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Synthesis and Antiinflammatory Activity of Some Novel Benzo(b)thiophene Substituted Thiazolidinones

T. SHIVARAJ GOUDA*, JAGADISH, MD. SALAHUDDIN and S.M. SHANTAKUMAR
Department of Pharmaceutical Chemistry, V.L. College of Pharmacy, Raichur-584 103, India
Fax: (91)(8532)240405; Tel: (91)(8532)240952
E-mail: tsgoudavlcp@rediffmail.com

The 2-amino-4,5,6,7-tetrahydrobenzo(b)thiophene-3-carboxylate (**I**) was prepared by treating an equimolar concentration of cyclohexanone, ethylcyanoacetate, sulphur and diethylamine in dry alcohal. The compound (**II**) was refluxed for about 18-20 h with different aromatic aldehydes in absolute alcohol to obtain **III(a-f)**. The obtained intermediates are treated with mercapto acetic acid to get **IV(a-f)**. The synthesized compounds were evaluated for antiinflammatory activity. The compound $\mathbf{IV_d}$ and $\mathbf{IV_e}$ showed significant activity when compared to standard diclofenac sodium.

Key Words: Synthesis, Thiazolidinones, Antiinflammatory.

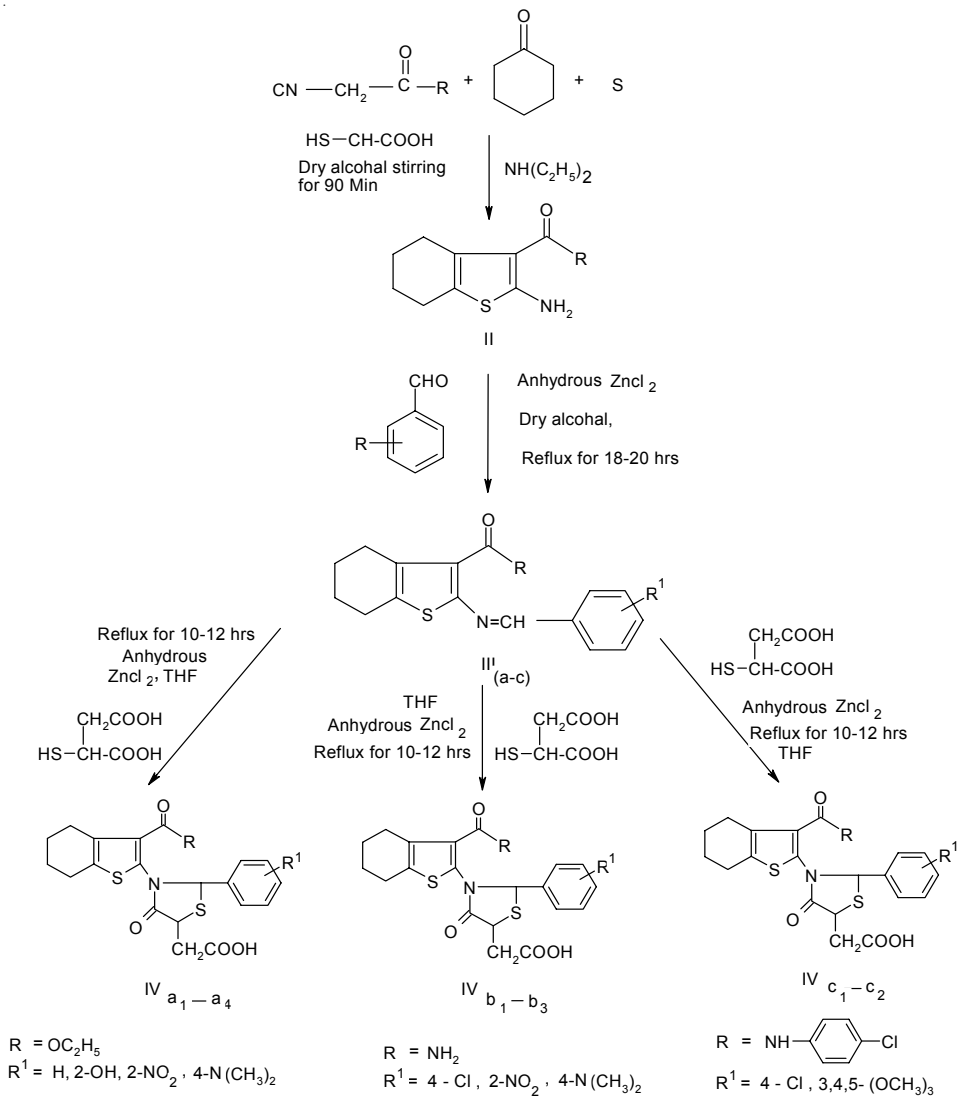
INTRODUCTION

It is well documented that substituted tetrahydro benzo(b)thiophenes have received considerable attention during the last few decades as they are endowed with variety of biological activities and have wide range of therapeutic properties. Tetrahydro benzo(b)thiophene derivatives showed interesting biological activities. A literature survey indicates that tetrahydro benzo(b)thiophene derivatives posses different biological activities like antimalerial[1], antiinflammatory[2], antibacterial[3], anticancer[4], antifungal[5], anticonvulsant[6] and potent analgesic activity[7].

Hence, it is planned to synthesize tetrahydro benzo(b)thiophenes by incorporating thiazolidinone moiety. It is contemplated that this combination is expected to result in a significant increase in antiinflammatory activity.

EXPERIMENTAL

