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A SIMPLE ROUTE FOR THE SYNTHESIS OF OXAZEPINE-2-ONE SYSTEMS USING CHLOROSULFONYL ISOCYANATE

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Abstract: Reaction between the 1-aroyl-2-arylcyclopropane (cyclopropyl chalcone) with chlorosulfonyl isocyanate leads to the formation of seven membered heterocyclic product, namely, oxazepine-2-one.

There are only few reports in the literature for the preparation of seven membered ring compounds in a single step process.[1,2] Herein we report the simple synthesis of oxazepine-2-one systems by the interaction of chlorosulfonyl isocyanate (CSI) and 1-aroyl-2-arylcyclopropane **1a-d** (*vide* Scheme). It was observed that the chlorosulfonyl isocyanate reacted with 1-benzoyl-2-(4-methoxyphenyl)cyclopropane **1a** in dichloromethane at -15°C, to give N-sulfonylchloride-cycloadduct **3a**, which upon reductive hydrolysis, using benzenethiol and

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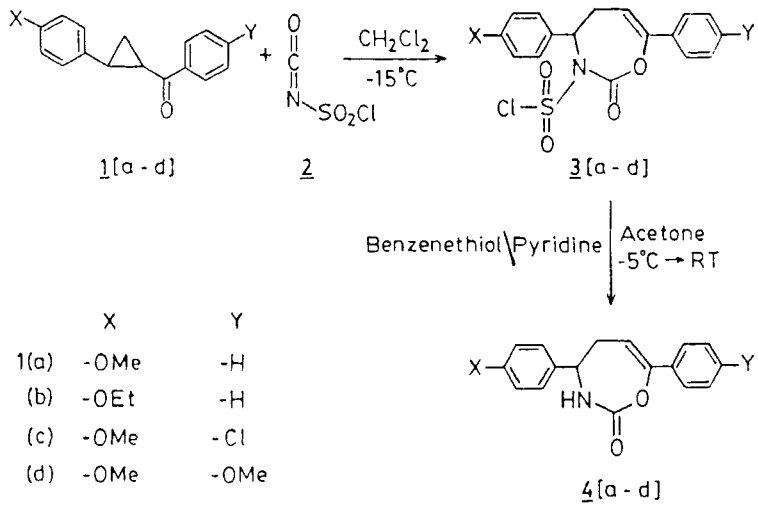
pyridine, furnished the corresponding seven membered heterocyclic compound **4a** in 50% yield.

SCHEME



	X	Y
1(a)	-OMe	-H
(b)	-OEt	-H
(c)	-OMe	-Cl
(d)	-OMe	-OMe

EXPERIMENTAL SECTION

The IR spectra were recorded on Perkin-Elmer (Model 1320). ^1H NMR spectra were recorded on Brüker WP 80 (80 MHz) instrument. Mass spectra were recorded on Jeol (JMS 600-D) mass spectrometer at 70 eV.

All reactions were carried out with dry solvents. Dichloromethane and acetonitrile were distilled from P_2O_5 separately, and stored over molecular sieves (4A°) Chlorosulfonyl isocyanate was purchased from Fluka and was used as such. 1-Aroyl-2-aryl-cyclopropanes[3,4] **1a-d** are prepared by the known procedures reported in the literature.

Reaction of 1-benzoyl-2-(4'-methoxyphenyl)cyclopropane (1a) with CSI: Preparation of 3a: (General Procedure)

To a magnetically stirred solution of **1a** (0.354g, 1.50 mmol) in 10 ml dry dichloromethane was added dropwise a solution of CSI (0.213g, 1.51 mmol), in 2 ml dichloromethane at -15°C. The solution acquired a yellow colour. Stirring was continued for 15h, by maintaining the temperature below 0°C. The reaction mixture was then concentrated to a small volume (≃ 5 ml), under reduced pressure and dry ethyl ether(20 ml) was added to it. It was kept in a refrigerator for two days. Light yellow crystals were deposited on the walls of the flask. The crystals were filtered in cold and washed twice with small volume of cold dry ether, and then dried in vacuum to yield N-sulfonyl chloride adduct (**3a**). Yield 0.295g (50%); mp 112-114°C.

