REACTION OF CHLORO-ARYLTHIO ADDUCTS OF 1,1-DIMETHYLALLENE WITH TRIMETHYLSILYL ENOL ETHERS – A METHOD OF 2-ARYLTHIOPRENYLATION OF CARBONYL COMPOUNDS

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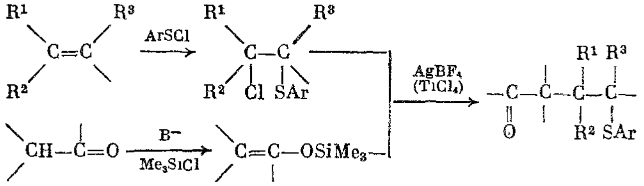
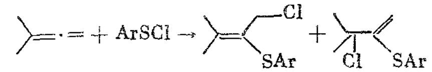
UDC 542.91:547.315.1:547.1'128

The reaction of β-chloroalkylaryl thioethers with trimethylsilyl enol ethers (TMSE) has been proposed as a new method for preparing complex polyfunctional compounds from simple predecessors [1, 2]



Alkyl-, aryl-, and alkoxy-substituted olefins were used for this purpose. In the present work, we studied the possible carrying out of a similar scheme using 1,1-dimethylallene (I) (DMA).

It is known that the reaction of (I) with PhSCl and CH_2Cl_2 preferentially gives 3-chloro-3-methyl-2-phenylthiobut-2-ene (IIIb) (a tertiary chloro-arylthio adduct) in a yield of 70% [3], while the addition of $2,4\text{-}(O_2N)_2C_6 \cdot H_3SCl$ in CCl_4 leads to the primary chloroadduct – 1-chloro-2-(2,4-dinitrophenylthio)-3-methylbut-2-ene (IId) in a 60% yield [4]



(I) (IIa–d) (IIIa–d)

Ar = 4-ClC$_6$H$_4$ (a); Ph (b); 4-MeC$_6$H$_4$ (c); 2,4-(NO$_2$)$_2$C$_6$H$_3$ (d)

However, we were unable to reproduce these data. It was shown that, in fact, the composition of the products formed from (I) and ArSCl is largely dependent on the reaction conditions and on the nature of the aryl substituent in the reagent (Table 1), and that in most cases not only II and III are formed, but also admixtures of an unestablished structure (according to PMR data, up to 30% of the reaction mixtures). The optimal conditions for the preferential preparation of adduct (IIa) are a reaction in $C_2H_2Cl_4$ at 20°C. The preferential formation of the tertiary chloro adduct (IIIc) is observed if the reaction is carried out at −78°C.

Possible alkylation of TMSE by a mixture of adducts (II + III) was studied for the example of reaction with 2-trimethylsiloxypropene (IV) (a TMSE of acetone). In analogy with previous data, the reaction was carried out in the presence of both $AgBF_4$ (method A) and $ZnCl_2$ (method B) [1, 2]. Best results are obtained with method B, and the yield of the required end product 2-methyl-3-(aryl)hept-en-6-one (V) is mainly determined by the content in the initial mixture of the primary chloro adduct (II). It is probable that the tertiary isomer is either less active in this reaction, or it undergoes secondary transformations in the presence of Lewis acids*

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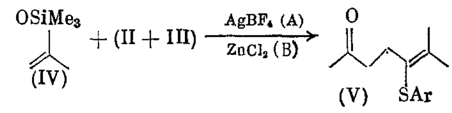
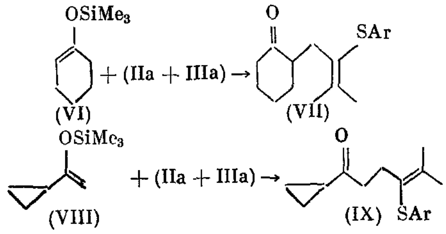
*After the reaction mixture is treated, compound (III) is not present in it; the isomer of adduct (V), corresponding to the condensation of (III) with (IV) at the tertiary C atom, was not detected.

N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 2, pp. 392-395, February, 1985. Original article submitted December 12, 1983.