All the melting points were recorded in open capillary tube and are uncorrected. IR spectra were recorded on a thermo Niolet Nexus 670 spectrometer. ^{1}H NMR spectra were recorded on Amx-400 NMR spectrometer at 400 MHz with DMSO as the solvent and TMS as internal standard. The purity was checked by thin layer chromatography using silica gel G. All the compounds were synthesized according to **Scheme-I**.



Scheme-I

Synthesis of ethyl-2-amino-4,5,6,7-tetrahydro benzo(b)thiophene-3-carboxylate (IIa)[8]: An equimolar mixture of cyclohexanone (0.1 mol), sulphur (0.1 mol), ethyl cyanoacetate (0.1 mol) and diethyl amine (0.1 mol), in dry ethanol (20 mL) is taken in a 500 mL round bottomed flask and stirred for 1.5 h. The mixture is then poured into ice water with constant stirring and set aside for 3 h at room temperature. The separated solid was collected by filtration, dried and recrystallized from ethanol. Yield: 75.83 % m.p. 118 ºC.

IIa: IR (KBr, ν_{max}, cm^{-1}): 3384 (NH *str.*), 2930 (CH *str.*), 3050 (Ar-H *str.*), 2935-2863 [CH of NH (CH_3)], 1680 (CH of $CONH_2$), 1645 (NH bending), 1620 (C=N), 1590, 1530, 1470 (Ar-ring *str.*), 812 (substituted benzene), 608 (C-S). ^{1}H NMR (DMSO-d_6) δ: 7.4(m, 2H of NH_2), 4.3 (m, 2H of CH_2 OC_2H_5), 2.6-2.7 (m, of tetrahydrobenzothiophene), 1.7 (m, 4H of tetrahydrobenzothiophene), 1.2 (d, 3H of CH_3 of OC_2H_5). MS m/z (%): M+1 = 226.

Synthesis of ethyl, 2-amino-4,5,6,7-tetrahydro benzo(b)thiophene-3-carboxamide (IIb)[8]: An equimolar mixture of cyclohexanone (0.1 mol), sulphur (0.1 mol), cyanoacetamide (0.1 mol) and diethyl amine (0.1 mol), in dry ethanol (20 mL) is taken in a 500 mL round bottom flask and stirred for 1.5 h at 40-50 ºC. The reaction mixture is then poured into ice cold water with constant stirring and set aside for 3 h. The separated solid was collected by filtration, dried and recrystallized with ethanol. Yield: 64.39 %, m.p. 175-180 ºC.

