Brief Communications

Vicarious nucleophilic substitution of hydrogen in aldehydes and Knoevenagel reaction of iminium salts with α-halocarbanions

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Iminium salts derived from aromatic aldehydes react with α-chlorocarbanions *via* two different pathways: reaction with secondary carbanion of halomethyl sulfones proceeds as the Knoevenagel condensation, while tertiary α-chlorocarbanions gave products of vicarious nucleophilic substitution of hydrogen in parent aldehydes.

Key words: vicarious nucleophilic substitution, Knoevenagel condensation, aldehydes, carbanions.

Carbanions containing the leaving group X at the carbanionic center react with nitroarenes *via* the formation of σ^H-adducts and the subsequent β-elimination of HX to give products of the vicarious nucleophilic substitution of hydrogen (VNS).[1] A similar process was reported to occur in electrophilic alkenes, although, in these cases, the formation of cyclopropanes is a much more common reaction.[2] It could be of great interest to expand the VNS reaction on electrophilic carbon—heteroatom double bonds, such as in aldehydes or aldimines. However, the reaction of α-chlorocarbanions with these electrophilic partners gave usually oxiranes and aziridines. Recently we have reported that VNS does occur in the reaction of some highly electrophilic aldimines with carbanions of chloromethyl *p*-tolylsulfone and chloroform.[3]

Aromatic aldehydes treated with perchlorates of secondary aliphatic amines in refluxing toluene form the corresponding dialkyliminium perchlorates,[4] which are much more active electrophilic reactants than parent aldehydes and form readily adducts with some C-nucleophiles.[5—8] The addition of α-halocarbanions to these salts would give substituted trialkylamines, which show much less tendency for intramolecular substitution than analogous anionic adducts to aldehydes or imines, one can therefore expect that base-induced β-elimination would occur readily to give the VNS products.

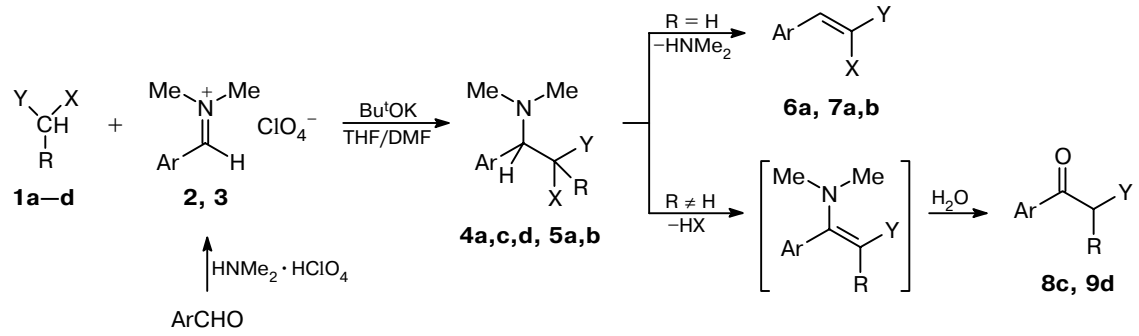
Results and Discussion

Indeed, the addition of pre-formed carbanions of halomethyl tolylsulfones **1a**,**b** to iminium salts **2** and **3** (Scheme 1) gave the expected adducts (**4a, 5a,b**), which could be isolated and purified, for example, **5a,b**. Treatment of these adducts with a base resulted, however, in the elimination of dimethylamine, not HX, to give

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 11, pp. 2136—2138, November, 2001.

