SYNTHESES AND REACTIONS OF ALKYLACETYLENIC ALCOHOLS AND KETONES OF THE THIOPHENE SERIES

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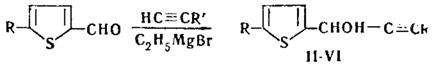
UDC 547.362'732.772:543.422.4

The reaction of thiophene-2-carbaldehyde and 5-ethylthiophene-2-carbaldehyde with alkylethynylmagnesium halides has given thienyl acetylenic alcohols, and these have been oxidized to the corresponding ketones. The reactions of the latter with hydrazine and their hydrogenation have been studied.

We have previously studied the reaction of thiophene-2-carbaldehyde and its 5-nitro and 5-bromo derivatives with phenylethynylmagnesium bromide [1]. The phenylethynylthienyl alcohols obtained proved to be extremely unstable compounds and, without preparative isolation, were oxidized by manganese dioxide to the corresponding ketones.

It appeared of interest to obtain and study the properties of alkyl-substituted thienyl acetylenic alcohols and ketones. Attempts to carry out the reaction of thiophene-2-carbaldehyde (I) with alkylacetylenes using sodium in liquid ammonia were unsuccessful. It is likely that in an alkaline medium the thienylacetylenic alcohols formed during the reaction isomerize into thienyl vinyl ketones, which readily polymerize under the action of sodium amide. The IR spectra of the amorphous polymers obtained have a strong carbonyl absorption band in the 1720 cm^{-1} region and lack absorption bands for C = C and C ≡ C bonds.

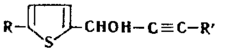
Alkyl-substituted thienylacetylenyl alcohols were obtained in good yields (40-70%) by the Iotsich reaction using tetrahydrofuran as solvent:



II-VI

$R = H, C_2H_5;\ R' = CH_3, C_3H_7, C_4H_9, C_5H_{11}$

TABLE 1.



Compound	R	R'	bp, °C (mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calc.	Empirical formula	Found, % C	Found, % H	Found, % S	Calc., % C	Calc., % H	Calc., % S	Yield, %
II	H	CH_3	107—108	1,5710	1,1723	42,41	42,49	C_8H_8OS	61,95	5,13	21,22	63,15	5,26	21,05	70
III	C_2H_5	CH_3	117—119	1,5554	1,0957	51,73	52,02	$C_{10}H_{12}OS$	67,05	6,45	17,80	66,67	6,66	17,77	42
IV	H	C_3H_7	124—125	1,5507	1,0930	52,03	52,46	$C_{10}H_{12}OS$	66,68	6,70	17,74	66,67	6,66	17,77	42
V	H	C_4H_9	129—130	1,5424	1,0625	56,65	57,45	$C_{11}H_{14}OS$	68,11	7,75	16,45	68,04	7,78	16,51	63
VI	H	C_5H_{11}	145—146	1,5505	1,0650	62,22	61,97	$C_{12}H_{16}OS$	70,08	7,72	15,14	69,23	7,69	15,36	30

Institute of Organic Chemistry, Siberian Division, Academy of Sciences of the USSR, Irkutsk. Translated from Khimiya Geterotsiklicheskikh Soedinenii, Vol. 6, No. 7, pp. 894-897, July, 1970. Original article submitted January 3, 1969.

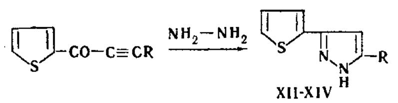
TABLE 2. Thienyl Ethynyl Ketones 

Compound	R	R′	bp, °C (mm)	n_D^{20}	d_4^{20}	Found, % C	Found, % H	Found, % S	Calc., % C	Calc., % H	Calc., % S	Empirical formula	2,4-Dinitrophenylhydrazone* mp, °C	N, % found	N, % calc.	Yield, %
VII	H	CH_3	110—111 (1)	1,6010	1,1573	64,12	4,11	21,05	64,00	4,00	21,33	C_8H_6OS	250—251	17,13	16,98	78
VIII	C_2H_5	CH_3	155—157 (5) mp 37—39.	—	—	67,50	5,58	18,20	67,41	5,61	17,97	$C_{10}H_{10}OS$	152—153	16,23	15,66	75
IX	H	C_3H_7	121—122 (1)	1,5733	1,0918	67,35	5,62	18,37	67,41	5,61	17,97	$C_{10}H_{10}OS$	204—206	15,96	15,66	60
X	H	C_4H_9	136—137 (1)	1,5641	1,0694	69,02	6,20	17,00	68,75	6,25	16,69	$C_{11}H_{12}OS$	151—152	15,12	15,05	67
XI	H	C_5H_{11}	152—153 (1)	1,5569	1,0566	69,55	6,89	15,75	69,88	6,84	15,34	$C_{12}H_{14}OS$	129—131	14,58	14,50	80

*The 2,4-DNPHs were crystallized from ethanol.