IIb: IR (KBr, ν_{max}, cm^{-1}): 3380 (NH *str.*), 2940 (CH *str.*), 3045 (Ar-H *str.*), 1675 (C=O), 1650 (NH bending), 1635 (C=N), 1595, 1530, 1460 (Ar-ring *str.*), 820 (substituted benzene) 610 (C-S). ^{1}H NMR (DMSO-d_6) δ: 7.4 (m, 2H of NH_2), 7.2 (s, 2H of $CONH_2$), 2.6-2.7 (m, of tetrahydrobenzothiophene), 1.7 (d, 4H of tetrahydrobenzothiophene). MS m/z (%): M+1 = 265.

Synthesis of ethyl, 2-amino-4,5,6,7-tetrahydro benzo(b)thiophene-3-carboxylate (IIc)[8]: An equimolar mixture of cyclohexanone (0.1 mol), sulphur (0.1 mol), N-(P-chloro phenyl)-cyanoacetamide (0.1 mol) and diethyl amine (0.1 mol), in dry ethanol (20 mL) is taken in a 500 mL round bottomed flask and stirred for 1.5 h for 40-50 ºC. The mixture is then poured into ice water with constant stirring and kept aside for 3 h. The separated solid was collected by filtration, dried and recrystallized with ethanol. Yield: 65 %, m.p. 202 ºC.

IIc: IR (KBr, ν_{max}, cm^{-1}): 3390 (NH *str.*), 2950 (CH *str.*), 3050 (Aro-H *str.*), 1685 (C=O), 1655 (NH bending), 1635 (C=N), 1570, 1540, 1465 (Ar-ring *str.*), 812 (substituted benzene) 605 (C-S). ^{1}H NMR (DMSO-d_6) δ: 7.4 (m, 2H of NH_2) 9.5 (s, 1H of NH) 7.4-7.7 (m, 4H of Ar-H) 2.6-2.7 (m, of tetrahydrobenzothiophene) 1.7 (d, 4H of tetrahydrobenzothiophene). MS m/z (%): M+1 = 275.

Synthesis of Schiff base (IIIa$_1$-a$_4$): An equimolar mixture of compound **IIa** (0.1 mol) and appropriate aromatic aldehydes (0.1 mol), in absolute alcohol was refluxed for 20 h in the presence of catalytic amount of zinc chloride (100 mg). The mixture was cooled and poured into ice-cold water with stirring, the separated solid was collected and washed with cold water, dried and recrystallized with appropriate solvent.

IIIa$_1$: IR (KBr, ν_{max}, cm^{-1}): 3375 (NH *str.*), 2965 (CH *str.*) 3040 (Ar-H *str.*), 1675 (C=O), 1665 (NH bending), 1635 (C=N), 1590, 1530, 1470 (Ar-ring *str.*), 805 (substituted benzene) 608 (C-S). ^{1}H NMR (DMSO-d_6) δ: 8.3 (s, 1H of -CH-N-) 7.2-7.8 (m, 5H of Ar-H) 4.1-4.2 (m, 2H of CH_2 of $COOCH_2CH_3$) 2.6-2.7 (d, 4H of tetrahydrobenzothiophene) 1.7 (m, 4H of tetrahydrobenzothiophene) 1.2 (d, 3H of CH_3 of $COOCH_2CH_3$). MS m/z (%): M+1 = 314.

IIIa$_2$: IR (KBr, ν_{max}, cm^{-1}): 3395 (NH *str.*), 2955 (CH *str.*), 3085 (Ar-H *str.*), 1700 (C=O), 1665 (NH bending), 1605 (C=N), 1590, 1545, 1485 (Ar-ring *str.*), 815 (substituted benzene) 625 (C-S). ^{1}H NMR (DMSO-d_6) δ: 11.2 (s, 1H of OH) 8.7 (s,1H of -CH-N-) 7.0-7.6 (m, 4H of Ar-H) 4.2-4.3 (m, 2H of CH_2 of $COOCH_2CH_3$) 2.4-2.6 (d, 4H of tetrahydrobenzothiophene) 1.7 (m, 4H of tetrahydrobenzothiophene) 1.3 (d, 3H of CH_3 of $COOCH_2CH_3$). MS m/z (%): M+1 = 330.

