SYNTHESIS OF 5-SUBSTITUTED FURANS ON THE BASIS OF THE REACTIONS OF 1,3-ALKADIYNES WITH β-DICARBONYL COMPOUNDS*

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The reaction of 1,3-hexadiyne, 1,3-heptadiyne, and 1,3-octadiyne with acetylacetone and acetoacetic ester in the presence of manganese(III) and copper(II) acetates proceeds with the participation of both triple bonds and leads to substituted 5-alkynyl- and 5-(5-furyl)furans: in the case of 5-hydroxy-5-methyl-1,3-hexadiyne the terminal triple bond participates selectively in the process as a result of the effective protection of the disubstituted triple bond by the dimethylhydroxymethyl group.

1,3-Alkadienes and 1-alkene-3-ynes have been investigated intensively in reactions with α,α-dioxoalkyl radicals generated by the oxidation of β-dicarbonyl compounds with manganese(III) acetate [2-8]. This made it possible to: 1) create accessible methods for the synthesis of alkyl- and functionally substituted derivatives of 5-alkenyl- [2-4], 5-alkynyl- [5-8], and 5(5-furyl)-4,5-dihydrofuran [2,6] and hexahydrobenzofuran [8]; establish the dependency of the regiochemistry of the process on the type and degree of substitution of the substrates, particularly 1-alken-3-ynes [5-8]; 3) detect inversion of cis-oriented double bonds by means of stereochemical testing of the reactions of 1,3-alkadienes [4]. In the present research we subjected 1,3-alkadiynes** to reaction with β-dicarbonyl compounds in order to establish the regiochemistry of the reactions and to ascertain their synthetic potential. We used acetylacetone and acetoacetic ester as the carbonyl components and manganese(III) and copper(II) acetates as the oxidizing agents. The reactions were carried out at 30°C in acetic acid at the empirically found diacetylenic compound:β-dicarbonyl compound:Mn(OAc)$_3$:Cu(OAc)$_2$ molar ratios, viz., 1:8:4:4 in the case of 1,3-alkadiynes and 1:2.4:1.2:1.2 in the case of 5-hydroxy-5-methyl-1,3-hexadiyne.

3-Carbethoxy(acetyl)-5-(1-alkynyl)-2-methylfurans (I-V) and 3,3'-carbethoxy(acetyl)-4 alkyl-2,2'-methyl-5,5'-bifuryls (VIII-XII) are formed in the reaction of 1,3-alkadiynes-1,3-hexadiyne, 1,3-heptadiyne, and 1,3-octadiyne – with acetylacetone and acetoacetic ester. Compounds I-V are the result of intramolecular cyclization of radical adducts of the A type obtained as a result of the addition of α,α-dioxoalkyl radicals to the terminal triple bond of the substrate molecules ($C_{(1)}$ attack). The formation of bifuryl derivatives VIII-XII is a multistep scheme that includes the following steps: 1) addition of α,α -dioxoalkyl radicals to the disubstituted triple bond of the substrate molecules /C(4) attack/; 2) oxidative cyclization of radical adducts of the B type to 5-ethynylfuran derivatives with structure C; 3) reaction of the latter with a second molecule of the β-dicarbonyl compound, which leads to radical-adducts of the D type ($C_{(1)}$ attack); 4) repeated intramolecular cyclization under the influence of copper(II) acetate. An alternative scheme for the formation of VIII-XII should be excluded, since it was demonstrated by a separate experiment that 5-(1-alkynyl)furans I-V are not converted to difuryl derivatives VIII-XII under the reaction conditions.

The passivity of I-V is evidently due either to the fact that, in view of the combination of steric and electronic factors, these structures do not coordinate with the manganese(III) ion sufficiently effectively or to the fact that a step involving incorporation of the substrate at the manganese—β-dicarbonyl compound does not occur in the π complex formed [3,10,11].**

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*Communication 148 in the series "Reactions of unsaturated compounds"; see [1] for Communication 147.

**See [9] for our preliminary communication.

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TABLE 1. Physicochemical Characteristics of I-XII

Compound	Empirical formula	n_D^{20}	R_f	Yield, %
I	$C_{12}H_{14}O_3$	1,5120	0,56*1	13
II	$C_{12}H_{14}O_2$	1,5281	0,51*2	29
III	$C_{13}H_{16}O_3$	1,5070	0,64*1	31
IV	$C_{13}H_{16}O_2$	1,5248	0,55*2	32
V	$C_{14}H_{18}O_3$	1,5082	0,56*1	30
VI	$C_{12}H_{14}O_3$	1,5170	0,68*3	37
VII	$C_{13}H_{16}O_4$	1,5115	0,59*3	40
VIII	$C_{18}H_{22}O_6$	65 . . . 66*4	0,40*1	5
IX	$C_{17}H_{20}O_4$	64 . . . 65*4	0,26*2	28
X	$C_{19}H_{24}O_6$	57 . . . 58*4	0,51*1	13
XI	$C_{18}H_{22}O_4$	55 . . . 56*4	0,27*2	30
XII	$C_{20}H_{26}O_6$	43 . . . 44*4	0,42*1	14

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*1Hexane—ether (2:1).
*2Hexane—ether (1:1).
*3Hexane—ether (1:3).
*4Melting point (°C).