The alcohols obtained consist of viscous light green liquids darkening on storage in the air. The constants of II-VI are given in Table 1. When II-VI were oxidized with active manganese dioxide in ether for 6 h, good yields (60-80%) of the corresponding thienyl acetylenic ketones VII-IX were obtained; their constants are given in Table 2. The exaltation of the molecular refraction of the ketones obtained is 3.0-3.3 units.

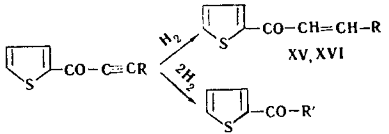
The alkyl-substituted ethynyl thienyl ketones readily react with hydrazine in aqueous ethanol, undergoing intramolecular cyclization with the formation of the corresponding pyrazoles:



XII-XIV

XII R=CH_3 XIII R=C_4H_9 XIV R=C_5H_{11}

To prove their structure, the ethynyl thienyl ketones were hydrogenated selectively over a Pd/$BaCO_3$ catalyst to thienyl vinyl ketones. Exhaustive hydrogenation gave the saturated thienyl ketones.



XV, XVI

XVII-XIX

XV R=CH_3 XVI R=C_4H_9 XVII R′=C_3H_7

XVIII R′=C_6H_{13} XIX R′=C_7H_{15}

The IR spectra of compounds II-VI have a broad absorption band of an associated hydroxy group in the 3390-3420 cm^{-1} region. In the IR spectra of the ethynyl thienyl ketones VII-XI there is a strong absorption band at 1645 cm^{-1}. The lowering of the carbonyl frequency indicates that the carbonyl group in the ethynyl thienyl ketones is conjugated with the π-electronic system of the heterocycle, on the one hand, and with the acetylenic bond, on the other hand. The stretching vibrations of the C ≡ C bond in compounds II-XI give a narrow absorption band in the usual region of the spectrum – 2220-2230 cm^{-1}. The frequencies of the vibrations of the thiophene nucleus are found within the following ranges: 690, 885-840, 1055-1043, and 3112-3090 cm^{-1}.

The 5-alkyl-3-(2′-thienyl)pyrazoles XII-XIV exhibit strong absorption consisting of a series of bands in the 1420-1580 cm^{-1} region. These can be ascribed to the vibrations of the C = C and C = N bonds of the pyrazole ring.

EXPERIMENTAL

1-(2′-Thienyl)but-2-yn-1-ol (II). With vigorous stirring, methylacetylene was passed for 5 h through a solution of the Grignard reagent from 1.6 g of magnesium and 7.4 g of ethyl bromide in 50 ml of tetrahydrofuran at −20°C. Then a solution of 5 g (0.045 mole) of thiophene-2-carbaldehyde in 20 ml of dry tetrahydrofuran was slowly added with the continued passage of methylacetylene. The mixture was stirred for 1 h and was left overnight. The complex obtained was decomposed with saturated ammonium chloride solution, the organic layer was separated off, and the aqueous layer was extracted with ether. The organic layer and the ethereal extracts were treated with 5% acetic acid and with water and were dried with potassium carbonate. The ether was evaporated off and the residue was distilled in vacuum giving 4.8 g (70%) of II. 1-(5'-Ethyl-2'-thienyl)but-2-yn-1-ol (III) was obtained similarly.

1-(2'-Thienyl)hex-2-yn-1-ol (IV). With cooling (0°C), a solution of 4.08 g (0.05 mole) of propylacetylene in 15 ml of dry tetrahydrofuran was added to the Grignard reagent prepared from 1.44 g (0.06 g-atom) of magnesium and 7 g (0.065 mole) of ethyl bromide in 75 ml of dry tetrahydrofuran. The mixture was heated in the water bath for 3 h and cooled to 0°C, and a solution of 5.6 g (0.05 mole) of thiophene-2-carbaldehyde in 15 ml of dry tetrahydrofuran was slowly added. The resulting mixture was stirred for 1 h and left overnight. The reaction product was worked up in a similar manner to II. This gave 3.51 (42%) of IV. 1-(2'-Thienyl)hept-2-yn-1-ol (V) and 1- (2'-thienyl)oct-2-yn-1-ol (VI) were obtained similarly.