IIIa$_3$: IR (KBr, ν_{max}, cm^{-1}): 3375 (NH *str.*), 2960 (CH *str.*), 3085 (Ar-H *str.*), 1705 (C=O), 1635 (NH bending), 1645 (C=N), 1570, 1525, 1475 (Ar-ring *str.*), 810 (substituted benzene), 608 (C-S). ^{1}H NMR (DMSO-d_6) δ: 8.2 (s, 1H of -CH-N-) 6.8 (m, 4H of Ar-H), 4.1-4.2 (m, 2H of CH_2 of $COOCH_2CH_3$), 2.4-2.7 (d, 4H of tetrahydrobenzothiophene) 1.7 (m, 4H of tetrahydrobenzothiophene) 1.3 (m, 3H of CH_3 of $COOCH_2CH_3$), 3.1 (d, 6H of $N(CH_3)_2$. MS m/z (%): M+1 = 404.

IIIa$_4$: IR (KBr, ν_{max}, cm^{-1}): 3380 (NH *str.*), 2945 (CH *str.*), 3095 (Ar-H *str.*), 1715 (C=O), 1635 (NH bending), 1615 (C=N), 1575, 1535, 1465 (Ar-ring *str.*), 805 (substituted benzene), 605 (C-S). ^{1}H NMR (DMSO-d_6) δ: 9.4 (s, 1H of OH), 8.8 (s, 1H of -CH-N-) 6.7-7.4 (m, 4H of Ar-H) 4.2 (m, 2H of CH_2 of $COOCH_2CH_3$), 2.4-2.6 (d, 4H of tetrahydrobenzothiophene), 1.6 (m, 4H of tetrahydrobenzothiophene), 1.3 (d, 3H of CH_3 of $COOCH_2CH_3$). MS m/z (%): M+1 = 330.

Synthesis of Schiff base (IIIb$_1$-b$_3$): An equimolar mixture of compound **IIb** (0.1 mol) and appropriate aromatic aldehydes (0.1 mol), in absolute alcohol was refluxed for 20 h in the presence of catalytic amount of zinc chloride (100 mg). The mixture was cooled and poured into ice-cold water with stirring, the separated solid was collected and washed with cold water, dried and recrystallized with appropriate solvent.

IIIb$_1$: IR (KBr, ν_{max}, cm^{-1}): 3384 (NH *str.*), 2930 (CH *str.*) 3050 (Ar-H *str.*), 1680 (C=O), 1640 (NH bending), 1627 (C=N), 1592, 1559, 1475 (Ar-ring *str.*), 840 (substituted benzene) 668 (C-S), 608 (Cl). ^{1}H NMR (DMSO-d_6) δ: 8.2 (s, 1H of -CH-N-), 8.2 (s, 12H of $CONH_2$), 7.4-7.5 (m, 4H of Ar-H), 2.6-2.7 (m, 4H of tetrahydro benzo thiophene), 1.7 (d, 4H of tetrahydrobenzothiophene). MS m/z (%): M+1 = 387.

IIIb$_2$: IR (KBr, ν_{max}, cm^{-1}): 3380 (NH *str.*), 3040 (Ar-H *str.*), 1670 (C=O), 1640 (NH bending), 1612 (C=N), 1580, 1527, 1480 (Ar-ring *str.*), 840 (substituted benzene), 668 (C-S). ^{1}H NMR (DMSO-d_6) δ: 8.8 (s, 1H of -CH-N-), 7.8 (s, 2H of $CONH_2$), 6.8-7.5 (m, 4H of Ar-H), 2.6-2.7 (m, 4H of tetrahydrobenzothiophene), 1.7 (d, 4H of tetrahydrobenzothiophene) 3.1 [m, 6H of $N(CH_3)_2$]. MS m/z (%): M+1 = 428.

IIIb$_3$: IR (KBr, ν_{max}, cm^{-1}): 3398 (NH *str.*), 2945 (CH *str.*), 3060 (Ar-H *str.*), 1675 (C=O), 1630 (NH bending), 1625 (C=N), 1582, 1545, 1485 (Ar-ring *str.*), 835 (substituted benzene), 656 (C-S). ^{1}H NMR (DMSO-d_6) δ: 8.5 (s, 1H of -CH-N-) 7.9 (s, 2H of $CONH_2$) 7.9-8.1 (m, 4H of Ar-H), 2.7-2.8 (m, 4H of tetrahydrobenzothiophene) 1.8 (d, 4H of tetrahydrobenzothiophene). MS m/z (%): M+1 = 375.

