

SYNTHESIS OF SOME NEW HETEROCYCLIC COMPOUNDS WITH EXPECTED POTENTIAL BIOLOGICAL ACTIVITY

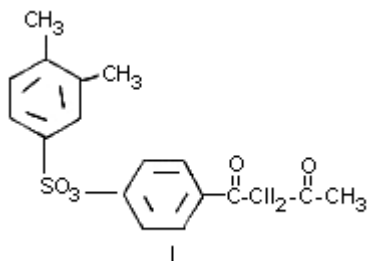
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SUMMARY: Condensation of 4-acetylphenyl-3', 4'-xylene sulphonate with ethyl acetate in presence of sodium metal gave the 1,3-diketone (1). Reaction of 1 with hydrazine hydrate, phenyl hydrazine, hydroxylamine, o-aminophenol and thiourea has been studied. Condensation of 3,4-xylene sulphonate ester of p-hydroxy benzaldehyde VI with p-aminobenzoic acid gave the corresponding Schiff base VII. Reaction of VII with thioglycolic acid and chloroacetylchloride has been also studied.

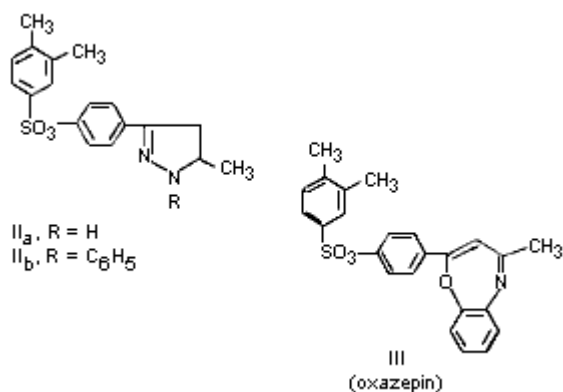
Key Word: Heterocyclic compounds.

INTRODUCTION

The promising usefulness of the pyrazole (1) isoxazole (2) and thiazole (3-6) derivatives as biologically active products has been previously reported. On the other hand, the aromatic esters of arylsulphonic acids are known to exhibit marked acaricidal (7), insecticidal (8) and bactericidal (9) activity. These observations have encouraged me to synthesize some new products containing the pyrazole, isoxazole and thiazole with aryl sulphonate moiety hoping to obtain new compounds with potential biological activity. This was followed by treatment of the 4-acetylphenyl-3', 4'-xylene sulphonate (10) with ethyl acetate in presence of sodium metal gave the corresponding 1,3-diketone derivative I. The structure of I has been established from the analytical data and i.r. spectrum which showed stretching frequencies at 1622 and 1618 cm^{-1} for tautomeric keto-enol forms (11).

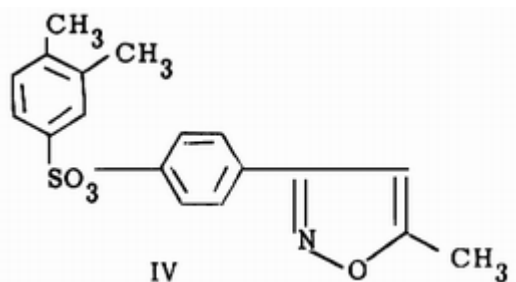


Treatment of I with hydrazine hydrate, phenylhydrazine and o-amino phenol in glacial acetic acid afforded the pyrazoles IIa, b and oxazepin III derivatives respectively. These products were identified by correct elemental analysis and i.r. spectra which showed bands at 1600 cm^{-1} , 1645 cm^{-1} corresponding to C=C and C=N and the band at 3300 cm^{-1} assignable to the OH group has disappeared.

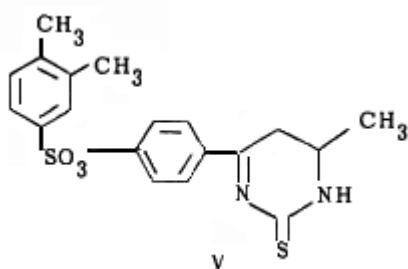


Treatment of I with hydroxyl amine hydrochloride in presence of sodium acetate afforded the corresponding oxazole derivative IV. Structure of IV was inferred by correct analytical results and i.r. spectrum, which revealed bands at 1620 cm^{-1} , 1945 cm^{-1} , and 2940 cm^{-1} corresponding to C=C, C=N and CH_3 groups, respectively.