Hydrolysis of N-sulfonylchloride adduct 3a

The adduct **3a** (0.225 g, 0.64 mmol) was dissolved in dry acetone (10 ml) and the resulting solution was cooled to -5°C. To this benzenethiol (0.307g. 2.79 mmol) was added with stirring. After a few minutes a solution of pyridine (0.2g, 2.54 mmol) in acetone (2 ml) was added over a period of 20 min. Stirring was continued for another 2h at this temperature and then overnight, at room temperature. The mixture was once again cooled and an equal amount of cold water (15 ml) was added dropwise. A precipitate was formed and found to contain a mixture of diphenyl disulphide and the required product by TLC. Washing the precipitate with ice-cold ether to remove the diphenyl disulphide,

leaving behind a colourless powdery material. The powdery material was dried under vacuum and then taken up in chloroform. Filtering it rapidly through a small column (5 mm diameter, 3 cm length) of TLC grade silica gel, followed by evaporation of the solvent afforded the compound (**4a**); yield: 0.10g (53%); mp (124-126°C).

Cycloadduct: (3a)

Yield: 50%; mp 112-114°C; ^{1}H NMR ($CDCl_3$): δ 2.1-2.4 (m, 1H), 3.03-3.37 (m, 1H), 3.81 (s, 3H, OCH_3), 4.85 (dd, 1H, J_1=6.25 Hz; J_2=10 Hz), 5.53 (dd, 1H, J_1=5 Hz; J_2=8.75 Hz, C_6H_5CH), 6.90-7.68 (m, 7H, Ar), 8.03-8.20 (m, 2H, *o*-phenyl H); IR (KBr): 1745 and 1675 (νC=O),1515, 1400 (νSO_2 asym), 1285, 1175 (νSO_2 sym) cm^{-1} Mass m/e (rel. int.): 395 (M^++1), 394 (M^+ 67.1), 296 (97.7), 295 (20), 251 (17.8), 105 (33.3). Anal for $C_{18}H_{16}ClNO_4S$ Calcd: C, 52.02; H, 4.06; N, 3.55%. Found: C, 52.10; H,4.15; N,3.62%.

4-(4'-Methoxyphenyl)-7-phenyl-4,5-dihydro-1,3-oxazepine-2-one: (4a)

Yield: 53%; mp 124-126°C; ^{1}H NMR ($CDCl_3$): δ 2.0-3.13 (m, 2H), 3.81 (s, 3H, OCH_3), 4.26-5.00 (m, 2H, Olefinic+benzylic), 6.53 (s, NH, D_2O exchangeable), 6.7-7.48 (m, 7H, Ar), 7.86-8.08 (m, 2H, *o*-Phenyl H); IR (KBr): 3200 (νNH), 1705 & 1680 (νC=O), 1600 (νC=C) cm^{-1} Mass m/e (rel. int.): 295 (M^+, 3.4), 220 (12.8), 218 (100), 109 (77.3), 105 (8.7). Anal for $C_{18}H_{17}NO_3$ Calcd: C, 73.22; H, 5.76; N, 4.74%. Found: C, 72.84; H, 5.59; N, 4.12%.

Cycloadduct: (3b)

Yield: 68%; mp 158-160°C; ^{1}H NMR ($CD_3CN/CDCl_3$): δ 1.33 (t, 3H, CH_3CH_2), 2.06-2.51 (m, 1H, CH_2), 2.80-3.28 (m, 1H, CH_2), 4.00 (q, 2H, CH_3CH_2), 5.00 (dd, J_1=7 Hz; J_2=10 Hz), 5.43 (dd, J_1=5 Hz;

J_2=7 Hz), 6.76-7.63 (m, 7H, Ar), 7.93-8.10 (m, 2H, *o*-phenyl H); IR (KBr): 1740 & 1670 (νC=O) 1400 (νSO_2 asym), 1170 (νSO_2 sym) cm^{-1} Mass m/e (rel. int.): 407 (M^+, 8.3), 308 ($M^+ - SO_2Cl$, 28.1), 264 (9.2), 105 (100). Anal for $C_{19}H_{18}ClNO_5S$ Calcd: C, 55.95; H, 4.42; N, 3.44%. Found: C, 55.61; H, 4.50; N, 3.48%.

4-(4'-Ethoxyphenyl)-7-phenyl-4,5-dihydro-1,3-oxazepine-2-one: (4b)

Yield: 24%; mp 142-143°C; ^1H NMR ($CDCl_3$): δ 1.36 (t, 3H, CH_3CH_2), 2.00-3.10 (m, 2H), 3.96 (q, 2H, CH_3CH_2), 4.33-5.00 (m, 2H, olefinic + benzylic), 6.53 (s, 1 NH, D_2O exchangeable), 6.68-7.45 (m, 7H, Ar), 7.88-8.08 (m, 2H, *o*-phenyl H); IR (KBr): 3200 (νNH) 1700 & 1670 (νC=O) cm^{-1} Mass m/e (rel. int.): 309 (M^+, 48.6), 204 (100), 163 (12.8). Anal for $C_{19}H_{19}NO_3$ Calcd: C, 73.78; H, 6.15; N, 4.53%. Found: C, 74.10; H, 6.21; N, 4.50%.