Synthesis of Schiff base (IIIc$_1$-c$_2$): An equimolar mixture of compound **IIc** (0.1 mol)[5] and appropriate aromatic aldehydes (0.1 mol), in absolute alcohol was

refluxed for 20 h in the presence of catalytic amount of zinc chloride (100 mg). The mixture was cooled and poured into ice-cold water with stirring, the separated solid was collected and washed with cold water, dried and recrystallized with appropriate solvent.

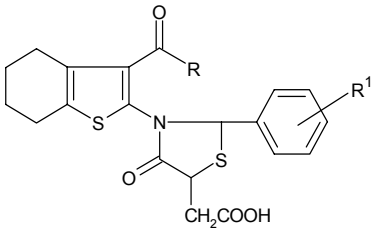
IIIc$_1$: IR (KBr, ν_{max}, cm^{-1}): 3485 (NH *str.*), 2945 (CH *str.*), 3055 (Ar-H, *str.*), 1675 (C=O), 1635 (NH bending), 1625 (C=N), 1595, 1547, 1477 (Ar-ring *str.*), 835 (substituted benzene), 655 (C-S). ^{1}H NMR (DMSO-d_6) δ: 10.2 (s, 1H of NH), 8.8 (s, 1H of -CH-N-), 7.5-7.7 (m, 8H of Ar-H), 2.6-2.7 (m, 4H of tetrahydrobenzothiophene), 1.8 (d, 4H of tetrahydrobenzothiophene). MS m/z (%): M+1 = 411.

IIIc$_2$: IR (KBr, cm^{-1}): 3480 (NH *str.*), 2925 (CH *str.*), 3040 (Ar-H, *str.*), 1670 (C=O), 1640 (NH bending), 1612 (C=N), 1580, 1527, 1480 (Ar-ring *str.*), 840 (substituted benzene), 658 (C-S). ^{1}H NMR (DMSO-d_6) δ: 10.3 (s, 1H of NH), 8.8 (s, 1H of -CH-N-), 7.2-7.6 (m, 6H of Ar-H), 2.6-2.7 (m, 4H of tetrahydrobenzothiophene), 1.7 (d, 4H of tetrahydrobenzothiophene), 3.8 (m, 9H of OCH_3). MS m/z (%): M+1 = 385.

Preparation of thiazolidinones (IVa$_1$-a$_4$) and (IVb$_1$-b$_3$): An equimolar mixture of compound **3a$_1$** (0.1 mol) and mercapto succinic acid (0.1 mol) in tetrahydro furan (30 mL) were refluxed for 10-12 h in the presence of catalytic amount of zinc chloride (100 mg). The mixture was cooled and poured into ice-cold water with stirring, the separated solid was collected and washed with cold water, dried and recrystallized with appropriate solvent.

Rest of compounds of series (**IVa$_1$-a$_4$**) and (**IVb$_2$-b$_3$**) are prepared by using same as given for **IIIa$_1$** and data is given in Table-1.

TABLE-1
CHARACTERIZATION DATA OF COMPOUND **IVa$_1$-IVc$_2$**:



Compd.	R	R^1	Solvent for recrystallization	m.p. (ºC)	Yield (%)
IVa$_1$	OC_2H_5	H	Ethanol	83	75
IVa$_2$	OC_2H_5	2-OH	Ethanol	96	70
IVa$_3$	OC_2H_5	4-N $(CH_3)_2$	Ethanol	88	80
IVa$_4$	OC_2H_5	4-OH	Ethanol + Acetone	92	69
IVb$_1$	NH_2	4-Cl	Ethanol + Acetone	246	72
IVb$_2$	NH_2	4-N $(CH_3)_2$	Ethanol + Acetone	155	74
IVb$_3$	NH_2	2-NO_2	Ethanol	165	78
IVc$_1$	NH-C_6H_5-Cl	4-Cl	Ethanol	159	66
IVc$_2$	NH-C_6H_5-Cl	3,4,5-$(OCH_3)_2$	Ethanol	170	72

