ALKYLATION OF π-DONORS BY (E)-1-METHOXYBUTADIENE ADDUCTS WITH ARYLSULFENYL CHLORIDES

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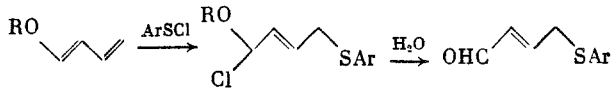
Electrophilic addition to π-donors such as silyl enol esters (TMSEE), silyl ketoacetal esters, and allylsilanes is an effective method for forming new C–C bonds [1-4]. The C-electrophiles commonly used are reagents capable of forming stable carbcations in the presence of Lewis acids (e.g., tert-alkyl, benzyl, allyl, α-alkoxy-, and α-arylthiocarbenium ions). Recently it was shown that various β-arylthioalkyl chlorides (adducts of alkenes with arylsulfenyl chlorides) could also be used in reactions of this type, forming electrophiles such as episulfonium ions in the presence of Lewis acids [5-9].

As a continuation of these investigations, in the present work we studied the possibility of obtaining C-electrophiles of a new type, based on adducts of (E)-1-alkoxybutadiene (I) with arylsulfenyl chlorides.

We know that Ad_E reactions of compound (I) with C-electrophiles such as acetals of aromatic and aliphatic aldehydes occur as 1,4-additions exclusively (see, for example, [10, 11]). Data about the course of this reaction for S-electrophiles are not available.

It was found that ArSCl adds readily to compound (I) to form 4-arylthio-1-alkoxybuten-2-yl chloride (II). Hydrolysis of (II) affords 4-arylthiobuten-2-al-1 (III) in a yield of up to 95%, E:Z = 30:1 (Scheme 1).

Scheme 1

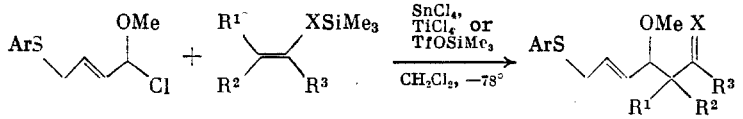


(Ia,b) (IIa,b) (IIIa,b)

R = Me (Ia), Et (Ib); R = Me, Ar = *p*-Tol ((IIa), (IIIb)), *p*-ClC_6H_4 ((IIb), (IIIb)); 71% (IIIa), 95% (IIIb).

Adducts (IIa, b) were used as C-electrophiles in reactions with typical π-donors: TMSEE of isobutyraldehyde (IV), acetone (V), methyl cyclopropyl ketone (VI), 2-methylcyclohexanone (VII), trimethylsilyl ketenacetal (VIII), obtained from methyl isobutyrate, and trimethylallylsilane (IX). In all cases the alkylation reactions proceeded readily at −78°C in the presence of Lewis acids such as $SnCl_4$ (2 equiv.), $TiCl_4$ (2 equiv.), or Me_3SiOTf (0.1 equiv.) and afforded the anticipated products (X)-(XV) in yields of 50-84% (Scheme 2).

Scheme 2



(IIa, b) (IV) — (IX) (X) — (XV)

R^1—R^3=H or Alkyl; X = O, CH_2

The reaction conditions and structures of the products obtained are shown in Table 1.

According to PMR spectroscopic data, the E isomer is the predominant product in all cases. Compound (XIII) is an individual diastereomer, which is an indication of the selectivity of formation of the new C–C bond.

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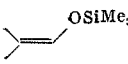
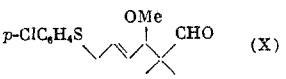
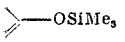
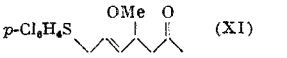
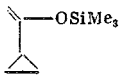
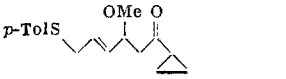
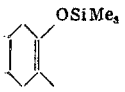
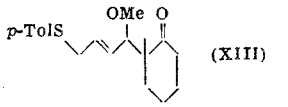
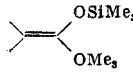
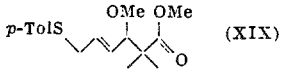
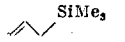
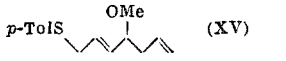
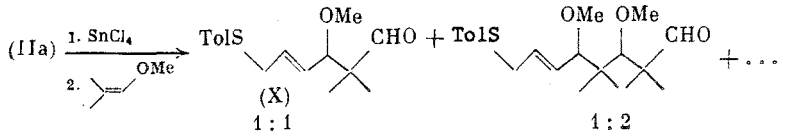
TABLE 1. Alkylation of π-Donors by Adducts (IIa, b)