1066-5285/01/5011-2236 $25.00

Scheme 1



2, 4, 6, 8: Ar = Ph
3, 5, 7, 9: Ar = 4-$MeOC_6H_4$

1—9	X	Y	R
a	Cl	Ts	H
b	Br	Ts	H
c	Cl	Ts	Cl
d	Cl	COOMe	COOMe

1-aryl-2-X-2-tosylethenes **6a, 7a,b** as single stereoisomers of the *Z*-configuration.[9] This Knoevenagel type reaction of halocarbanions is of some interest because the direct reaction of such carbanions with aldehydes gives usually oxiranes *via* intramolecular substitution in the initial adducts. Synthesis of the Knoevenagel type products with halogens at the double bond requires additional steps.[9]

At the same time, the addition of tertiary α-chlorocarbanions generated from dichloromethyl *p*-tolyl sulfone (**1c**) or dimethyl chloromalonate (**1d**) to iminium salts **2** and **3** produces the adducts which undergo the expected base-induced β-elimination of HCl giving enamines. These enamines hydrolyzed during the work-up procedure gave the products of VNS of hydrogen in aldehydes, *viz.*, α-chloro-α-tosylacetophenone (**8c**) and dimethyl (4-methoxybenzoyl)malonate (**9d**). According to ^{1}H NMR spectroscopy, compounds **8c** and **9d** exist in a $CDCl_3$ solution in the enolic form.

Thus, the general goal, vicarious substitution of hydrogen at the carbonyl group of aldehydes with α-chlorocarbanions, was realized *via* this indirect way.

Experimental

^{1}H NMR spectra were recorded on a Varian Gemini-200 (200 MHz) in $CDCl_3$. Column chromatography was carried out on silica gel (Merck, 70—230 mesh) using CH_2Cl_2 as an eluent. Precursors of carbanions, chloro-[10] and bromomethyl (*p*-tolyl)sulfones[11] and dichloromethyl (*p*-tolyl) sulfone,[12] were prepared by described procedures. Commercial dimethyl chloromalonate (Fluka) was used.

Reactions of α-halocarbanions with iminium salts 2, 3 and transformations of adducts formed. A solution of the corresponding carbanion precursor **1a—d** (2 mmol) in THF (5 mL) was added to a stirred solution of potassium *tert*-butoxide (235 mg, 2.1 mmol) in THF (4 mL) at −70 °C. To this solution iminium salt **2** or **3** (2 mmol) in DMF (1 mL) was added, and the reaction mixture was stirred for 1 h, while the temperature was increased to −20 °C. For isolation of the adducts, the mixture was poured into acidified water, and the product was extracted with methylene chloride, purified *via* column chromatography, and recrystallized. For direct conversion of the adducts of tertiary carbanions into the VNS products, additional potassium *tert*-butoxide (235 mg, 2.1 mmol) in THF (3 mL) was added, the whole mixture was stirred at −20 °C for 5 min and treated as above. Elimination of dimethylamine from adducts **4a**, **5a**,**b**: the adduct (0.5 mmol) was dissolved in a solution of sodium methoxide in methanol (prepared from Na (50 mg) and methanol (20 mL)), and after 2—4 h the mixture was poured into water and extracted with methylene chloride, and the product was purified *via* column chromatography. The yields of the compounds obtained are presented in Table 1. All compounds obtained gave satisfactory spectral and analytical data, some of them are presented below.

2-Chloro-1-dimethylamino-1-(4-methoxyphenyl)-2-(*p*-tolylsulfonyl)ethane (5a). M.p. 140 °C. Found (%): C, 58.69; H, 6.11; N, 3.91. $C_{18}H_{22}ClNO_3S$. Calculated (%): C, 58.77; H, 6.03; N, 3.81. ^{1}H NMR ($CDCl_3$), δ: 1.98 (s, 6 H, NMe_2); 2.45 (s, 3 H, C_6H_4—C$\underline{H}_3$), 3.81 (s, 3 H, OMe); 4.10 (d, 1 H, J = 9.1 Hz); 5.23 (d, 1 H, J = 9.1 Hz); 6.87 (m, 2 H); 7.13 (m, 2 H); 7.32 (m, 2 H); 7.80 (m, 2 H).

