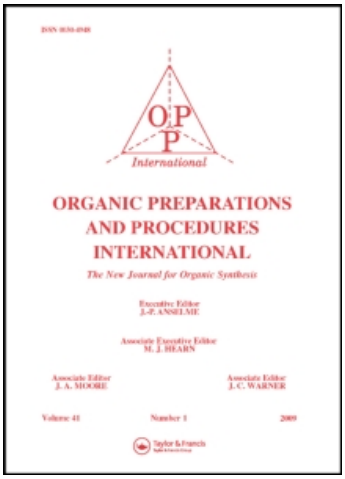

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ONE-POT SYNTHESIS OF 2-SPIROTHIAZOLIDIN-4-ONE DERIVATIVES

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ONE-POT SYNTHESIS OF 2-SPIROTHIAZOLIDIN-4-ONE DERIVATIVES

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(04/30/91)

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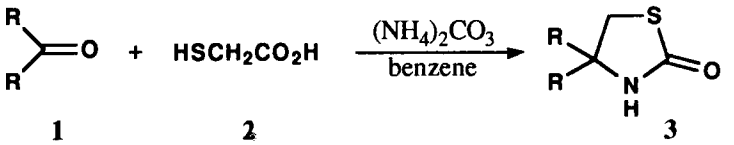
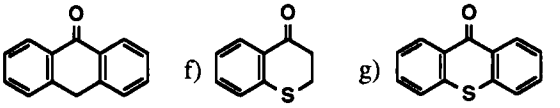
Several thiazolidinones have gained commercial importance as drugs (e. g. bactericidal, pesticidal, fungicidal, insecticidal, anticonvulsant, tuberculostatic, antiinflammatory, antithyroidal, and potentiation of pentobarbital-induced sleeping time).[1] Spiro derivatives of such compounds also exhibit interesting properties, such as photochromism, biological and optical activity.[2] Although the chemistry of thiazolidinones and of their derivatives has been studied intensely, very little is known about the synthesis of 2-spirothiazolid-4-ones. As an extension of our previous work,[3] coupled with our interest in sulfur chemistry,[4] the importance of the combination of spiro moieties with thiazolidin-4-ones led to the development of a one-step synthesis of 2-spirothiazolidin-4-one derivatives.

The synthesis was carried out by the reaction of thioglycolic acid with the cyclic carbonyl compounds in the presence of ammonium carbonate at reflux in dry benzene.



1 2 3

a) Cyclopentanone b) Cyclohexanone c) Cycloheptanone d) α-Tetralone



In a typical run, ammonium carbonate was added portionwise over 5 min to a mixture of the cyclic carbonyl compounds and thioglycolic acid in dry benzene. Thus cyclopentanone (**1a**) afforded 1-thia-4-azaspiro[4,4]nonan-3-one (**3a**) in 65% yield; similarly cyclohexanone (**1b**) gave 1-thia-4-azaspiro[4,5]decan-3-one (**3b**) in 67% yield. Cycloheptanone (**1c**) and α-tetralone (**1d**) yielded 1-thia-4-azaspiro[4,6]undecan-3-one (**3c**) and 3,4-dihydrospiro[naphthalene-1(2H)-2'-thiazolidin]-4'-one (**3d**) in 55% and 45% yields respectively. Anthrone (**1e**), thiochromanone (**1f**) and thioxanthone (**1g**) also gave corresponding spiro[anthracene-9(10H),2'-thiazolidin]-4'-one (**3e**), spiro[thiazolidine-2,4'-thiochroman]-4-one (**3f**) and spiro[thiazolidine-2,9'-thioxanthen]-4-one (**3g**) in 65%, 30% and 25% yields respectively. All the spirothiazolidin-4-ones were identified IR, ^{1}H NMR and elemental analysis.

EXPERIMENTAL SECTION

Melting points are uncorrected. ^{1}H NMR spectra were measured on EM-360 90-MHz spectropho-

tometer using TMS as an internal standard. IR spectra were recorded as KBr pellets on a Pye-Unicam SP 200-G spectrophotometer. UV absorbances were measured on a Perkin-Elmer 552 spectrophotometer. Elemental analyses were determined on a Perkin-Elmer 240C microanalyser.

Reaction of Cyclic Ketones with Thioglycolic Acid. General Procedure.- A mixture of the cyclic ketone (0.01 mole), thioglycolic acid (0.01 mole) and ammonium carbonate (0.012 mole) in dry benzene was refluxed for 24 hrs on water bath and the liberated water was removed using a Dean-Stark trap. The reaction mixture was cooled to room temperature and the solution was concentrated by evaporation under reduced pressure using a rotary evaporator. The product was collected and crystallized from the appropriate solvent.