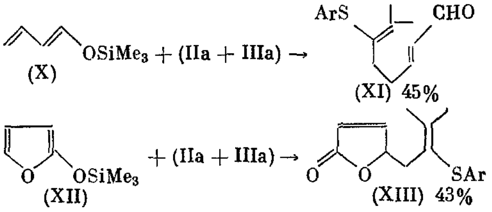


(IIIb):(IIb)	Yield (V), %	(IIIa):(IIa)	Yield (V), %
95 : 5	0 (A)	2 : 1	39 (A)
4 : 1	26 (A)	1 : 2	48 (B)

Similarly, the reaction of a mixture of (IIa + IIIa) (ratio 2:1) with cyclohexanone TMSE (VI) led to 2-[3-methyl-2-(4-chlorophenylthio)but-2-enyl]cyclohexan-1-one (VII) and the reaction with cyclopropyl methyl ketone TMSE (VIII) gave 3-(4-chlorophenylthio)-4-methylpent-3-enyl cyclopropyl ketone (IX) (yield 44% by method A and 61% by method B).



The reaction studied can also be extended to trimethylsiloxy-1,3-dienes. It was shown that in the presence of $ZnCl_2$, the alkylation of 1-trimethylsiloxybutadiene (X) (a crotonaldehyde TMSE) and 1-trimethylsiloxyfuran (XII) (a crotonolactone TMSE) with the (IIa + IIIa) mixture proceed smoothly, and in both cases γ-alkylation is exclusively observed



In all the cases studied, as a result of the alkylation of TMSE by a mixture of adducts (II + III), the 2-arylthioprenyl substituent is introduced into the molecule of the carbonyl predecessor. Adducts of 1,1-dimethylallene with ArSCl can thus be used as C_5-electrophilic synthons in the preparation of various isoprenoid blocks containing the synthetically useful vinyl sulfide grouping.

EXPERIMENTAL

The GLC analyses were carried out on the XE-60 phase (5%), column 1 m × 4 mm, flame-ionization detector, LKhM-8 MD apparatus. The PMR spectra were run on a Varian DA-60-IL (60 MHz) and Bruker WM-250 (250 MHz) spectrometers with TMS as the internal standard. The mass spectra were run on a Varian CH-6 apparatus. Preparative separation of the products was carried out on 250 × 300 mm glass plates with a 2-mm-thick SiO_2 stationary layer.

Trimethylsilyl enol ethers of acetone (IV), cyclohexanone (VI), and cyclopropyl methyl ketone (VIII) were obtained from the corresponding ketones by the method in [5]. Trimethylsilyl enol ethers of crotonaldehyde (X) and crotonolactone (XII) were obtained by the method in [6].

1,1-Dimethylallene (I) was obtained from dimethylethynylcarbinol as described in [7].

Reaction of 1,1-Dimethylallene (I) with 4-Chlorophenylsulfenyl Chloride. A solution of 2.68 g (15 mmoles) of $4\text{-}ClC_6H_4SCl$ in 10 ml of $C_2H_2Cl_4$ was added at ~20°C to a solution of 1.36 g (20 mmoles) of DMA in 15 ml of $C_2H_2Cl_4$. The PMR spectrum shows that the mixture obtained contains 3-chloro-3-methyl-2-(4-chlorophenylthio)but-1-ene (IIIa) and 1-chloro-2-(4-chlorophenylthio)-3-methylbut-2-ene (IIa) in a ratio of 1:2. PMR spectrum (60 MHz, CCl_4) of (IIa): 4.08 s and 4.43 s (2H), 1.95 d (6H). (IIIa): 5.6 d and 4.78 d (2H), m 1.83 s (6H). The ratio of the adducts (II) and (III), depending on solvent, temperature, and ArS, is given in Table 1.

TABLE 1

Experiment	Adduct	ArS	Solvent	T., °C	Ratio (III):(II)*
1 †	(IIa) + (IIIa)	4-ClC_6H_4S	CH_2Cl_2	–78	5 : 1
2 ‡	the same	the same	CH_2Cl_2	–78	2 : 1
3	»	»	CH_2Cl_2	–30	1 : 1
4	»	»	C_6D_6	22	1 : 2
5	»	»	$C_2H_2Cl_4$	22	1 : 2
6	»	»	CCl_4	0	1 : 3
7	(IIb) + (IIIb)	PhS	CH_2Cl_2	–78	>95 : 5
8	the same	the same	CH_2Cl_2	22	4 : 1
9	»	»	CH_2Cl_2	36	2 : 1
10	»	»	CCl_4	22	1 : 2
11 †	(IIc) + (IIIc)	4-MeC_6H_4S	CH_2Cl_2	–78	>95 : 5
12	(IId) + (IIId)	2,4-$(NO_2)_2C_6H_3S$	CH_2Cl_2	–78	2 : 1

*The (III):(II) ratio was obtained from the data of PMR spectra of the reaction mixtures when the reaction was carried out directly in the ampul of the NMR spectrometer, or after removal of the solvent at low temperature; the absence of (II) $\rightleftharpoons$ (III) isomerization was shown by control experiments.