1-(2'-Thienyl)but-2-yn-1-one (VII). With vigorous stirring, 10.6 g of active manganese dioxide was added to a solution of 1.52 g (0.01 mole) of II in 40 ml of ether. The mixture was stirred at room temperature for 6 h. Then the precipitate was filtered off and washed repeatedly with ether. The ethereal solution was dried with magnesium sulfate and evaporated, and the residue was distilled in vacuum. This gave 1.16 g (77.5%) of VII. 1-(5'-Ethyl-2'-thienyl)but-2-yn-1-one (VIII), 1-(2'-thienyl)hex-2-yn-1-one (IX), 1-(2'-thienyl)hept-2-yn-1-one (X), and 1-(2'-thienyl)oct-2-yn-1-one (XI) were obtained similarly.

5-Methyl-3-(2'-thienyl)pyrazole (XII). A mixture of 0.35 g (2.3 mmoles) of VII and 0.3 g (2.3 mmoles) of hydrazine sulfate in 20 ml of ethanol was heated to the boiling point of the solvent, and then a small amount of water was added to render it homogeneous. To this boiling solution was added in drops a saturated solution of 0.32 g (2.3 mmoles) of potassium carbonate, and the mixture was heated in the water bath for 3 h, cooled, and treated with 30 ml of water. The precipitate that deposited was filtered off and was washed on the glass filter with water, cold ethanol, and ether. Then it was recrystallized from ethanol, giving 0.34 g (90%) of XII. mp 137-138°C. Found %: N 17.27. $C_8H_8N_2S$. Calculated %: N 17.07.

5-Butyl-3-(2'-thienyl)pyrazole (XIII). This was obtained in a similar manner to XII from 1 g (5.2 mmoles) of X and 0.68 g (5.2 mmoles) of hydrazine sulfate. Yield 0.89 g (85%). bp 180-182°C (1 mm); mp 64-65°C (from ethanol). Found %: N 13.61. $C_{11}H_{14}N_2S$. Calculated %: N 13.58.

5-Pentyl-3-(2'-thienyl)pyrazole (XIV). This was obtained in a similar manner to XII from 1.5 g (7.6 mmoles) of XI and 0.99 g (7.6 mmoles) of hydrazine sulfate. Yield 1.39 g (87%). bp 193-195°C (1 mm); mp 65-66°C (from ethanol). Found %: N 12.81. $C_{12}H_{16}N_2S$. Calculated %: N 12.72.

1-(2'-Thienyl)but-2-en-1-one (XV). A vessel for catalytic hydrogenation was charged with 1.5 g (0.01 mole) of VII, 30 ml of methanol, and 1.2 g of $Pd/BaCO_3$ catalyst (5% of Pd), and hydrogen was passed in with shaking. After the absorption of 258 ml of hydrogen, the hydrogenation was stopped, the catalyst was filtered off, the solvent was evaporated off, and the residue was distilled in vacuum, giving 1.21 g (80%) of XV. bp 102-103°C (3 mm); n_D^{20} 1.5900. Found %: C 63.61; H 5.35; S 21.10. C_8H_8OS. Calculated %: C 63.15; H 5.30; S 21.05.

The selective hydrogenation of X similarly gave 1-(2'-thienyl)hept-2-en-1-one (XVI). bp 125-127°C (1 mm), n_D^{20} 1.5387. Found %: C 67.98; H 7.30; S 16.46. $C_{11}H_{14}OS$. Calculated %: C 68.02; H 7.27; S 16.49.

1-(2'-Thienyl)butan-1-one (XVII). This was obtained by the exhaustive hydrogenation of 1 g (7 mmoles) of VII, as for the preparation of XV. The yield of XVII was 0.87 g (87%). bp 92°C (3 mm), n_D^{20} 1.5449. Literature data [2]; bp 91-92°C (3 mm), n_D^{20} 1.5413.

1-(2'-Thienyl)heptan-1-one (XVIII). This was obtained in a similar manner to XVII from 1.64 g (8 mmoles) of X in the presence of 0.8 g of $Pd/BaCO_3$ catalyst (5% of Pd). The yield of XVIII was 1.2 g (70%). bp 120°C (1 mm); n_D^{20} 1.5240. Found %: C 67.30; H 8.18; S 15.28. $C_{11}H_{16}OS$. Calculated %: C 67.32; H 8.15; S 15.23.

1-(2'-Thienyl)octan-1-one (XIX). This was obtained in a similar manner to XVII from 1 g (4.8 mmoles) of XI in the presence of 0.8 g of $Pd/BaCO_3$ catalyst (5% of Pd). The yield of XIX was 0.65 g (68%). bp 125-126°C (1 mm); n_D^{20} 1.5232. Found %: C 68.51; H 8.70; S 16.28. $C_{12}H_{18}OS$. Calculated %: C 68.54; H 8.63; S 16.34.

LITERATURE CITED

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2. H. D. Hartough and A. J. Kosak, J. Am. Chem. Soc., 69, 3093 (1947).