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SYNTHESIS OF β-SUBSTITUTED TETRAHYDROFURANS BY THE PRINS REACTION

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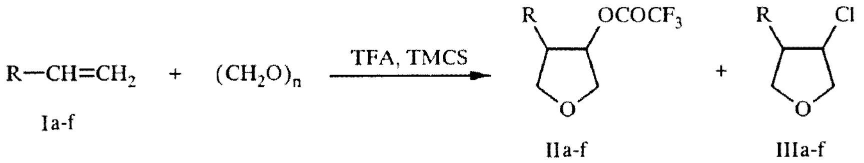
Mixtures of 3-trifluoroacetoxy- and 3-chloro-4-alkyltetrahydrofurans were synthesized by the reaction of a series of α-olefins with formaldehyde in trifluoroacetic acid and trimethylchlorosilane.

Earlier we described the synthesis of β-substituted 2,5-dihydro- and tetrahydrofurans by the reaction of α-olefins with formaldehyde in trifluoroacetic acid [1-3] (see also [4]). In the present communication we give the results obtained when the reaction was conducted in the presence of trimethylchlorosilane.



Ia-f IIa-f IIIa-f

I—III a R = C_4H_9, b R = C_5H_{11}, c R = C_6H_{13}, d R = C_7H_{15}, e R = C_8H_{17}, f R = C_9H_{19}

TABLE 1. The Characteristics of Compounds (IIa-f, IIIa-f)*

Compound	Molecular formula	Found % / Calculated %			bp, °C (760 mm Hg)	n_D^{20}	Yield, %
		C	H	Cl			
IIa	$C_{10}H_{15}O_3F_3$	50,20 50,00	6,33 6,29	—	228...232	1,4065	35
IIb	$C_{11}H_{17}O_3F_3$	52,36 51,96	6,70 6,73	—	231...234	1,4098	38
IIc	$C_{12}H_{19}O_3F_3$	54,26 53,72	7,19 7,13	—	235...238	1,4135	40
IId	$C_{13}H_{21}O_3F_3$	54,92 55,31	7,44 7,40	—	240...242	1,4182	39
IIe	$C_{14}H_{23}O_3F_3$	57,19 56,74	7,87 7,82	—	242...246	1,4242	37
IIf	$C_{15}H_{25}O_3F_3$	58,40 58,05	8,09 8,11	—	254...256	1,4283	34
IIIa	$C_8H_{15}OCl$	58,60 59,07	9,36 9,29	21,99 21,79	195...198	1,4518	49
IIIb	$C_9H_{17}OCl$	61,79 61,18	9,75 9,69	20,16 20,06	196...199	1,4532	50
IIIc	$C_{10}H_{19}OCl$	63,17 62,98	10,09 10,04	18,48 18,59	196...200	1,4560	48
IIId	$C_{11}H_{21}OCl$	65,11 64,53	10,26 10,33	17,45 17,31	196...200	1,4662	54
IIIe	$C_{12}H_{23}OCl$	66,14 65,88	10,65 10,59	16,28 16,20	198...200	1,4688	53
IIIf	$C_{13}H_{25}OCl$	66,80 67,07	10,90 10,82	15,13 15,22	198...200	1,4702	53

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*The characteristics of the mixtures of cis and trans isomers are given, and the n_D^{20} values are given for the trans isomers.

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TABLE 2. The ^1H NMR Spectra of the Mixture of cis and trans Isomers of Compounds (IIa, c, d, f, IIIa, c-f)

Compound	Signals of protons, δ, ppm, spin—spin coupling constant (J), Hz							
	heterocycle							R
	$2\text{-}H_a$, m	$2\text{-}H_e$, m	$5\text{-}H_a$, m	3-H, m	$5\text{-}H_e$, dd	4-H, m	J_{45}	
trans IIa*	3,95...4,05	3,69...3,80	3,49...3,57	4,86...4,91	3,22	1,74...1,98	9,4	0,89 (3H, t, CH_3, $J = 6,5$), 1,17...1,45 (6H, m, CH_2)
IIb	3,15...4,18			4,86...4,91	*2	1,69...1,99	—	0,89 (3H, t, CH_3), 1,09...1,51 (10H, m, CH_2)
IIIa	3,33...3,99			—	3,03	1,42...1,71	10,3	0,89 (3H, t, CH_3, $J = 6,7$), 1,30...1,42 (6H, m, CH_2)
IIIc	3,35...3,94			—	3,10	1,48...1,82	10,1	0,88 (3H, t, CH_3, $J = 6,7$), 1,15...1,41 (10H, m, CH_2)
IIId*3	3,37...4,04			—	3,11	1,67...1,99	9,7	0,88 (3H, t, CH_3, $J = 6,7$), 1,18...1,28 (12H, m, CH_2)

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*The spectra of the trans-IId, f compounds were identical with the given spectrum, $J_{34} = 8.7$ Hz.

*2The spectrum is overlapped by a multiplet at 3.15-4.18.

*3The spectra of the mixtures of cis and trans isomers of compounds (IIIe, f) are identical with the given spectrum.