TABLE 2. Spectral Characteristics of I-XII

Compound	IR spectrum	PMR spectrum
I*	2245 ($C\equiv C$); 1720 ($COOC_2H_5$); 1610, 1565 (C=C furan ring)	1,20 (3H, t, $J=7{,}4$, CH_3), 1,27 (3H, t, $J=7{,}2$, $COOCH_2CH_3$), 2,37 (2H, q, $CH_2C\equiv C$), 2,50 (3H, s, 2-CH_3), 4,20 (2H, q, $COOCH_2CH_3$), 6,62 ppm (1H, s, 4-H)
II	3130 (C—H furan ring); 2245 ($C\equiv C$); 1675 (C=O); 1588, 1550 (C=C furan ring)	0,95 (3H, t, $J=6{,}4$, CH_3), 1,55 (2H, sextet, CH_2), 2,22 (3H, s, CH_3CO), 2,32 (2H, t, $CH_2C\equiv C$), 2,46 (3H, s, 2-CH_3), 6,55 ppm (1H, s, 4-H)
III	3145 (C—H furan ring); 2245 ($C\equiv C$); 1718 ($COOC_2H_5$); 1605, 1560 (C=C furan ring)	0,97 (3H, t, $J=6{,}9$, CH_3), 1,25 (3H, t, $J=7{,}3$, $COOCH_2CH_3$), 1,55 (2H, sextet, CH_2), 2,31 (2H, t, $J=6{,}8$, $CH_2C\equiv C$), 2,48 (3H s, 2-CH_3), 4,14 (2H, q., $COOCH_2CH_3$), 6,53 ppm (1H, s, 4-H)
IV	3135 (C—H furan ring); 2245 ($C\equiv C$); 1675 (C=O); 1585, 1550 (C=C furan ring)	0,77 (3H, t, $J=5.0$, CH_3), 1,03 . . . 1,55 (4H, m, $2CH_2$), 2,13 (3H, s, CH_3CO), 2,25 (2H, t, $CH_2C\equiv C$), 2,37 (3H, s, 2-CH_3), 6,44 ppm (1H, s, 4-H)
V	3142 (C—H furan ring); 2240 ($C\equiv C$); 1712 ($COOC_2H_5$); 1605, 1560 (C=C furan ring)	0,89 (3H, t, $J=5.0$, CH_3), 1,24 (3H, t, $J=7{,}3$, $COOCH_2CH_3$), 1.03 . . . 1,66 (4H, m, $2CH_2$), 2,33 (2H, t, $J=6{,}7$, $CH_2C\equiv C$), 2,49 (3H, s, 2-CH_3), 4,18 (2H, q, $COOCH_2CH_3$), 6,57 ppm (1H, s, 4-H)
VI*	3470 br. (O—H); 3130 (C—H furan ring); 2235 ($C\equiv C$); 1668 (C=O); 1582, 1552 (C=C furan ring)	1,49 (6H, s, $2CH_3$), 2,23 (3H, s, CH_3CO), 2,46 (3H, s, 2-CH_3), 3,47 (1H, br.s, OH), 6,57 ppm (1H, s, 4-H)
VII	3440 br. (O—H); 3140 (C—H furan ring); 2242 ($C\equiv C$); 1715 ($COOC_2H_5$); 1602, 1555 (C=C furan ring)	1,26 (3H, t, $J=7{,}3$, $COOCH_2CH_3$), 1,48 (6H, s, $2CH_3$), 2,48 (3H, s, 2-CH_3), 2,72 (1H, br. s, OH), 4,18 (2H, q, , $COOCH_2CH_3$), 6,62 ppm. (1H, s, 4-H)
VIII**	3150 (C—H furan ring): 1712 br. ($COOC_2H_5$); 1600 br, 1535 w, 1512 w (C=C furan ring);	1,12 (3H, t, $J=7{,}3$, CH_3), 1,31 (6H, t, $J=7{,}3$, $2COOCH_2CH_3$), 2,51 (3H, s, 2-CH_3), 2,56 (3H, s, 2-CH_3), 2,76 (2H, q, CH_2), 4,25 (4H, q, $2COOCH_2CH_3$), 6,60 ppm. (1H, s, 4-H)
IX	3140 (C—H furan ring); 1675 br. (C=O); 1580 br. 1540 w 1518 w. (C=C furan ring)	0,88 (3H, t, $J=7{,}1$, CH_3), 1,48 (2H, m, CH_2), 2,28 (3H, s, CH_3CO), 2,32 (3H, s, CH_3CO), 2,52 (3H, s, 2-CH_3), 2,55 (3H, s, 2-CH_3), 2,71 (2H, t, $J=6{,}8$, CH_2), 6,55 ppm (1H, s, 4-H)
X	3150 (C—H furan ring); 1715 br ($COOC_2H_5$); 1600 split, 1540 w; 1518 w (C=C furan ring)	0,89 (3H, t, $J=6{,}7$, CH_3), 1,28 (6H, t, $J=7{,}3$, $2COOCH_2CH_3$), 2,48 (3H, s, 2-CH_3), 2,55 (3H, s, 2-CH_3), 2,71 (2H, t, $J=7{,}4$, CH_2), 4,18 (4H, q, $2COOCH_2CH_3$), 6,53 ppm (1H, s, 4-H)
XI	1675 br. (C=O); 1580 br, 1505 w (C=C furan ring)	0,84 (3H, t, $J=5{,}0$, CH_3), 1,02 . . . 1,64 (4H, m, $2CH_2$), 2,24 (3H, s, CH_3CO), 2,28 (3H, s, CH_3CO), 2,49 (6H, s, 2-CH_3), 2,67 (2H, br. t, CH_2), 6,48 ppm (1H, s, 4-H)
XII	3148 (C—H furan ring); 1720 br. ($COOC_2H_5$); 1602 br. 1515 w (C=C furan ring);	0,88 (3H, t, $J=4{,}7$, CH_3), 1,30 (6H, t, $J=7{,}3$, $2COOCH_2CH_3$), 1,08 . . . 1,71 (4H, m, $2CH_2$), 2,51 (3H, s, 2-CH_3), 2,57 (3H, s, 2-CH_3), 2,72 (2H, br.t, CH_2), 4,22 (4H, w, $2COOCH_2CH_3$), 6,57 ppm (1H, s, 4-H)

