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Stereoselective Synthesis of (2Z)-Cinnamanilides via Desulfonylation of (2E)-α-Amido-α,β-Unsaturated Sulfones by Sodium Hydrogen Telluride

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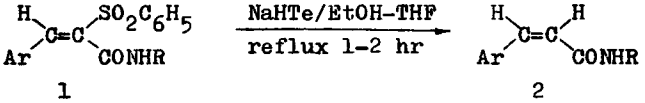
ABSTRACT

(2E)-α-Amido-α,β-unsaturated sulfones, which are easily prepared by the condensation of α-amido-sulfones with aldehydes, can be desulfonylated by sodium hydrogen telluride to give (2Z)-cinnamanilides with excellent stereoselectivity and in good yields.

(2E)-Cinnamanilides can be synthesized by many methods [1–5]. Recently, we reported that reactions of dibutyl(arylcarbamoylmethyl)tellurium halides with aldehydes in the presence of potassium carbonate also afford a convenient stereoselective synthesis of (2E)-cinnamanilides [6]. However, there are only a few reports in the literature on the stereoselective synthesis of (2Z)-cinnamanilides [7,8]. In this article, we describe work in which we have attempted to develop a convenient method of synthesis of (2Z)-cinnamanilides by using tellurium reagents.

The α-Amido-α,β-unsaturated sulfones can easily be prepared through the Knoevenagel condensation of α-amidosulfones with aldehydes [9]. They contain both the sulfonyl group and a carbon–carbon double bond, which may be reduced. Recently, we found that sodium hydrogen telluride is both a selective reducing agent and a desulfonylating agent for α,β-unsaturated compounds [10,11]. Thus, we studied the selective reduction of α-amido-α,β-unsaturated sulfones by sodium hydrogen telluride. The experimental results showed that, upon reaction of α-amido-α,β-unsaturated sulfones with sodium hydrogen telluride, reductive desulfonylation took place to give α,β-unsaturated amides preferentially but with the conjugated C=C double bond remaining unaffected (method A).

This procedure gave excellent stereoselectivity. Starting from (2E)-α-amido-α,β-unsaturated sulfones **1**, desulfonylation afforded Z-isomers (with almost 100% stereospecificity) of cinnamanilides **2** which cannot be prepared by the Wittig reaction or by a condensation reaction.



1 2

The possible mechanism is that the hydrotelluride anion makes a nucleophilic attack on the sulfonyl group of the amido-α,β-unsaturated sulfones **1** to form a vinyl anion which then captures a proton to give cinnamanilides **2** with retention of the configuration.

Dedicated to Prof. Yao-Zeng Huang on the occasion of his eightieth birthday.

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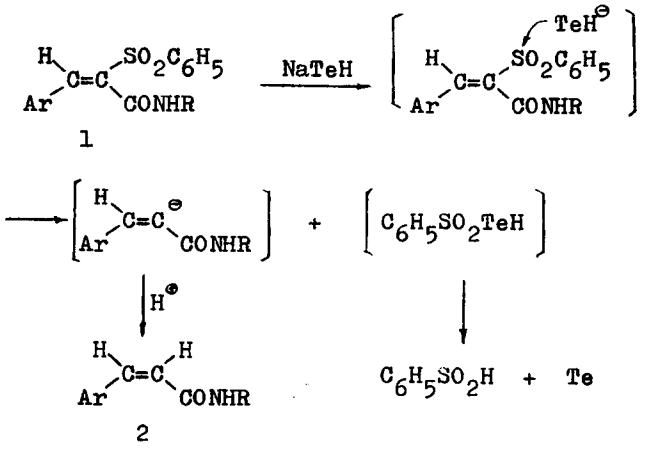
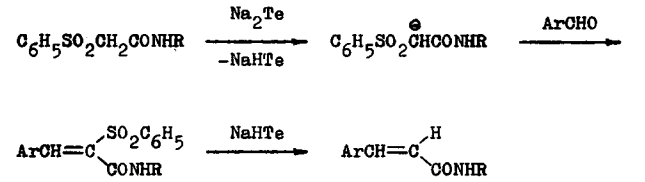
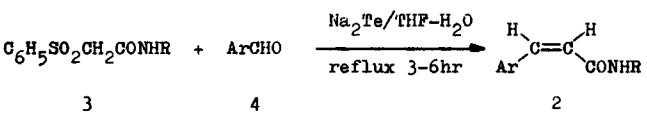


In view of the basicity of sodium telluride, we thought that it might cause amidosulfones to undergo condensation with aldehydes to give α-amido-α,β-unsaturated sulfones, the reagent itself being changed into sodium hydrogen telluride. Since sodium hydrogen telluride can effect reductive desulfonylation of α-amido-α,β-unsaturated sulfones, we reasoned that the tandem reactions of condensation and desulfonylation, which start from the reaction of α-amido-sulfones with aromatic aldehydes, can take place in a one-pot reaction under the action of sodium telluride.