IVa$_1$: IR (KBr, ν_{max}, cm^{-1}): 3485 (NH *str.*), 2935 (CH *str.*), 3035 (Ar-H *str.*), 1685 (C=O), 1645 (NH bending), 1615 (C=N), 1575, 1530, 1470 (Ar-ring *str.*), 845 (substituted benzene), 660 (C-S). ^{1}H NMR (DMSO-d_6) δ: 11.8 (s, 1H of OH of CH_2COOH), 6.5 (s, 1H of -CH-N-), 7.4-8.5 (m, 5H of Ar-H and IH of thiozolidinone $CH\text{-}CH_2\text{-}COOH$), 4.2-4.4 (d, 2H of CH_2 of $COOC_2H_5$), 2.4-2.7 (d, 4H of thiophene and 2H of CH_2 of CH_2COOH), 1.7-1.9 (d, 4H of tetrahydrothiophene), 1.3-1.5 (m, 3H of CH_3 of $COOC_2H_5$). MS m/z (%): M+1 = 446.

IVa$_2$: IR (KBr, ν_{max}, cm^{-1}): 3385 (NH *str.*), 2935 (CH *str*.), 3035 (Ar-H, *str.*), 1685 (C=O), 1645 (NH bending), 1615 (C=N), 1575, 1530, 1470 (Ar-ring *str.*), 845 (substituted benzene), 660 (C-S). ^{1}H NMR (DMSO-d_6) δ: 11.9 (s,1H of OH of CH_2COOH), 9.7 (s, 1H of 2-OH), 8.6 (s, 1H of -CH-N-), 6.8-7.2 (m, 4H, of Ar-H and 1H of $-CH\text{-}CH_2\text{-}COOH$), 4.3-4.4 (d, 2H of CH_2 of $COOC_2H_5$), 2.5-2.7 (d, 4H of thiophene and 2H of CH_2 of CH_2COOH), 1.7-1.9 (d, 4H of tetrahydrothiophene), 1.3-1.5 (m, 3H of CH_3 of $COOC_2H_5$). MS m/z (%): M+1 = 462.

IVa$_3$: IR (KBr, ν_{max}, cm^{-1}): 3415 (NH *str.*), 2975 (CH *str.*), 3035 (Ar-H, *str.*), 1695 (C=O), 1645 (NH bending), 1630 (C=N), 1585, 1545, 1485 (Ar-ring *str.*), 850 (substituted benzene), 670 (C-S). ^{1}H NMR (DMSO-d_6) δ: 11.7 (s, 1H of OH of CH_2COOH), 8.7 (s, 1H-CH-N-), 6.6-7.5 (m, 4H of Ar-H and 1H of $-CH\text{-}CH_2\text{-}COOH$), 4.2-4.4 (d, 2H of CH_2 of $COOC_2H_5$), 2.4-2.7 (d, 4H of tetrahydrothiophene and 2H of CH_2 of CH_2COOH), 1.7-1.9 (d, 4H of tetrahydrothiophene), 1.3-1.5 (m, 3H of CH_3 of $COOC_2H_5$), 3.1 [m, 6H of $N(CH_3)_2$]. MS m/z (%): M+1 = 489.

IVa$_4$: IR (KBr, ν_{max}, cm^{-1}): 3380 (NH *str.*), 2965 (CH *str.*), 3040 (Ar-H *str.*), 1645 (C=O), 1665 (NH bending), 1608 (C=N), 1576, 1545, 1435 (Ar-ring *str.*), 840 (substituted benzene), 665 (C-S). ^{1}H NMR (DMSO-d_6) δ: 11.7 (s, 1H of OH of CH_2COOH), 9.4 (s, 1H of 4-OH), 8.7 (s, 1H of -CH-N-), 6.6-7.8 (m, 4H, Ar-H and 1H of $-CH\text{-}CH_2\text{-}COOH$), 4.3-4.4 (d, 2H of CH_2 of $COOC_2H_5$), 2.5-2.7 (d, 4H of tetrahydrothiophene and 2H of CH_2 of CH_2COOH), 1.7-1.9 (d, 4H of tetrahydrothiophene), 1.3-1.5 (m, 3H of CH_3 of $COOC_2H_5$). MS m/z (%): M+1 = 462.