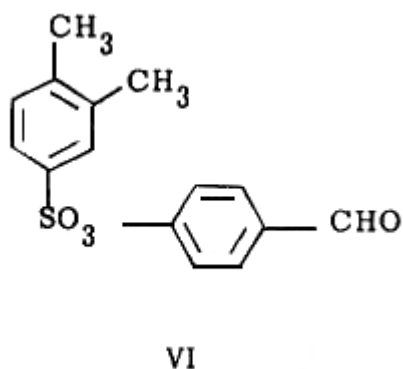
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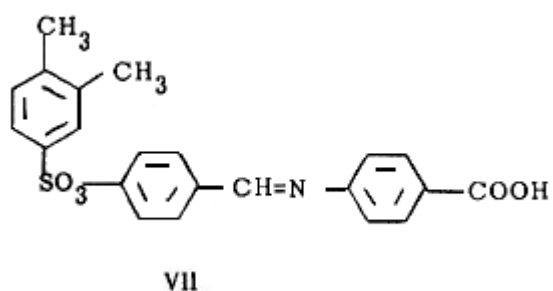
Condensation of I with thiourea afforded the thiopyrimidine derivative V. Structure V has been established from analytical data and i.r. spectrum which showed absorption bands at 1645, 3100 cm^{-1} corresponding to C=N and NH groups.



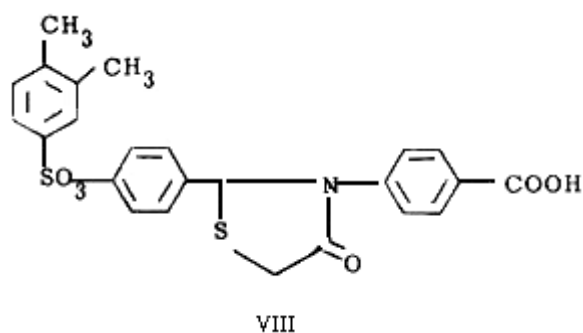
On the other hand, treatment of the 3,4-xylene sulphonyl chloride (12) with p-hydroxybenzaldehyde in presence of sodium hydroxide afforded 3,4-xylene sulphonate ester of p-hydroxy benzaldehyde (13) VI. Structure VI was characterised by correct elemental analysis and i.r. spectrum which revealed absorption bands at 1340, 1710 cm^{-1} attributable to the SO_3 and CHO groups.



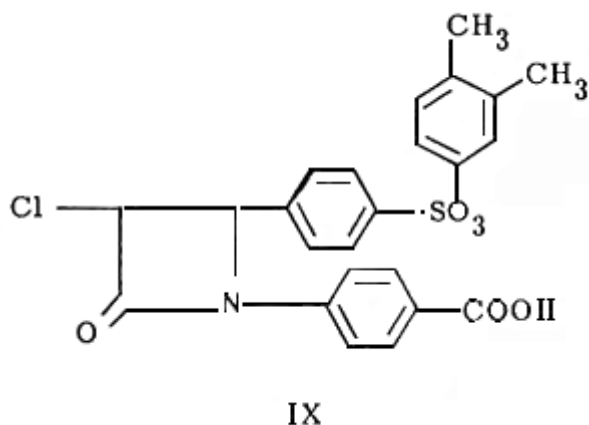
Condensation of compound VI with p-aminobenzoic acid in absolute ethanol gave corresponding xylenyl Schiff base VII. Beside correct elemental analysis, the i.r. spectrum of VI showed a band at 1670 cm^{-1} due to the C=N group.



Reaction of compound VII with both of thioglycolic acid in dry benzene and chloroacetyl chloride in dry dioxane afforded the corresponding thiazolidinone VIII and azetidinone IX derivatives. These products were characterised correct analytical results and i.r. spectra which showed absorption bands in the region 1700-1695 cm^{-1} attributed to the C = O group of the thiazolidin-4-one (14) and bands assigned to the stretching vibration of the carbonyl group of monocyclic β -lactam near 1700-1630 cm^{-1} (15,16).



Thiazolidine-4-one derivative



3-chloro-4-substituted-1-(4'-carboxy)-phenylazetidine-2-one (β -lactam).

EXPERIMENTAL

Melting points are uncorrected. Analytical data were determined by the Microanalytical Unit, Faculty of Science, Mansoura University. The infra-red spectra were recorded on a Unicam Spectrophotometer Model SP 1200 using KBr wafer technique.

Reaction of 4-acetylphenyl-3', 4'-xylene sulphonate with ethyl-acetate. Formation of the 1,3-diketone I.

A suspension of 4-acetylphenyl-3', 4'-xylene sulphonate (0.01 mole) in freshly distilled ethyl acetate (50 ml, 0.57 mole) was slowly added to powdered sodium metal (4 gm, 0.17 gm atom). The reaction mixture was refluxed for five hours cooled then acidified with acetic acid. The precipitated solid product was separated and crystallized from ethanol as white crystals, m.p. 280°C in 73.5% yield.

Analysis: for $C_{18}H_{18}O_5S$ (346)
 Calcd.: C, 62.42; H, 5.20; S, 9.24
 Found : C, 62.31; H, 5.15; S, 9.12

Reaction of I with hydrazine hydrate and phenyl hydrazine. Formation of compounds IIa, b.

