spectra (in ethanol)** λ_{max} ($\varepsilon \cdot 10^{-3}$)	Source
R – (CH_3–CH_2)– (IX)	22	225 (decomp.)	Mixture of dimethylformamide and alcohol	$C_9H_{11}N_2O_4Cl$	–	–	–	–	21.20	21.13		
R – (CH_3–CH_2)– (X)	38	232–233	Acetic acid	$C_{12}H_{11}NO_4$	61.87	4.75	4.70	6.01	6.32		232 (8.08), 306 (22.88), 405 (38.25)	
R – (CH_3–CH_2)– (XI)	32	225 (decomp.)	Mixture of dimethylformamide and alcohol	$C_9H_{13}N_2O_4Cl$	–	–	–	–	18.61	18.77		
R – (CH_3–CH_2)– (XII)	60	232–233	Acetic acid	$C_{14}H_{13}NO_4$	65.28	5.05	4.38	5.40	5.39		217 (8.75), 247 (11.55), 331 (36.75), 422 (79.00)	

Structural formula R = O_2N— ⟨ furan ring	Yield, %	M.p., °C	Solvent for recrystallization	Empirical formula	Cl, % calc.	Cl, % found	H, % calc.	H, % found	N, % calc.	N, % found	Ultraviolet absorption spectra (in ethanol)** λ_{max} ($\varepsilon \cdot 10^{-3}$)	Source
R — (CH=CH)$_2$— C(=NNHCONH$_2$)— (XIII)	70	227 (decomp.)	Mixture of dimethylformamide and alcohol	$C_6H_5ClN_4O$	—	—	—	—	17.65	17.90		
R — CH=CH—COOC$_2$H$_5$ (XIV)	66	123	Alcohol	$C_9H_9NO_5$	—	—	—	—	—	—	237 (7) (12.95), 277 (6.73), 342 (18.76)	
R — CH=CH—COOH (XV)	74	236 (decomp.)	Acetic acid	$C_7H_5NO_5$	—	—	—	—	—	—		(7)
R — (CH=CH)$_2$— COOC$_2$H$_5$ (XVI)	75	122—123	Alcohol	$C_{11}H_9NO_5$	56.03	4.67	4.64	5.91	5.88		267 (15.43), 375 (23.63)	
R — (CH=CH)$_2$— COOH (XVII)	63	216—218 (decomp.)	Dioxane	$C_9H_7NO_5$	51.87	3.37	3.47	6.70	6.71		—	
R — (CH=CH)$_3$— COOC$_2$H$_5$ (XVIII)	79	137—138.5	Alcohol	$C_{13}H_{11}NO_5$	59.40	4.98	4.92	5.32	5.40		227 (8.63), 300 (24.00), 390 (34.50)	

Structural formula $R = O_2N-\langle$ furan ring	Yield, %	M.p., °C	Solvent for recrystallization	Empirical formula	Cl, % calc.	C, % found	H, % calc.	H, % found	N, % calc.	N, % found	Ultraviolet absorption spectra (in ethanol)** λ_{max} ($\varepsilon \cdot 10^{-3}$)	Source
$R-(CH=CH)_4-COOC_2H_5$ (XIX)	66	157	—	$C_{15}H_{15}NO_5$	—	62.46	5.23	5.32	4.84	4.98	244 (7.45), 324 (3.05), 415 (36.25)	

* Obtained by acid hydrolysis of the esters.

** We express our gratitude to M. B. Tytlyano for recording the ultraviolet absorption spectra.

with carbethoxymethylenetriphenylphosphorane (V), we were able, without affecting the double bonds, to synthesize very readily and in good yields 5-nitrofurylpolyenones and esters of 5-nitrofurylpolyenecarboxylic acids (VI–XIX), containing up to four vinylidene groups in the side chain. The properties of these compounds are given in Table 1.

$$O_2N\text{-furyl(O)-}(CH{=}CH)_n\text{-CHO} + (C_6H_5)_3P{=}CHX \longrightarrow O_2N\text{-furyl(O)-}(CH{=}CH)_{n+1}\text{-X} + (C_6H_5)_3PO$$

(IIIb) $(n = 0, 1, 2, 3)$ (IV) $X = COCH_3$ (IIa) $X = COCH_3$

(V) $X = COOC_2H_5$ (IIb) $(X = COOC_2H_5)$

By acid hydrolysis of the esters of β-(5-nitrofuryl-2)-acrylic (XIV) and 5-(5′-nitrofuryl-2′)-pentadiene-2,4-carboxylic (XVI) acids, the corresponding acids (XV and XVII) were obtained. It has not yet been possible to hydrolyze the esters of the higher 5-nitrofurylpolyenecarboxylic acids XVIII and XIX in the same way, which indicates the considerable sensitivity of these compounds to various chemical effects.

Compounds VI–XIII are of interest as highly active antimicrobial preparations, and compounds XIV–XIX as potential anthelmintics. Information on the physiological and pharmacological properties of these compounds will be presented in a separate communication.

Experimental Part

Conditions for carrying out the Wittig reaction. To a solution of 0.01 mole of acetylmethylenetriphenylphosphorane (IV) or, respectively, carbethoxymethylenetriphenylphosphorane (V) in 20 ml of anhydrous methylene chloride, a solution of 0.01 mole of a 5-nitrofuran aldehyde IIIb ($n = 0, 1, 2, 3$) in anhydrous methylene chloride (20–60 ml) was added over 10 min with stirring in a nitrogen atmosphere. The mixture was heated under reflux for 5 hr, cooled to room temperature, purified by passage through a column filled with 7 g of activated alumina moistened with 5% water, and, after removal of the solvent, the resulting mixture of the 5-nitrofuran derivative IIa or IIb and triphenylphosphine oxide was recrystallized from alcohol. The yields and properties of the substances synthesized in this way are shown in Table 1.

Acid hydrolysis of the esters. 0.01 mole of the ethyl ester of a 5-nitrofurylpolyenecarboxylic acid IIb was added to a mixture of 8 ml of 98% acetic acid and 0.3 ml of conc. sulfuric acid and heated on a water bath under reflux with stirring for 6 hr. After completion of the reaction, the mixture was cooled to room temperature, filtered, washed with water, and dried first in air and then in a vacuum desiccator over phosphorus pentoxide.

Institute of Organic Synthesis
Academy of Sciences of the Latvian SSR

Received
20 VI 1961

References Cited

1. S. A. Giller, K. K. Venter, *Izv. AN LatvSSR*, No. 12, 115 (1958).
2. K. K. Venter, S. A. Giller, N. O. Saldabol, *Izv. AN LatvSSR*, No. 8, 99 (1959).
3. K. K. Venter, S. A. Giller, *DAN*, **137**, 83 (1961).
4. S. S. Novikov, G. A. Shvekhgeimer, *Izv. AN SSSR, OKhN*, **1960**, 673.
5. S. S. Novikov, G. A. Shvekhgeimer, *Izv. AN SSSR, OKhN*, **1960**, 2061.
6. U. Schöllkopf, *Angew. Chem.*, **71**, 260 (1959).
7. H. Gilman, G. F. Wright, *J. Am. Chem. Soc.*, **52**, 2550 (1930).

Note: Figure translations are in progress. See original paper for figures.