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Synthesis of 4 - (Substituted benzene)-1(substituted sulfonyl) Semicarbazides in Aqueous Medium

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Abstract: An expeditious solvent less approach for the synthesis of 4-(Substituted benzene)-1(substituted-sulfonyl) semicarbazides **3a-f** from substituted phenyl semicarbazide **1a-b** with substituted sulfonylurea chloride **2a-c** in water was studied. There is increase in yield and reaction time was reduced. These compounds have been characterized on the basis of elemental analysis, IR, ^{1}H NMR and M.S.

Key words: Semicarbazides

INTRODUCTION

The well-known classic sulfonylurea,sulfo- nyl semicarbazides, sulfonylaminopyrimidines display a hypoglycemic activity [1-3]. The aim of this work is to synthesis of novel sulfonylurea semicarbazide; by a convenient procedure (solvent free condition).Organic synthesis under solvent free condition is of great relevance because of emerging environmental issues [4-7]. The current global awareness in developing environmentally friendly technologies and our philosophy is developing such technologies. It was decided to carry out the reaction in non-hazardous solvent. Performing a reaction in water is the ultimate dream of an organic chemist.This communication describes our effort toward this [8-9].

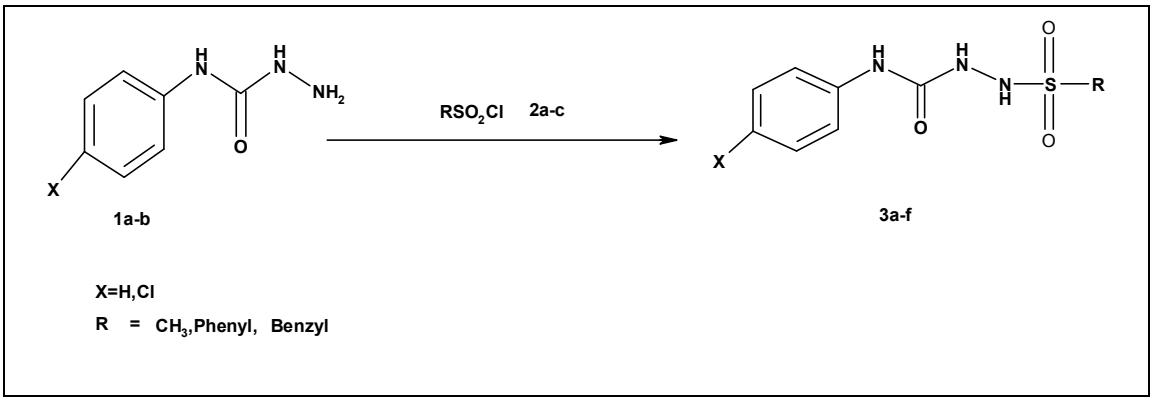
RESULTS AND DISCUSSION

The sulfonyl semicarbazide derivatives 3a-f were synthesized by refluxing appropriately substituted phenyl semicarbazide 1a-b and substituted sulfonyl chloride 2a-c in THF in the presence of pyridine for 5-6 hours [10] in this method the yields are poor. The crude product was purified by crystallizing the Solid product in appropriate amount of methanol. We now report a modified and convenient procedure for the reaction of substituted phenyl semicarbazide 1a-b with substituted sulfonyl chloride 2a-c using water but not organic solvent. Compound 3a-f formed within 1-1.5 hours in 90-95% overall yield and remarkable advantages because of easier workup.

EXPERIMENTAL

All the melting points are uncorrected and recorded on BÜCHI Melting Point apparatus (Model No. B-540); The IR Spectra were recorded in cm^{-1} for KBr pellets on Perkin Elmer (Model No.1000). The ^{1}H NMR Spectra were recorded on Bruker 400 MH_Z spectrophotometer in deuteriochloroform using TMS as internal standard and the chemical shift are expressed in ppm. MS spectra were recorded on Agilent 1100 Mass spectrophotometer.

SCHEME 1:



General Procedure for the synthesis of:

4-(Substitutedbenzene)-1 (substituted sulfonyl) semicarbazides 3a-3f (General method):

The solid mixture of substituted phenyl semicarbazide 1a-b (5 mmol, 1.0 equiv.) and substituted sulphonyl chloride 2a-c (5mmol, 1.0equiv.) was suspended in 25 ml water. The pH of the suspension was adjusted and was maintained at 8.0 by adding 1 mol/L Na_2CO_3 aqueous solution at room temperature. It took 1.0-1.5 hours for the reaction to complete. Concentrated HCl was added slowly to adjust pH=2.0. The precipitate was collected by filtration, washed with water and dried to afford the title compound. No further purification was needed.