† Experiment with addition of catalytic amounts of $CaCO_3$ (to bind traces of HCl).

‡ Experiment with reverse order of mixing the reagents (DMA was added to ArSCl).

6-Methyl-5-(4-chlorophenylthio)hept-5-en-2-one (V). Method A. A 0.26-g portion (2 mmoles) of 2-trimethylsiloxypropene (IV) and 3 mmoles of $AgBF_4$ (a solution in dichloroethane) were added to a solution of the mixture of 0.25 g (1 mmole) of (IIa + IIIa) (1:2) in 5 ml of CH_2Cl_2. After 30 min, the mixture was treated with an aqueous solution of Na_2CO_3, extracted by $CHCl_3$, and dried over Na_2SO_4. The residue after the removal of the solvent was separated by TLC (SiO_2, hexane–ether, 2:1). Yield, 0.1 g (39%) of (V). m/z 268 (M^+). PMR spectrum (250 MHz, $CDCl_3$): 1.94 d (3H, J = 1, MeC=), 1.99 d (3H, J = 1, MeC=), 2.2 s (3H, MeC=O), 2.55 m (4H, CH_2CH_2), 7.17 m (4H, J = 9, C_6H_4). Found: C 62.46; H 6.44%. $C_{14}H_{17}ClOS$. Calculated: C 62.56; H 6.37%.

Method B. A 0.26-g portion (2 mmoles) of TMSE (IV) and 0.136 g (1 mmole) of $ZnCl_2$ was added at 0°C to a mixture of 0.25 g (1 mmole) of (IIa + IIIa) (2:1) in 5 ml of $MeNO_2$. After 30 min, the mixture was treated as in method A. Yield, 0.13 g (48%) of (V). The physical constants are similar to those given above.

2-[3-Methyl-2-(4-chlorophenylthio)but-2-enyl]cyclohexan-1-one (VII). From 0.5 g (2 mmoles) of the (IIa + IIIa) mixture (2:1) and 0.68 g (4 mmoles) of TMSE (VI), 0.38 g (60%) of V(II) was obtained by method A. m/z 308 (M^+). PMR spectrum (60 MHz, CCl_4): 1.4-2.3 m (17H), 7.13 d (4H, J = 2). Found: C 65.90; H 7.12%. $C_{17}H_{21}ClOS$. Calculated: C 66.10; H 6.85%.

3-(4-Chlorophenylthio)-4-methylpent-3-enyl Cyclopropyl Ketone (IX). From 0.25 g (1 mmole) of the (IIa + IIIa) mixture (2:1) and 0.316 g (2 mmoles) of TMSE (VIII), 0.18 g (61%) of (IX) was obtained by method B. m/z 294 (M^+). PMR spectrum (250 MHz, $CDCl_3$): 0.87-1.09 m (5H of the ring), 1.93 s and 1.99 s (6H, Me_2C=), 2.62 d.t (4H, CH_2CH_2), 71.6 m (4H, C_6H_4). Found: C 65.15; H 6.72%. $C_{16}H_{19}ClOS$. Calculated: C 65.18; H 6.50%.

7-Methyl-6-(4-chlorophenylthio)octa-2,6-dien-1-al (XI). From 0.25 g (1 mmole) of the (IIa + IIIa) mixture (2:1) and 0.282 g (2 mmoles) of TMSE (X), 0.126 g (45%) of (XI) was obtained by method B. m/z 280 (M^+). PMR spectrum (250 MHz, $CDCl_3$): 1.81 s and 1.92 s (6H, Me_2C=), 2.34 m (4H, CH_2CH_2), 6.05 d.d (1H, $C\underline{H}CHO$), 6.72 d.t (1H, $C\underline{H}$-CHCHO), 7.06 m (4H, C_6H_4), 9.48 d.d (1H, J = 10, $C\underline{H}O$). Found: C 64.52; H 6.51%. $C_{15}H_{17}ClOS$. Calculated: C 64.16; H 6.10%.