The experimental results showed that α-amidosulfones do indeed undergo a one-pot reaction with aromatic aldehydes to give cinnamanilides in the presence of sodium telluride (method B).



The one-pot reaction gave excellent stereoselectivity, Z-isomers being formed preferentially, with little or no E-isomers being detected by ^1H NMR spectroscopy. This method has the advantages of convenient operation, mild conditions, good yields, and the fact that tellurium can be recovered for subsequent utilization.

EXPERIMENTAL

All melting points are uncorrected. Proton nuclear magnetic resonance (^1H NMR) spectra were determined with a JEOL FX 90Q or an XL-200 spectrometer using tetramethylsilane as the internal standard. Infrared (IR) spectra were recorded on a Perkin-Elmer 983 instrument.

TABLE 1 Synthesis of (2Z)-Cinnamanilides **2a–i**

Product	Ar	R	Yield (%) Method A	Yield (%) Method B
2a	C_6H_5	C_6H_5	87	81
2b	4-$CH_3OC_6H_4$	C_6H_5	82	75
2c	4-ClC_6H_4	C_6H_5	84	76
2d	2-ClC_6H_4	C_6H_5	72	67
2e	3-BrC_6H_4	C_6H_5	81	73
2f	4-BrC_6H_4	C_6H_5	78	71
2g	C_6H_5	i-C_4H_9	79	71
2h	4-$CH_3OC_6H_4$	i-C_4H_9	81	70
2i	4-ClC_6H_4	i-C_4H_9	82	72

The α-Amido-α,β-unsaturated sulfones (**1a–i**) were prepared according to the method described in the literature [9].

*Synthesis of (2Z)-Cinnamanilide (**2a**) (Typical Procedure)*

Method A. A solution of (2E)-α-phenylamido-β-phenyl-ethenyl phenyl sulfone (**1a**; 3.63 g, 10 mmol) in THF (30 mL) was added to a solution of sodium hydrogen telluride, prepared from tellurium (1.30 g, 10 mmol) and sodium borohydride (0.9 g, 24 mmol) in ethanol (20 mL) under nitrogen, and the mixture was stirred under reflux for 1 hour. The reaction was quenched by the addition of water (20 mL), and the mixture was kept open to air to cause precipitation of tellurium powder. After 20 minutes, the mixture was filtered and the filtrate was extracted with chloroform (3 × 20 mL). The combined organic phase was dried ($MgSO_4$) and concentrated to give the crude product **2a**, which was purified by column chromatography on silica gel using chloroform as eluent. Yield: 1.94 g (87%), mp 99–101°C (Ref [7], 101–102°C). IR (KBr), 1665, 1625 cm^{-1}; ^1H NMR ($CDCl_3$), δ 6.05 (d, 1H, J = 12 Hz), 6.77 (d, 1H, J = 12 Hz), 7.04–7.80 (m, 11H, ArH, NH).

Method B. A solution of α-phenylsulfonylacetanilide (**3a**; 2.75 g, 10 mmol) and benzaldehyde (**4a**; 1.27 g, 12 mmol) in THF (20 mL) was added to a solution of sodium telluride, prepared by heating a mixture of tellurium (1.30 g, 10 mmol), sodium borohydride (0.9 g, 24 mmol), and water (10 mL) at 60–70°C under nitrogen. An instaneous reaction occurred, and the color of the reaction mixture changed from colorless to violet. The mixture was then stirred under reflux for 4 hours. The completion of the reaction was detected by TLC (silica GF, benzene as eluent). The remaining workup was

analogous to that given for method A and gave **2a**. Yield: 1.8 g (81%); mp 99–101°C.

*(2Z)-4-Methoxycinnamanilide (**2b**).* Yield, 82% (method A), 75% (method B); mp 84–86°C; IR (KBr), 1655, 1630 cm^{-1}; ^1H NMR ($CDCl_3$), δ 3.86 (s, 3H, OCH_3), 6.90 (d, 1H, J = 12 Hz), 6.75 (d, 1H, J = 12 Hz), 6.78–7.85 (m, 10H, ArH, NH); $C_{16}H_{15}NO$. Calcd C 75.87; H, 5.97; N, 5.53. Found C, 75.49; H, 6.21; N, 5.66.