π-Donor	Adduct	Reaction conditions	Yield, %
 (IV)	 (X)	$SnCl_4$, 10 min	66
 (V)	 (XI)	$TfOSiMe_3$, 3 h $SnCl_4$, 10 min	84, 56
 (VI)		$TfOSiMe_3$, 3,5 h	81
 (VII)	 (XIII)	$TfOSiMe_3$, 4 h	50
 (VIII)	 (XIX)	$TiCl_4$, 10 min $TfOSiMe_3$, 10 min	75, 71
 (IX)	 (XV)	$TfOSiMe_3$, 4 h	70

The data obtained by us show the high reactivity of compound (II) as an electrophile in reactions with different types of π-donors. In these reactions compound (II) appears as the equivalent of the polyfunctional syntone $ArSCH_2\overset{+}{C}H{=}CHCH(OMe)$. Products (X)-(XV) obtained in this reaction contain different types of functional groups, which permits subsequent selective reactions with any of these functions.

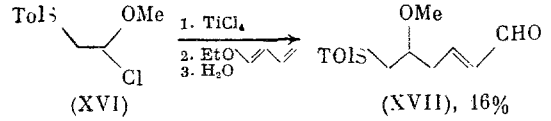
In addition to the previously mentioned π-donor compounds, the reaction has also been carried out with vinyl ethers, e.g., 2-methyl-1-methoxypropene-1. However, in these reactions a significant amount of oligomerization products is formed in addition to the 1:1 adduct (Scheme 3, cf. [8]).

Scheme 3



We also studied the possibility of using 1-ethoxybutadiene as a nucleophile in the reaction with 1-methoxy-2-p-tolylthioethyl chloride (XVI) (an adduct of methyl vinyl ether with ArSCl). As in the previous case, the major course of this reaction is oligomerization; the 1:1 product, (E)-5-methoxy-6-p-tolylthiohexen-2-al-1 (XVII), was isolated in a low yield (Scheme 4).

Scheme 4



(XVI) (XVII), 16%

EXPERIMENTAL

PMR spectra of solutions in $CDCl_3$ were recorded on a Bruker WM-250 apparatus. Mass spectra were obtained on a Varian MAT CH-6 instrument.

The characteristics of the adducts obtained (R_f, n_D^{22}, M^+, and elemental analysis data) are shown in Table 2.

4-p-Tolylbuten-2-al-1 (IIIa). A 98-mg portion (1 mmole) of (E)-1-ethoxybutadiene in 2 ml abs. CH_2Cl_2 was added dropwise to 159 mg (1 mmole) p-ToSCl in 10 ml abs. CH_2Cl_2 at −78°C in an Ar atmosphere (till the disappearance of the characteristic ArSCl color). The reaction

TABLE 2. Characteristics of the Synthesized Adducts

Compound	R_f^*	n_D^{22}	Found/Calculated, % C	H	S	Empirical formula	M+
(IIIa)	0,42	1,5969	68,56	6,64		$C_{11}H_{12}SO$	192
			68,71	6,29			
(X)	0,66	1,5520	59,98	6,48		$C_{15}H_{19}SO_2Cl$	298, 300
			60,29	6,41			
(XI)	0,29	1,5520	59,14	6,01	10,95	$C_{14}H_{17}SO_2Cl$	284, 286
			59,04	6,02	11,26		
(XII)	0,45	1,5485	70,62	7,78	10,68	$C_{17}H_{22}SO_2$	290
			70,31	7,64	11,04		
(XIII)		1,5565	71,69	8,26		$C_{19}H_{26}SO_2$	318
			71,66	8,23			
(XIV)	0,51	1,5388	66,42	7,84		$C_{17}H_{24}SO_3$	308
			66,20	7,84			
(XV)	0,81	1,5441	72,62	8,20	12,75	$C_{15}H_{20}SO$	248
			72,54	8,12	12,91		
(XVII)	0,46 †	1,5590	67,41	7,39		$C_{14}H_{18}SO_2$	250
			67.17	7.25			

*Silufol; eluent: ether–hexane, 1:1.
†Silufol; eluent: ether–hexane, 2:1.

mixture was treated for 10 min with saturated $NaHCO_3$ cooled to 0°C; it was then extracted with ether and dried over $CaCl_2$. After removal of solvent, the residue was chromatographed on SiO_2; eluent: hexane–ether, 2:1. A 135-mg yield (71%) of compound (IIIa) was obtained; E:Z = 30:1.‡ PMR spectrum (δ, ppm, J, Hz): 2.32 s (3H, CH_3), 3.67 dd (2H, SCH_2, J_1 = 7.25, J_2 = 1.5), 5.95 ddt (1H, =CHCHO, J_1 = 15.5, J_2 = 7.5, J_3 = 1.5), 6.78 dt (1H, $CHCH_2$, J_1 = 15.5, J_2 = 7.25), 7.19 m (4H, H_{arom}), 9.50 d (1H, CHO, J = 7.5).