TABLE 3. The ^{13}C NMR Spectra of the cis and trans Isomers of Compounds (IIc, d, f, IIId, e)

Compound	Signals of carbon atoms, δ, ppm				
	heterocycle*				R*2
	$C_{(2)}$, t	$C_{(3)}$, d	$C_{(4)}$, d	$C_{(5)}$, t	C(α), t
trans-IIc	69,84	78,71	40,67	65,54	26,37
cis-IIc	67,73	74,64	39,19	62,97	25,68
trans-IId	69,14	78,77	40,61	65,52	26,56
cis-IId	67,71	74,75	39,14	62,95	24,99
trans-IIf	69,85	78,76	40,70	65,56	26,49
cis-IIf	67,76	77,73	39,22	62,99	25,07
trans-IIId	71,03	62,53	44,95	66,99	37,23
cis-IIId	67,19	60,76	41,02	62,53	34,63
trans-IIIe	71,42	61,90	44,94	66,96	37,22
cis-IIIe	67,10	60,69	41,01	62,50	34,61

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*The chemical shifts of the C═O group in compounds (IIc, d, f) lie in the region of 157.2-157.6 ppm.

*2The chemical shifts of Cβ and so forth are typical of alkanes.

It was shown that the main reaction products were mixtures of 3-trifluoroacetoxy- and 3-chloro-4-alkyltetrahydrofurans (IIa-f) and (IIIa-f), which were separated by preparative GLC. The mixtures contained the cis and trans isomers of the compounds, and the trans isomers predominated (approximate cis:trans ratio 1:5). The characteristics of the synthesized tetrahydrofurans are given in Table 1. The products were identified and the isomers were assigned by ^{1}H and ^{13}C NMR spectroscopy (Tables 2 and 3) and also by chromato-mass spectrometry [in the case of the isomers (IIIb)]. In particular, the appreciable difference between the chemical shifts of the C_3 and C_4 atoms of the ring and also the C(α) substituent for the cis and trans isomers (up to 2-4 ppm) made it possible to achieve a stereochemical assignment of the signals in the ^{13}C NMR spectra. The upfield chemical shifts of the indicated atoms in the cis isomers are due to the steric cis-coupling of the vicinal substituents at C_3 and C_4 [5]. The signals for the carbon atoms of the CF_3 and CO groups take the form of quartets with spin—spin coupling constants $^{1}J_{^{13}C-^{19}F} = 285.3$ Hz and $^{2}J_{^{13}C-^{19}F} = 42.7$ Hz.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were recorded on an AM-300 instrument at 300 MHz in deuterochloroform with TMS as internal standard. Chromato-mass spectrometric analysis was conducted at 70 eV on a Finnigan 4021 instrument. Preparative GLC was realized on a PAKhV-08 instrument (stainless steel columns, 8 × 2000 mm, 5% of SE-30 on Tsvetokhrom, evaporator temperature 270°C, column thermostat temperature 180°C, helium, 180 cm^3/min, katharometer).

3-Trifluoroacetoxy- and 3-Chloro-4-alkyltetrahydrofurans (IIa-f and IIIa-f). To a 20% solution of 100 mmole of formaldehyde in trifluoroacetic acid at room temperature we added dropwise a mixture of 50 mmole of the olefin and 50 mmole of trimethylchlorosilane. The reaction mixture was stirred for a further 4 h and neutralized with 37% aqueous potassium hydroxide. The organic layer was separated, and the aqueous layer was extracted with ether (3 × 50 ml). The combined extract was combined with the organic layer and dried with calcium chloride. After distillation of the ether the products were separated by preparative GLC.

Mass spectrum of trans-(IIIb), m/z (%): M^+ 176(4), 147(1), 140(2), 98(4), 84(11), 83(25), 81(67), 69(28), 68(50), 56(21), 55(100), 54(21), 53(11), 41(68).

Mass spectrum of cis-(IIIb), m/z (%): M^+ 176(1), 147(0.5), 140(1, 5), 98(3), 84(15), 83(50), 81(96), 70(11), 69(42), 68(52), 56(34), 55(100), 54(31), 53(19), 41(71).

REFERENCES

1. R. F. Talipov, A. S. Starikov, I. A. Gorina, N. A. Akmanova, and M. G. Safarov, Zh. Org. Khim., **29**, 1024 (1993).
2. R. F. Talipov, A. S. Starikov, A. V. Gorin, and M. G. Safarov, Zh. Org. Khim., **29**, 748 (1993).
3. R. F. Talipov, M. Z. Igdavletova, A. S. Starikov, N. A. Akmanova, and I. M. Safarov, Neftekhimiya, No. 5, 436 (1993).
4. R. F. Talipov, I. V. Vakulin, I. M. Safarov, and M. G. Safarov, Bashkirskii Khim. Zh., **1**, 57 (1994).
5. J. K. Whitesell and M. A. Minton, Stereochemical Analysis of Alicyclic Compounds by C-13 NMR Spectroscopy, Chapman and Hall, London–New York (1987), p. 231.