2-Bromo-1-dimethylamino-1-(4-methoxyphenyl)-2-(*p*-tolylsulfonyl)ethane (5b). M.p. 124 °C (decomp.). Found (%):

Table 1. Yields of obtained adducts and elimination products

Adduct	Yield[a] (%)	Elimination product	Yield[a] (%)
4a	—[b]	**6a**	72
5a	81	**7a**	76
5b	64	**7b**	63
4c	—[b]	**8c**	40
4d	—[b]	**9d**	54

[a] Isolated yields.
[b] Not isolated.

C, 52.38; H, 5.52; N, 3.38%. $C_{18}H_{22}BrNO_3S$. Calculated (%): C, 52.43; H, 5.38; N, 3.40. ^{1}H NMR ($CDCl_3$), δ: 1.88 (s, 6 H, NMe_2); 2.45 (s, 3 H, C_6H_4—C<u>H</u>$_3$); 3.81 (s, 3 H, OMe); 4.14 (d, 1 H, J = 9.5 Hz); 5.34 (d, 1 H, J = 9.5 Hz); 6.87 (m, 2 H); 7.10 (m, 2 H); 7.31 (m, 2 H); 7.82 (m, 2 H).

***Z*-β-Chloro-β-(*p*-tolylsulfonyl)styrene (6a)**. M.p. 63—65 °C. Found (%): C, 61.38; H, 4.59. $C_{18}H_{22}ClNO_3S$. Calculated (%): C, 61.54; H, 4.48. ^{1}H NMR ($CDCl_3$), δ: 2.48 (s, 3 H, C_6H_4—C<u>H</u>$_3$); 7.2—7.5 (m, 4 H); 7.6—7.8 (m, 5 H); 8.01 (s, 1 H, CH).

***Z*-β-Chloro-β-(*p*-tolylsulfonyl)-4-methoxystyrene (7a)**. M.p. 94—95 °C (*cf.* Ref. 9: 92—94 °C). ^{1}H NMR ($CDCl_3$), δ: 2.46 (s, 3 H, C_6H_4—C<u>H</u>$_3$); 3.86 (s, 3 H, OMe); 6.95 (m, 2 H); 7.36 (m, 2 H); 7.79 (m, 2 H); 7.87 (m, 2 H); 7.98 (s, 1 H, CH). ^{13}C NMR ($CDCl_3$), δ: 21.75, 55.43, 114.16, 123.83, 127.52, 128.82, 129.71, 132.34, 134.09, 134.55, 144.89, 161.55.

***Z*-β-Bromo-β-(*p*-tolylsulfonyl)-4-methoxystyrene (7b)**. M.p. 88—89 °C. Found (%): C, 52.18; H, 4.29. $C_{16}H_{15}BrO_3S$. Calculated (%): C, 52.33; H, 4.12. ^{1}H NMR ($CDCl_3$), δ: 2.47 (s, 3 H, C_6H_4—C<u>H</u>$_3$); 3.83 (s, 3 H, OMe); 6.94 (m, 2 H); 7.37 (m, 2 H); 7.83 (m, 2 H); 7.88 (m, 2 H); 8.01 (s, 1 H, CH).

α-Chloro-α-(*p*-tolylsulfonyl)acetophenone (8c). M.p. 139 °C (*cf.* Ref. 13: 139 °C). ^{1}H NMR ($CDCl_3$), δ: 2.49 (s, 3 H, Me); 6.21 (s, 1 H, CH); 7.38 (m, 2 H); 7.54 (m, 2 H); 7.69 (m, 1 H); 7.80 (m, 2 H); 8.05 (m, 2 H).

Dimethyl 4-methoxybenzoylmalonate (9d). M.p. 51 °C. Found (%): C, 58.73; H, 5.37. $C_{14}H_{14}O_6$. Calculated (%): C, 58.65; H, 5.30. ^{1}H NMR ($CDCl_3$), δ: 3.85 (s, 3 H, OMe); 3.89 (s, 6 H, 2 COOMe); 7.00 (m, 2 H); 7.83 (m, 2 H); 9.88 (s, OH (enol)).

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Received January 31, 2001