1-Phenyl-4-methylsulphonylsemicarbazide (3a).
mp190-192 ^{o}C;
ir(potassiumbromide):3342(SO_2NH),
3204**(**CONH),1654(C=O),1317
(S=O)cm-^{1};^{1}Hnmrdimethylsulfoxide-d_6)**:** δ2.99(s,3H),
6.96-6.99(t,1H),7.24-7.28(t, 2H),
7.48-7.50 (d.2H), 8.58(s, 1H), 8.66 (s, 1H), 9.21(s, 1H). ms: m/z 228.5 (base peak),229.4. *Anal* Calcd. For $C_8H_{11}N_3O_3S$: C, 41.91; H, 4.84; N, 18.33.Found: C, 41.90; H, 4.82; N, 18.38.

1-Phenyl-4-benzenesulphonyl semicarbazide (3b).
mp 210-212^{o}C ;ir (potassiumbromide):
3355(SO_2NH),3209**(**CONH),1600(C=O),1337
(S=O)cm^{1};^{1}Hnmr(dimethylsulfoxide-d_6)**:**
δ 6.92-6.96(t,1H),7.19-7.23(t,2H),7.34-7.36 (d.2H), 7.58-7.62(t, 2H), 7.65-7.69(t, 2H),7.85-7.87(d.2H), 8.34(s, 1H), 8.52(s, 1H), 9.66(s, 1H); ms: m/z 291.2, 290.3(base peak) ,141.
Anal. Calcd. For $C_{13}H_{13}N_3O_3S$: C, 53.60; H, 4.50; N, 14.42.Found: C, 53.64; H, 4.58; N, 15.32.

1-Phenyl-4-benzyl sulphonyl semicarbazide (3c).
mp 198 ^{o}C; ir (potassiumbromide):
3299 (SO_2NH)**,**3130**(**CONH),1663(C=O),1337
(S=O)cm-^{1};^{1}H nmr (dimethyl sulfoxide-d_6)**:** δ 4.44(s, 2H), 6.97-7.00 (t, 1H), 7.26-7.30 (t, 2H), 7.37-7.41(d, 3H), 7.46-7.57(m, 4H), 8.62(s, 1H), 8.69(s, 1H), 9.33(s, 1H); ms: m/z 306 (base peak), 323, 328 .
Anal. Calcd. For $C_{14}H_{15}N_3O_3S$: C, 55.07; H, 4.95; N, 13.76.Found: C, 55.17; H, 4.98; N, 13.86.

Parachloro1-phenyl-4-methylsulphonyl semicarbazide (3d).
mp 263-266 ^{o}C; ir (potassium bromide):
3339 (SO_2NH)**,** 3258 **(**CON-H) 1656 (C=O), 1317(S=O) cm-^{1};^{1}H nmr (dimethyl sulfoxide-d_6)**:** δ 2.99(s, 3H), 7.29-7.31 (d, 2H), 7.54-7.57(d, 2H), 8.71 (s.1H), 8.89 (s,1H), 9.24 (s,1H) ms: m/z 262.5, 264.3.
*Anal.*Calcd.for $C_8H_{10}N_3O_3SCl$: C, 36.44; H, 3.82; N, 15.93.Found: C, 36.48; H, 3.86; N, 16.00.

Para-chloro1-phenyl-4-benzenesulphonyl semicarbazide (3e).
mp 230-233 ^{o}C; ir (potassiumbromide):
3332(SO_2NH)**,**3299**(**CON-H),1678 (C=O),1320 (S=O) cm-^{1};
^{1}Hnmr(dimethylsulfoxide-d_6): δ 7.25-.28(d,2H),7.40-7.42(d,2H), 7.57-7.61(t, 2H),), 7.64-7.68(t, 1H), 7.83-7.86 (d, 2H), 8.47(s,1H), 8.75(s, 1H), 9.71(s,1H).
ms:m/z 324.1, 326.1.
*Anal.*Calcd.For $C_{13}H_{12}N_3O_3SCl$: C, 47.93; H, 3.71; N, 12.90 Found: C, 47.98; H, 3.75; N, 13.02.

1-Phenyl-4-benzil sulphonyl semicarbazide (3f).
mp228-230 ^{o}C ;ir(potassiumbromide):
3347(SO_2NH)**,**3253**(**CON-H),1693(C=O),1317(S=O)cm-^{1}**;**
^{1}Hnmr. (dimethyl sulfoxide-d_6) δ 4.44(d, 2H), 7.31-7.33(d, 2H), 7.36-7.41(m, 3H), 7.44- 7.46(m, 2H), 7.55-7.58(d, 2H), 8.76(s, 1H), 8.91(s, 1H), 9.36(s, 1H), ms: m/z 340 (base peak), 362.2, 364.1,
*Anal.*Calcd.For $C_{14}H_{14}N_3O_3SCl$: C, 49.49 H, 4.15; N, 12.37 Found: C, 50.02.; H, 4.20; N, 12.70.

CONCLUSION

In conclusion, the water serves as an excellent medium for the condensation of phenyl semicarbazide with sulphonyl chloride for the synthesis of sulphonyl semicarbazide.

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