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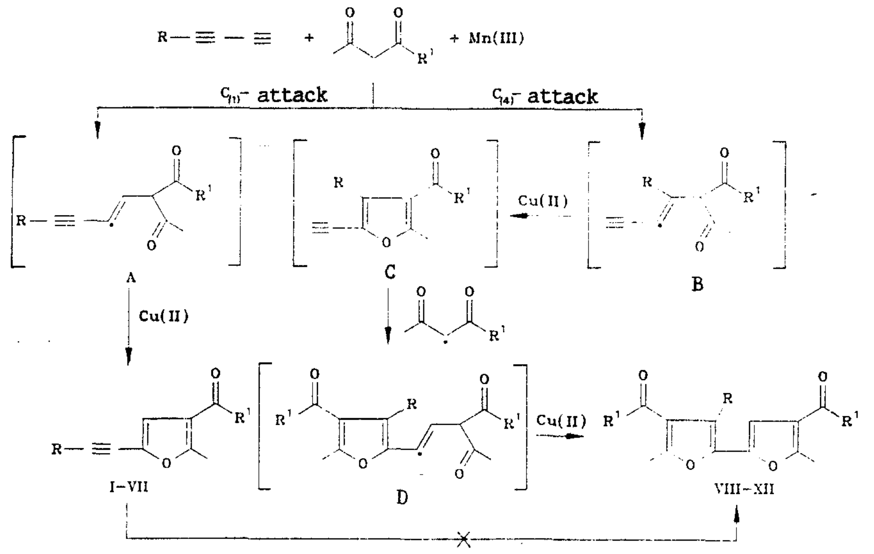
*Resinifies readily at room temperature.
**Mass spectrum, m/z: M^+ 334.



I, VIII $R=C_2H_5$, $R^1=OC_2H_5$; II, IX $R=C_3H_7$, $R^1=CH_3$; III, X $R=C_3H_7$, $R^1=OC_2H_5$; IV, XI $R=C_4H_9$, $R^1=CH_3$; V, XII $R=C_4H_9$, $R^1=OC_2H_5$; VI $R=(CH_3)_2C(OH)$, $R^1=CH_3$; VII $R=(CH_3)_2C(OH)$, $R^1=OC_2H_5$

The ratios of the yields of products I-V and VIII-XII, which provide evidence for the relative participation of the terminal and disubstituted triple bonds in the reaction ($C_{(1)}$ and $C_{(4)}$ attack), differ significantly for the investigated β-dicarbonyl compounds. When acetylacetone participates in the process, the desired ratios for 1,3-hexadiyne, 1,3-heptadiyne, and 1,3-octadiyne are 1.06:1 [9], 1.06:1, and 1.08:1, as compared with 2.66:1, 2.37:1, and 2.16:1, respectively, in the case of acetoacetic ester. In the first case the reaction is nonregioselective, since approximately identical participation of both triple bonds in the reaction occurs, whereas in the second case the regioselectivity of the process is considerably higher, and the addition of the α-carbethoxy-α-acetylmethyl radical occurs primarily at the terminal triple bond ($C_{(1)}$ attack).