TABLE 1. Yields, mps and Elemental Analyses of Thiazolidinones

Cmpds	mp[a] (°C)	Yield (%)	Elemental Analysis (Found) C	H	N	S
3a	158-160	65	55.00(55.30)	7.00(7.13)	8.91(8.91)	20.38(20.42)
3b	180-182	67	56.14(56.07)	7.60(7.61)	8.18(8.13)	18.71(18.59)
3c	130-132	55	58.37(58.21)	8.10(8.01)	7.56(7.42)	17.29(17.08)
3d	172-174	45	65.75(65.42)	5.93(5.72)	6.39(6.21)	14.61(14.31)
3e	170-172[b]	65	71.91(71.72)	4.86(4.64)	5.24(5.17)	11.98(11.92)
3f	210-212[b]	30	55.69(55.41)	4.64(4.48)	5.90(5.82)	27.00(26.98)
3g	180-182[b]	25	63.15(63.10)	3.85(3.62)	4.91(4.75)	22.45(22.24)

a) Recrystallized from ethanol. b) From 1:1 ethanol-water.

1-Thia-4-azaspiro[4,4]nonan-3-one (3a): IR: 1685, 2925, 3200 cm^{-1}. ^1H NMR ($CDCl_3$/TMS): δ 1.8 (m, 4H), 2.2 (m, 4H), 3.8 (s, 2H), 4.3 (s, 1H).

1-Thia-4-azaspiro[4,5]decan-3-one (3b): IR: 1695, 2925, 3220 cm^{-1}. ^1H NMR (CF_3COOH/TMS): δ 1.7-1.9 (m, 6H), 2-2.2 (m, 4H), 3.9 (s, 2H), 4.3 (s, 1H).

1-Thia-4-azaspiro[4,6]undecan-3-one (3c): IR: 1695, 2930, 3220 cm^{-1}. ^1H NMR (CF_3COOH): δ 1.8-2 (m, 8H), 2.2 (m, 4H), 3.8 (s, 2H), 4.1 (s, 1H).

3,4-Dihydrospiro[naphthalene-1(2H)-2'-thiazolidin]-4'-one (3d): IR: 1700, 2850, 2980-3010, 3150-3200 cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.1-2.4 (m, 2H), 2.6 (m, 2H), 2.8 (t, 2H), 3.7 (s, 2H), 4.2 (s, 1H), 7-7.5 (m, 2H), 7.8-8 (d, 1H).

Spiro[anthracene-9(10H)-2'-thiazolidin]-4'-one (3e): IR: 1695, 2810, 3020, 3320 cm^{-1}. ^1H NMR (CF_3COOH): δ 3.6 (s, 2H), 4.1 (s, 1H), 4.3 (s, 2H), 7.2-7.7 (m, 6H), 8.15 (d, 2H).

Spiro[thiazolidine-2,4'-thiochroman]-4-one (3f): IR: 1680, 2830, 3010, 3315 cm^{-1}. ^1H NMR (CF_3COOH): δ 2.8 (t, 2H), 3 (t, 2H), 3.8 (s, 2H), 4.1 (s, 1H), 7-7.6 (m, 3H), 7.9-8.1 (d, 1H).

Spiro[thiazolidine-2,9'-thioxanthen]-4-one (3g): IR: 1705, 2800, 2980, 3250 cm^{-1}. ^1H NMR (CF_3COOH): δ 3.7 (s, 2H), 4.1 (s, 1H), 7.2-7.7 (m, 6H), 8.15 (d, 2H).

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PHASE TRANSFER CATALYZED N-ALKYLATION OF *sym*-N,N'-DIARYLUREAS†

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sym-N,N'-Diethyldiphenylurea (Centralite I) is used commercially as stabilizer for a number of explosives.[1] Recently a non-phosgene route involving the N-ethylation of *sym*-N,N'-diphenylurea (DPU) using phase-transfer catalyst (PTC) has been reported.[2] As an extension of our work on the N-alkylation of benzanilides[3] and aminoanthraquinones,[4] we now describe the alkylation of diarylureas (DAU, **1a-d**) in the presence of base and phase-transfer catalysts.

Alkylation of DAU with diethyl sulfate, in presence of triethylbutylammonium bromide (TEBuAB), was studied using different alkalis. The results are summarized in Table 1. The use of a mixture of powdered sodium hydroxide and potassium carbonate as alkali proved to be ideal. Alkylation of **1a** with diethyl sulfate in the presence of a mixture of powdered sodium hydroxide and