6-(4-Chlorophenylthio)-7-methylocta-2,6-dien-4-olide (XIII). From 0.25 g (1 mmole) of the (IIa + IIIa) mixture (2:1) and 0.316 g (2 mmoles) of TMSE (XII), 0.125 g (43%) of (XIII) was obtained by method B. m/z 294 (M^+). PMR spectrum (60 MHz, CCl_4): 1.9 d and 2.07 d (6H, Me_2C), 2.66 d (2H, J = 7, CH_2), 4.37 t.t (1H, CHO), 6.15 d.d (1H, ($C\underline{H}CHO$), 7.2 s (4H, C_6H_4), 7.47 d. (1H, CHC=O).

CONCLUSIONS

The adduct of 1,1-dimethylallene with arylsulfenyl chlorides can be used to introduce the 2-aryltyioprenyl residue into molecules of carbonyl compounds.

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SYNTHESIS AND STRUCTURE OF DIASTEREOMERS OF Λ- AND Δ-BIS[N-3-R'-SALICYLIDENE-(Z,E)-DEHYDROAMINOBUTYRATO]COBALTATE(III)

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UDC 542.91+541.6:541.49:547.9:577.15

Dehydroamino acids are currently attracting attention as important constituents of physiologically active compounds [1], and as intermediates in pyridoxal-catalyzed enzymic β-elimination and the synthesis of amino acids containing electronegative substituents in the β position [2]. No attempt has hitherto been made to study the stereochemistry of these reactions in systems modeling pyridoxal catalysis.

As the first step in this direction, we have synthesized and examined the structures of the diastereomeric complexes sodium Λ- and Δ-bis[N-3-R'-salicylidene-(Z,E)-dehydroaminobutyrato]cobaltate(III), obtained by the β elimination of the acyl group from the complexes sodium Λ- and Δ-bis[N-3-R'-salicylidene-(S)-O-acylthreoninato]cobaltate(III). We have also obtained preliminary data on the reactivity of the dehydroaminobutyrate moiety in nucleophilic addition reactions.

In these compounds, salicylaldehyde functions as the simplest analog of pyridoxal, and the chiral environment of the dehydroaminobutyric moiety in these complexes imitates the chiral environment of the active site in the enzyme. The stereochemical inertness of the complexes enables the formation and reactivity of dehydroamino acids to be studied in water, over a wide range of pH values, and under conditions in which the free dehydroamino acids decompose to the keto acid and ammonia.

EXPERIMENTAL

The Sephadex LH-20 used was from Pharmacia Fine Chemicals. The amino acids (Reanal, Budapest) were used without further purification; 1,4-diazabicyclooctane (dabco) was obtained from Merck. 3-Methylsalicylaldehyde was prepared as described in [3]. Alumina was prepared as described in [4].

The mixed diastereomers sodium Λ- and Δ-bis[N-salicylidene-(S)-threoninato]cobaltate(III) (BSTC) and sodium Λ- and Δ-bis[N-3-methylsalicylidene-(S)-threoninato]cobaltate(III) (MSTC) were obtained as described in [5]. The diastereomers were separated by column chromatography on LH-20 in the system C_6H_6:EtOH = 3:1. First eluted was the Λ-(SS) isomer, followed by the Δ-(SS) isomer. The diastereomers had the same electronic spectral parameters, PMR spectra, and ORD plots as those described in [5].

The PMR spectra were obtained on Tesla-467A and Bruker WP-200 instruments. Experiments on the Overhauser effect were carried out on a Bruker WP-200 using previously degassed samples. Electronic spectra were obtained on a Specord UV-VIS instrument, and ORD plots were obtained with a Jasco-ORD/VV-5. Polarimetric measurements were made on a Perkin–Elmer-241 polarimeter. The configurational component of the ORD plots of the complexes SATC and MSATC was calculated in the usual way [5]. The pH-stat used was a Radiometer SBR-2/SBU-1/TTT-1.

A. N. Nesmeyanov Institute of Heteroorganic Compounds, Academy of Sciences of the USSR, Moscow. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 2, pp. 395-404, February, 1985. Original article submitted February 7, 1984.