IVb$_1$: IR (KBr, ν_{max}, cm^{-1}): 3405 (NH *str.*), 2936 (CH *str.*), 3045 (Ar-H *str.*), 1685 (C=O), 1655 (NH bending), 1635 (C=N), 1595, 1550, 1475 (Ar-ring *str.*), 860 (substituted benzene), 665 (C-S), 608 (Cl). ^{1}H NMR (DMSO-d_6) δ: 12.1 (s, 1H of OH of CH_2COOH), 8.7 (s, 1H-CH-N-), 7.2 (s, 2H of $CONH_2$), 7.4-8.5 (m, 4H of Ar-H and IH of $-CH\text{-}CH_2\text{-}COOH$), 2.4-2.7 (d, 4H of tetrahydrothiophene and 2H of CH_2 of CH_2COOH), 1.7-1.9 (d, 4H of tetrahydrothiophene). MS m/z (%): M+1 = 451.

IVb$_2$: IR (KBr, ν_{max}, cm^{-1}): 3385 (NH *str.*), 2930 (CH *str.*), 3045 (Ar-H *str.*), 1689 (C=O), 1640 (NH bending), 1630 (C=N), 1585, 1570, 1455 (Ar-ring *str.*), 855 (substituted benzene), 670 (C-S). ^{1}H NMR (DMSO-d_6) δ: 11.9 (s, 1H of OH of CH_2COOH), 8.7 (s, 1H-CH-N-), 7.2 (s, 2H of $CONH_2$), 7.4-8.5 (m, 4H of Ar-H and 1H of $-CH\text{-}CH_2\text{-}COOH$), 2.5-2.7 (d, 4H of tetrahydrothiophene and 2H of CH_2 of CH_2COOH), 1.2-1.4 (m, 4H of tetrahydrothiophene), 3.1 [m, 6h of $N(CH_3)_2$. MS m/z (%): M+1 = 460.

IVb$_3$: IR (KBr, ν_{max}, cm^{-1}): 3395 (NH *str.*), 2955 (CH *str.*), 3055 (Ar-H *str.*), 1690 (C=O), 1625 (NH bending), 1625 (C=N), 1555 1545, 1435 (Ar-ring *str.*), 840 (substituted benzene), 665 (C-S). ^{1}H NMR (DMSO-d_6) δ: 11.8 (s, 1H of OH of CH_2COOH) 8.7 (s, 1H,-CH-N-) 7.4-8.5 (m, 4H of Ar-H and 1H of -CH-CH_2-COOH), 7.2 (s, 2H of $CONH_2$), 2.4-2.7 (d, 4H of tetrahydrobenzothiophene and 2H of CH_2 of CH_2COOH), 1.7-1.9 (m, 4H of tetrahydrothiophene). MS m/z (%): M+1 = 462.

Preparation of thiazolidinones (IVc$_1$ and IVc$_2$): An equimolar mixture of compound **IIIc$_1$** and **IIIc$_2$** (0.1 mol) and mercapto-succinic acid (0.1 mol) in tetrahydro furan (30 mL) were refluxed for 10-12 h in the presence of catalytic amount of zinc chloride (100 mg). The mixture was cooled and poured into ice-cold water with stirring, the separated solid was collected and washed with cold water, dried and recrystallized with appropriate solvent.

IVc$_1$: IR (KBr, ν_{max}, cm^{-1}): 3380 (NH *str.*), 2925 (CH *str.*), 3040 (Ar-H *str.*), 1670 (C=O), 1640 (NH bending), 1612 (C=N), 1580, 1527, 1480 (Ar-ring *str.*), 840 (substituted benzene), 668 (C-S), 605 (Cl). ^{1}H NMR (DMSO-d_6) δ: 11.7 (s, 1H of OH of CH_2COOH), 8.7 (s, 1H of -CH-N-), 7.4-8.5 (m, 4H of Ar-H and 1H of -CH-CH_2-COOH), 2.4-2.7 (d, 4H of tetrahydrobenzothiophene and 2H of CH_2 of CH_2COOH), 1.7-1.9 (d, 4H of tetrahydrothiophene). MS m/z (%): M+1 = 562.