Cycloadduct: (3c)

Yield: 60%; mp 148-150°C; ^1H NMR ($CDCl_3$): δ 2.12-2.53 (m, 1H, CH_2), 3.00-3.53 (m, 1H, CH_2), 3.85 (s, 3H, OCH_3), 5.06 (dd, J_1=7.5 Hz; J_2=10 Hz), 5.56 (dd, J_1=5 Hz; J_2=8.75 Hz), 7.80-8.21 (m, 8H, aromatic); IR (KBr): 1765 & 1680 (νC=O) 1460 (νSO_2 asym), 1250, 1140 (νSO_2 sym) cm^{-1} Mass m/e (rel. int.): 428 (M^+, 6.9), 322 ($M^+ - SO_2Cl$, 21), 285 (89.5), 162 (76.9), 139 (100). Anal for $C_{18}H_{15}Cl_2NO_5S$ Calcd C, 50.46; H, 3.50; N, 3.27%. Found: C, 51.20; H, 3.54; N, 3.14%.

4-(4'-Methoxyphenyl)-7-(4'-chlorophenyl)-4,5-dihydro-1,3-oxazepine-2-one: (4c)

Yield: 20%; mp 159-161°C; ^1H NMR ($CDCl_3$): δ 2.00-3.12 (m, 2H, CH_2), 3.75 (s, 3H, OCH_3), 4.34-4.97 (m, 2H, Olefinic + benzylic),

6.17 (s, 1H, NH, D_2O exchangeable), 7.47 (aromatic 8H); IR (KBr): 3190 (νNH), 1690 & 1665 (νC=O) 1600, 1120 cm^{-1} Mass m/e (rel. int.): 330 (M^++1), 329 (M^+, 26.7), 190 (100), 136 (42.6). Anal for $C_{18}H_{16}ClNO_3$ Calcd: C, 65.65; H, 4.86; N, 4.25%. Found: C, 65.20; H, 4.62; N, 4.08%.

Cycloadduct: (3d)

Yield: 56.6%; mp 160-162°C; ^{1}H NMR (CD_3CN): δ 2.06-2.41 (m, 1H, CH_2) 2.84-3.28 (m, 1H, CH_2), 3.70 (s, 3H, *p*-OCH_3), 3.79 (s, 3H, *p'*-OCH_3), 4.89 (dd, 1H, J_1=7.5 Hz; J_2=10 Hz), 5.40 (dd, 1H, J_1=5 Hz; J_2=8.7 Hz) 7.45 (m, 8H, A_2B_2); IR (KBr): 1755 & 1660 (νC=O) 1590, 1405 (νSO_2 asym) 1190, 1175 (νSO_2 sym) cm^{-1} Mass m/e (rel. int.): 325 (M^+ - SO_2Cl, 15.8), 280 (7.6), 190 (36.7), 135 (92), 49 (100). Anal for $C_{19}H_{19}ClNO_6S$ Calcd: C, 53.9; H, 4.25; N, 3.30%. Found: C, 53.9; H, 4.20; N, 3.15%.

4,7-Di(4'-methoxyphenyl)-4,5-dihydro-1,3-oxazepine-2-one: (4d)

Yield: 52%; mp 150-152°C; ^{1}H NMR ($CDCl_3$): δ 2.0-3.12 (m, 2H, CH_2), 3.75 (s, 3H, OCH_3), 4.37-5.00 (m, 2H, olefinic + benzylic), 6.25 (s, 1H, NH, D_2O exchangeable), 6.81-7.34 (m, 8H, aromatic); IR (KBr): 3150, 3080 (νNH), 1695 & 1665 (νC=O) , 1590, 1040 cm^{-1} Mass m/e (rel. int.): 325 (M^+, 23.5), 297 (16), 290 (57.7), 139 (100). Anal for $C_{19}H_{19}NO_4$ Calcd: C, 70.15; H, 5.84; N, 4.31%. Found: C, 70.20; H, 5.65; N, 4.28%.

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