*(2Z)-4-Chlorocinnamanilide (**2c**).* Yield, 84% (method A), 76% (method B); mp 122–124°C; IR (KBr), 1665, 1628 cm^{-1}; ^1H NMR ($CDCl_3$), δ 6.28 (d, 1H, J = 12 Hz), 6.86 (d, 1H, J = 12 Hz), 6.95–7.83 (m, 10H, ArH, NH); $C_{15}H_{12}ClNO$. Calcd C, 69.91; H, 4.69; N, 5.43. Found C, 70.28; H, 4.31; N, 5.82.

*(2Z)-2-Chlorocinnamanilide (**2d**).* Yield, 72% (method A), 67% (method B); mp 151–153°C; IR (KBr), 1664, 1627 cm^{-1}; ^1H NMR ($CDCl_3$), δ 6.12 (d, 1H, J = 12 Hz), 6.73 (d, 1H, J = 12 Hz), 7.02–7.98 (m, 10H, ArH, NH); $C_{15}H_{12}ClNO$. Calcd C, 69.91; H, 4.69; N, 5.43. Found C, 69.72; H, 4.43; N, 5.83.

*(2Z)-3-Bromocinnamanilide (**2e**).* Yield, 81% (method A), 73% (method B); mp 126–128°C; IR (KBr), 1665, 1626 cm^{-1}; ^1H NMR ($CDCl_3$), δ 6.10 (d, 1H, J = 12 Hz), 6.88 (d, 1H, J = 12 Hz), 6.72–7.55 (m, 10H, ArH, NH); $C_{15}H_{12}BrNO$. Calcd C, 59.63; H, 4.00; N, 4.64. Found C, 59.28; H, 3.73; N, 5.02.

*(2Z)-4-Bromocinnamanilide (**2f**).* Yield, 78% (method A), 71% (method B); mp 162–164°C; IR (KBr), 1666, 1628 cm^{-1}, ^1H NMR ($CDCl_3$), δ 6.29 (d, 1H, J = 12 Hz), 6.84 (d, 1H, J = 12 Hz), 7.06–7.76 (m, 10H, ArH, NH); $C_{15}H_{12}BrNO$. Calcd C, 59.63; H, 4.00; N, 4.64. Found C, 59.30; H, 4.32; N, 4.98.

*(2Z)-N-Isobutylcinnamanilide (**2g**).* Yield, 79% (method A), 71% (method B); mp 77–79°C; IR (KBr), 1650, 1625 cm^{-1}; ^1H NMR ($CDCl_3$), δ 0.95 [d, 6H, J = 6.5 Hz, $CH(CH_3)_2$], 1.80 [m, 1H, $CH(CH_3)_2$], 3.20 (m, 2H, $NHCH_2CH$), 5.75 (br, 1H, NH), 5.90 (d, 1H, J = 12 Hz), 6.82 (d, 1H, J = 12 Hz), 5.82–7.52 (m, 5H, ArH); $C_{13}H_{17}NO$. Calcd C, 76.81; H, 8.43; N, 6.89. Found C, 76.45; H, 8.12; N, 7.23.

*(2Z)-N-Isobutyl-4-methoxycinnamanilide (**2h**).* Yield, 80% (method A), 70% (method B); mp 70–72°C; IR (KBr), 1655, 1625 cm; ^1H NMR ($CDCl_3$), δ 0.92 [d, 6H, J = 6.5 Hz, $CH(CH_3)_2$], 1.81 [m, 1H, $CH(CH_3)_2$], 3.21 (m, 2H, $NHCH_2CH$), 3.79 (s, 3H, OCH_3), 5.85 (br, 1H, NH), 5.90 (d, 1H, J = 12 Hz), 6.84 (d, 1H, J = 12 Hz), 6.86–7.53 (m, 4H, ArH); $C_{14}H_{19}NO_2$. Calcd C, 72.08; H, 8.21; N, 6.00. Found C, 71.73; H, 7.98; N, 6.38.

*(2Z)-N-Isobutyl-4-chlorocinnamanilide (**2i**).* Yield, 82% (method A), 72% (method B); mp 86–88°C; IR (KBr), 1670, 1635 cm; ^1H NMR ($CDCl_3$), δ 0.95 [d, 6H, J = 6.5 Hz, $CH(CH_3)_2$], 1.83 [m, 1H, $CH(CH_3)_2$], 3.22 (m, 2H, $NHCH_2CH$), 5.68 (br, 1H, NH), 6.15 (d, 1H, J = 12 Hz), 6.91 (d, 1H, J = 12 Hz), 6.80–7.54 (m, 4H, ArH); $C_{13}H_{16}ClNO$. Calcd C, 65.68; H, 6.78; N, 6.89. Found C, 65.93; H, 6.42; N, 6.23.

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