IVc$_2$: IR (KBr, ν_{max}, cm^{-1}): 3385 (NH *str.*), 2950 (CH *str.*), 3045 (Ar-H *str.*), 1695 (C=O), 1675 (NH bending), 1640 (C=N), 1580, 1545, 1455 (Ar-ring *str.*), 870 (substituted benzene), 655 (C-S). ^{1}H NMR (DMSO-d_6) δ: 11.8 (s, 1H of OH of CH_2COOH), 8.9 (s, 1H of -CH-N-), 7.4-8.5 (m, 4H of Ar-H & IH of -CH-CH_2-COOH), 2.4-2.7 (d, 4H of thiophene and 2H of CH_2 of CH_2COOH), 1.7-1.9 (d, 4H of tetrahydrothiophene), 3.8 [m, 9H of $(OCH_3)_2$]. MS m/z (%): M+1 = 617.

RESULTS AND DISCUSSION

Table-2 shows antiinflammatory activity data. The compounds under the study exhibited significant antiinflammatory activity. Compound **IVa$_2$**, **IVa$_3$**, **IVa$_4$**, **IVb$_2$**, **IVb$_3$** and **IVc$_1$** shown maximum reduction in the paw oedema volume about 57.94, 83.00, 68.53, 74.48, 60.00 and 58.14 %, respectively and compound **IVa$_1$** and **IVc$_2$** exhibited a good reduction in the paw oedema volume 46.42 and 54.12 % compared to standard diclofenac sodium 96.96 % in carrageenin induced reduction in the paw oedema volume of the rats.

From antiinflammatory evaluation data Table-2 it is found that the compound **IVa$_2$**, **IVa$_3$**, **IVa$_4$**, **IVb$_2$**, **IVb$_3$** and **IVc$_1$** have shown significant antiinflammatory activity and compound **IVa$_1$** and **IVc$_2$** shown good antiinflammatory activity. The significant activity of the compound **IVa$_3$** and **IVb$_2$** may be due to the presence of electron donating group N-$(CH_3)_2$ and significant activity of **IVa$_2$** and **IVa$_4$**, **IVb$_3$**, **IVc$_1$** may be due to the presence of the electron withdrawing group (OH, NO_2, Cl) substituted on phenyl nucleus, which is attached to the second position of the thiazolidinones ring system.

TABLE-2
ANTIINFLAMMATORY ACTIVITY OF COMPOUND **IV**$_{(a-d)}$ IN
CARRAGEENAN INDUCED ACUTE RAT PAW OEDEMA MODEL

Group	Treatment	Dose (mg/kg)	Paw oedema volume							
			After 0.5 h		After 1.0 h		After 2.0 h		After 3.0 h	
			Mean	%ROV	Mean	%ROV	Mean	%ROV	Mean	%ROV
1	Control	0.5 mL	0.180	-	0.51	-	0.58	-	0.55	-
2	Standard (Diclofenac)	20	0.101	45.45	0.16	67.74	0.116	80.00	0.016	96.96
3	IVa_1	100	0.220	25.00	0.35	35.71	0.45	41.66	0.37	46.42
4	IVa_2	100	0.130	23.23	0.30	42.85	0.40	50.00	0.30	57.94
5	IVa_3	100	0.075	75.00	0.10	78.57	0.15	78.57	0.15	83.00
6	$IV4a_4$	100	0.180	40.00	0.25	58.33	0.24	65.71	0.22	68.57
7	IVb_1	100	0.180	40.00	0.27	55.00	0.30	57.14	0.35	50.00
8	IVb_2	100	0.100	64.28	0.14	64.28	0.20	71.42	0.25	76.48
9	IVb_3	100	0.190	36.66	0.28	53.33	0.36	48.57	0.28	60.00
10	IVc_1	100	0.140	15.85	0.26	56.66	0.30	57.14	0.41	58.14
11	IVc_2	100	0.150	17.85	0.27	35.71	0.45	50.00	0.57	54.18

ROV = Reduction in paw oedema volume.

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