The reaction of 5-hydroxy-5-methyl-1,3-hexadiyne with acetylacetone and acetoacetic ester takes place exclusively at the terminal triple bond and leads to 3-acetyl(carbethoxy)-5-(3-hydroxy-3-methyl-1-butynyl)-2-methylfurans VI and VII. The observed regiospecificity of the reactions is due to the effective protection of the disubstituted triple bond by the dimethylhydroxymethyl group, which was previously demonstrated in the case of 1-alken-3-ynes [5]. It should be noted that in a study of the analogous reactions of unsaturated alcohols such as cis- and trans-$(CH_3)_2C(OH)CH{=}CHCH{=}CH_2$ [4], $(CH_3)_2C(OH)C{\equiv}CCH{\equiv}CH_7$ [5], $(CH_3)_2C(OH)C{\equiv}CC(CH_3){=}CH_2$ [7], and trans-$(CH_3)_2C(OH)CH{=}CHC{\equiv}CH$ [8]; this can be explained by the greater stability of the furylallyl carbonium from the reaction products. One should have expected a similar trend of the process for diacetylenic alcohol $(CH_3)_2C(OH)C{\equiv}CC{\equiv}CH$; however, as one can see from the structures of VI and VII, dehydration did not occur. The reason for this is evidently either the different stabilities of the furyallyl and furylpropargyl carbonium ions or the fact that 5-(1-alkynyl)-furans VI and VII do not coordinate with the manganese (III) ion sufficiently effectively.*

EXPERIMENTAL

The IR spectra of thin layers of the pure substances were recorded with a UR-20 spectrometer; the absorption frequencies are given in reciprocal centimeters. The PMR spectra were obtained with a Perkin—Elmer R-12B spectrometer (60 MHz); the chemical shifts (in parts per million) are presented relative to tetramethylsilane (TMS) (on the δ scale), and the spin-spin coupling constants (SSCC) (in hertz) are given. The mass spectrum was recorded with an MKh-1320 spectrometer at ionizing-electron energy of 70 eV. Analysis by TLC was carried out on Silufol UV-254 plates with development by means of a saturated solution of $KMnO_4$.

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*Dehydration presumably takes place in the coordination sphere of the transition metal, as in the analogous reaction of dicobalt hexacarbonyl complexes of propargyl alcohols [12].

The results of elementary analysis for C and H of I-XII were in agreement with the calculated values. The physicochemical characteristics of I-XII are presented in Table 1, and the spectral characteristics are presented in Table 2.

Typical Method. 3-Carbethoxy(acetyl)-5-(1-alkynyl)-2-methylfurans (I-V) and 3,3'-Carbethoxy(acetyl)-4-alkyl-2,2'-methyl-5,5'-difuryls (VIII-XII). An 80-mmole sample of $Mn(OAC)_3 \cdot 2H_2O$, 160 mmole of the β-dicarbonyl compound, and 20 mmole of the 1,3-alkadiyne were added to a solution of 80 mmole of $Cu(OAc)_2.2H_2O$ in 200 ml of glacial acetic acid, and the mixture was heated in an argon atmosphere at 30°C until the brown color vanished (3 h). The mixture was then cooled to 20°C and filtered, and the filtrate was diluted with water and extracted with ether. The ether extract was washed with water, a saturated solution of sodium carbonate, and water, and dried ($MgSO_4$). The ether was evaporated in vacuo, and the individual products I-V and VIII-XII were isolated by means of column chromatography on silica gel (40...100μ); the sample: sorbent ratio was 1:50, the separation was monitored by TLC, and the eluents were hexane—ether (5:1) for I and VIII and hexane—ether (3:1) for II-V and IX-XII.

3-Acetyl(carbethoxy)-5-(3-hydroxy-3-methyl-1-butynyl)-2-methylfurans (VI and VII). Similarly, VI (VII) was obtained from 6 mmole of $Cu(OAc)_2 \cdot 2H_2O$, 6 mmole of $Mn(OAc)_3 \cdot 2H_2O$, 12 mmole of the β-dicarbonyl compound, and 5 mmole of 5-hydroxy-5-methyl-1,3-hexadiyne in 50 ml of acetic acid; the eluent was hexane—ether (3:1).

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