4-p-Chlorophenylthiobuten-2-al (IIIb) was obtained from compound (Ia) in a manner analogous to (IIIa); yield, 95%: R_f 0.31 (ether–hexane, 1:1; Silufol), n_D^{22} 1.6045. PMR spectrum (δ, ppm, J, Hz): 3.68 dd (2H, SCH_2), 6.01 ddt (1H, =CHCHO, J_1 = 15.5, J_2 = 8, J_3 = 1.5), 6.75 dt (1H, =CH, J_1 = 15.5, J_2 = 7), 7.27 s (4H, H_{arom}), 9.48 d (1H, CHO, J = 8); E:Z = 9:2; M^+ 212, 214.

2,2-Dimethyl-3-methoxy-6-p-chlorophenylhexen-4-al-1 (X). An 84-mg portion (1 mmole) of (E)-1-methoxybutadiene in 2 ml CH_2Cl_2 was added dropwise to 179 mg (1 mmole) p-ClC_6H_4SCl in 20 ml CH_2Cl_2 at −78°C in an Ar atmosphere. Then a precooled solution (−78°C) containing 0.234 ml (2 mmoles) $SnCl_4$ in 2 ml CH_2Cl_2 was added, followed immediately by 173 mg (1.2 mmoles) of 2-methyl-1-trimethylsiloxypropene-1 in 2 ml CH_2Cl_2. After 10 min the mixture was decanted, with stirring, into saturated $NaHCO_3$ cooled to 0°C. It was then extracted with ether and dried over $CaCl_2$. After removal of solvent, the residue was purified by preparative TLC on SiO_2; eluent: ether–hexane, 1:1.** A 220-mg yield (66%) of compound (X) was isolated; E:Z = 9:1. PMR spectrum (δ, ppm, J, Hz): 0.82 s and 0.94 s (6H, $C(CH_3)_2$), 3.08 s (3H, OCH_3), 3.56 d (1H, $CHOCH_3$, J = 8.5), 3.58 dd (2H, SCH_2, J_1 = 7, J_2 = 1), 5.36 ddt (1H, =CH, J_1 = 15.5, J_2 = 8.5, J_3 = 1), 5.70 dt (1H, CH_2CH=, J_1 = 15.5, J_2 = 7), 7.27 s (4H, H_{arom}), 9.40 s (1H, CHO).

4-Methoxy-7-p-chlorophenylthiohepten-5-one-2 (XI). E:Z = 30:1. PMR spectrum (δ, ppm, J, Hz): 2.11 s (3H, CH_3), 2.64 (AB part of ABX system, 2H, CH_2, J_{AB} = 16.5, J_{AX} = J_{BX} = 9), 3.12 s (3H, OCH_3), 3.60 dd (2H, SCH_2, J_1 = 8, J_2 = 1.5), 4.30 dt (1H, $CHOCH_3$, J_1 = 11, J_2 = 9.5, J_3 = 4.5), 5.31 ddt (1H, =CH, J_1 = 11, J_2 = 8), 7.26 m (4H, H_{arom}).

1-Cyclopropyl-3-methoxy-6-p-tolylthiohexen-4-one-1 (XII). E:Z = 30:1. PMR spectrum (δ, ppm, J, Hz): 0.87 m and 1.02 m (4H, $CH(CH_2)_2$), 1.89 m (1H, $CH(CH_2)_2$), 2.02 s (3H, CH_3), 2.45 and 2.76 (AB part of ABX spectrum, 2H, CH_2CO, J_{AB} = 16, J_{AX} = 8, J_{BX} = 5), 3.12 s (3H, OCH_3), 3.48 ddd (2H, SCH_2, J_1 = 7.5, J_2 = 3, J_3 = 1.25), 4.02 ddd (1H, $CHOCH_3$, J_1 = J_2 = 8,

‡Here and below the E:Z ratios are obtained from PMR spectra; the spectra given are for E isomers.
**Adducts (XI)-(XV) were obtained in a similar manner (for reaction conditions, see Table 2).