Equimolar amounts of compound I (0.05 mole) and hydrazine hydrate or phenylhydrazine in 85 ml) glacial acetic acid were refluxed for three hours. The reaction mixture was diluted with 20 ml water and neutralized with sodium bicarbonate solution. The solid separated was crystallized from ethanol as white crystals for IIa m.p. 36°C in 80% yield and for IIb m.p. 72°C in 66% yield.

Analysis for IIa: $C_{18}H_{18}O_3S$ (342)
 Calcd.: C, 63.15; H, 5.26; S, 9.35
 Found : C, 63.01; H, 5.12; S, 9.23

Analysis for IIb: $C_{24}H_{22}N_2O_3S$ (358)
 Calcd.: C, 63.68; H, 6.14; S, 8.93
 Found : C, 63.51; H, 6.00; S, 8.81

Reaction of I with o-aminophenol. Formation of the oxazepin derivative III.

A mixture of compound I (0.01 mole) and o-aminophenol (0.01 mole) in 30 ml acetic acid, was heated at 80°C for one hour. The reaction mixture gave on cooling a solid product which on treatment with boiling methanol gave III as insoluble pale yellow crystals recrystallized from acetic acid, m.p. 140°C in 50% yield.

Analysis for : $C_{24}H_{21}NO_4S$ (419)
 Calcd : C, 68.73; H, 5.01; S, 7.63
 Found : C, 68.59; H, 5.00; S, 7.62

Reaction of I with hydroxylamine hydrochloride. Formation of the isoxazole derivative VI.

A solution of hydroxylamine hydrochloride (0.52 gm, 0.0075 mole) and sodium acetate (0.21 gm, 0.0025 mole) in the least amount of water was added to a suspension of compound I (0.005 mole) in ethanol (70 ml), the reaction mixture was refluxed for seven hours, cooled and diluted with water (50 ml). The obtained solid was crystallized from acetic acid as white crystals, m.p. > 300°C in 40% yield.

Analysis for : $C_{18}H_{17}NO_4S$ (343)
 Calcd. : C, 62.97; H, 4.95; S, 9.32
 Found : C, 62.79; H, 4.91; S, 9.22

Reaction of I with thiourea. Formation of compound V.

A mixture of compound I (0.0025 mole) and thiourea (1 gm, 0.016 mole) in ethanol (50 ml) refluxed for three hours. The reaction mixture was poured onto ice-cold water, and the obtained solid was crystallized from ethanol as white crystals, m.p. 156°C in 50% yield.

Analysis for : $C_{19}H_{20}N_2O_3S_2$ (388)
 Calcd. : C, 58.76; H, 5.15; S, 16.49
 Found : C, 58.61; H, 5.01; S, 16.32

Reaction of 3,4-xylene sulphonyl chloride with p-hydroxy-benzaldehyde. Formation of VI.

This was followed using the general procedure described in literature (13). It was recrystallized from aqueous ethanol as white crystals m.p. 87°C in 50% yield.

Analysis for : $C_{15}H_{14}O_4S$ (290)

Calcd. : C, 62.06; H, 4.82

Found : C, 62.05; H, 4.56

Reaction of VI with p-aminobenzoic acid. Formation of the xylene Schiff base VII.

A mixture of 3,4-xylene sulphonate ester of p-hydroxy benzaldehyde VI (0.01 mole) and the p-aminobenzoic acid (0.01 mole), in ethanol (20 ml) was refluxed for four hours. The precipitated solid filtered off and crystallized from ethanol as white crystals m.p. 200°C in a 63% yield.

Analysis for : $C_{22}H_{19}NO_5S$ (409)

Calcd. : C, 64.54; H, 4.68

Found : C, 64.25; H, 4.43

Reaction of VII with thioglycollic acid. Formation of the thiazolidine-4-one derivative VIII.

A mixture of the Schiff base VII (0.02 mole) and thioglycollic acid (0.02 mole) in 100 ml dry benzene was refluxed for twenty hours. The precipitated solid product was separated and crystallized from ethanol as white crystals m.p. 76°C in 50% yield.

Analysis for : $C_{24}H_{21}NO_6S_2$ (483)

Calcd. : C, 59.62; H, 4.34

Found : C, 59.51; H, 4.19

Reaction of VII with chloroacetyl chloride. Formation of azetidinone derivative IX.

A mixture of VII (0.01 mole), chloroacetyl chloride (0.02 mole) and trimethylamine (0.02 mole) in 50 ml dry dioxane was refluxed for seven hours. The obtained solid product was separated and crystallized from ethanol as white crystals, m.p. 67°C in 50% yield.

Analysis for : $C_{24}H_{20}NO_6SCI$ (485.5)

Calcd. : C, 59.32; H, 4.11

Found : C, 59.10; H, 4.00

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