J_3 = 5), 5.32 ddt (1H, =CH, J_1 = 15.5, J_2 = 8, J_3 = 1.25), 5.72 dt (1H, =C<u>H</u>CH_2, J_1 = 15.5, J_2 = 7.5), 7.17 m (4H, H_{arom}).

<u>2-Methyl-2-(1'-methoxy-4'-p-tolylthiobuten-2'-yl)cyclohexanone-1 (XIII)</u>. E:Z = 30:1. PMR spectrum (δ, ppm, J, Hz): 0.86 s (3H, CH_3), 1.6 m (6H, $-(CH_2)_3-$), 2.26 s (3H, CH_3), 2.4 m (2H, CH_2CO), 3.01 s (3H, OCH_3), 3.52 dd (2H, J_1 = 7, J_2 = 1.25), 3.89 d (1H, C<u>H</u>OCH_3, J = 8.25), 5.27 ddt (1H, =CH, J_1 = 15.5, J_2 = 8.25, J_3 = 1.25), 5.69 ddt (1H, $CH_2C\underline{H}=$, J_1 = 15.5, J_2 = 7, J_3 = 0.75), 7.24 m (4H, H_{arom}).

<u>2,2-Dimethyl-3-methoxy-6-p-tolylthiohexen-4-oic Acid Methyl Ester (XIV)</u>. E:Z = 30:1. PMR spectrum (δ, ppm, J, Hz): 0.91 s and 1.01 s (6H, $C(CH_3)_2$), 2.30 s (3H, CH_3), 3.08 s (3H, OCH_3), 3.52 dd (2H, SCH_2, J_1 = 7.5, J_2 = 1.75), 3.56 s (3H, OCH_3), 4.10 dd (1H, CHOMe, J_1 = 10, J_2 = 1.5), 5.33 ddt (1H, =CH, J_1 = 15.5, J_2 = 10, J_3 = 1.5), 5.69 dt (1H, =C<u>H</u>CH_2, J_1 = 15.5, J_2 = 7.5), 7.16 m (4H, H_{arom}).

<u>4-Methoxy-1-p-tolylthioheptadiene-2,6 (XV)</u>. E:Z = 30.1. PMR spectrum (δ, ppm, J, Hz): 2.21 m (2H, CH_2), 2.34 s (3H, CH_3), 3.14 s (3H, OCH_3), 3.52 m (3H, SCH_2 and C<u>H</u>OMe), 5.02 m (2H, $=CH_2$), 5.32 ddt (1H, =C<u>H</u>CHOMe, J_1 = 15.5, J_2 = 8, J_3 = 1.35), 5.67 m (2H, two =CH groups), 7.19 m (4H, H_{arom}).

<u>5-Methoxy-6-p-tolylthiohexen-2-al-1 (XVII)</u>. A 58-mg portion (1 mmole) of methyl vinyl ether in 2 ml CH_2Cl_2 was added dropwise to 159 mg (1 mmole) TolSCl in 10 ml abs. CH_2Cl_2 at −78°C in an Ar atmosphere. Then precooled solutions containing 0.13 ml (1.2 mmoles) $TiCl_4$ in 2 ml CH_2Cl_2 and 196 mg (2 mmoles) (E)-1-ethoxybutadiene in 2 ml CH_2Cl_2 were added. After 30 min the mixture was decanted into saturated $NaHCO_3$; it was then extracted with ether and dried over $CaCl_2$. After evaporating the solvent, the residue was purified by preparative TLC on SiO_2; eluent: ether–hexane, 2:1. A 40-mg yield (16%) of compound (XVII) was isolated. E:Z = 30:1. PMR spectrum (δ, ppm, J, Hz): 2.30 s (3H, CH_3), 2.68 m (2H, CH_2), 2.89 dd and 3.15 dd (2H, SCH_2, J_1 = 13.5, J_2 = 7, J_3 = 5), 3.37 s (3H, OCH_3), 3.50 m (1H, C<u>H</u>$(OCH_3)_2$), 6.15 ddt (1H, =C<u>H</u>CHO, J_1 = 15, J_2 = 8, J_3 = 1.5), 6.84 dt (1H, =C<u>H</u>−CH_2, J_1 = 15, J_2 = 7), 7.22 m (4H, H_{arom}), 9.50 d (1H, CHO, J = 8).

CONCLUSIONS

1,4-Adducts of 1-alkoxybutadiene with arylsulfenyl chlorides were obtained. It was shown that these adducts can be used as C-electrophiles to transfer 1-alkoxy-4-arylthiobuten-2-al groups in reactions with π-donors.

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