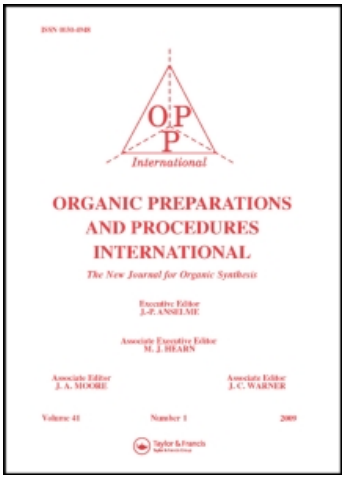

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A NOVEL SYNTHESIS OF 2,3-DIHYDRO[1,5]BENZOTHIAZEPIN-4(5H)-ONES

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2327(1988); b) K. Harano, I. Shinohara, S. Sugimoto, T.Matsuoka and T. Hisano, *Chem. Pharm. Bull. Japan*, **37**, 576 (1989) and references cited therein.

4) The activation enthalpy and entropy for the reaction of *O*-ethyl *S*-methyl xanthate with PP in DMSO are 24.7 kcal/mol and -11 e.u. respectively. In the reaction, a coloration due to a charge transfer complex[3b] was not observed in contrast to the case of pyridine *N*-oxides.

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6) Reaction of *O,S*-dimethyl xanthate with triethylenediamine gave the stable quaternary salt. The reaction with PP may proceed through the formation of a similar quaternary salt which may easily dissociate by heating.

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A NOVEL SYNTHESIS OF 2,3-DIHYDRO[1,5]BENZOTHIAZEPIN-4(5H)-ONES

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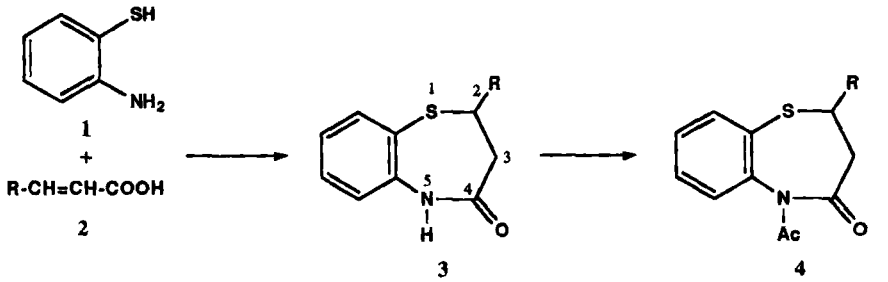
Benzothiazepines such as *Diltiazem*[1] or *Thiazesim*[2] are currently used as antidepressant, coronary vasodilator and antiangina agents. The present paper describes the preparation of new 2,3-dihydro[1,5]benzothiazepines diversely substituted at the 2-position.



a) R = 3-pyridyl
b) R = *p*-$NO_2C_6H_4$
c) R = *p*-FC_6H_4
d) R = 2-furyl
e) R = 2-thienyl
i) R = 5-methyl-2-thienyl
g) R = 5-bromo-2-thienyl
h) R = 3-thienyl
i) R = *n*-butyl

TABLE 1. 2,3-Dihydro[1,5]benzothiazepin-4(5H)-ones

Cmpd.	Yield (%)	mp.[a] (°C)	Time (hrs)	IR (cm^{-1})	^1H NMR (δ) ppm
3a	66	164	6	3160, 1660	9.78 (NH), 8.56, 8.46, 7.63, 7.60 (Ar, pyridyl), 7.50, 7.25 (Ar, H), 5.06 (1H, CH), 2.70 (2H, CH_2).
3b	76	192	6	3160, 1655	9.78 (NH), 7.90, 7.25, 6.87 (Ar, H), 4.90 (1H, CH), 2.43 (2H, CH_2).
3c	71	179	6	3160, 1660	9.96 (NH), 7.43, 7.00 (Ar, H), 5.03 (1H, CH), 2.63 (2H, CH_2).
3d	72	159[b]	7	3180, 1670	9.96 (NH), 7.46, 7.06 (Ar, H), 7.00, 6.36, 6.26 (Ar, furyl), 4.96 (1H, CH), 2.63 (2H, CH_2).
3e	70	171	7	3160, 1670	10.00 (NH), 7.46, 7.15, 7.03 (Ar, H), 7.03 (Ar, H), 5.30 (1H, CH), 2.73 (2H, CH_2).
3f	75	169	8	3160, 1655	9.93 (NH), 7.46, 7.1 0 (Ar, H), 6.67, 6.53 (Ar, thienyl), 5.16 (1H, CH), 2.66 (2H, CH_2), 2.33 (3H, CH_3).
3g	78	178	8	3180, 1660	10.00 (NH), 7.33, 7.16 (Ar, H), 6.96, 6.80 (Ar, thienyl), 5.16 (1H,CH), 2.66 (2H, CH_2).
3h	76	155[b]	6	3150, 1670	10.00 (NH), 7.45, 7.1 0 (Ar, H), 5.06 (1 H, CH), 2.70, (2H, CH_2).
3i	69	117[b]	4	3180, 1680	9.73 (NH), 7.36, 7.06 (Ar, H), 3.70 (1H, CH), 2.46 (2H, CH_2),1.46 (8H, CH_2), 0.96 (3H, CH_3).

a) Crystallized from acetonitrile unless otherwise noted. b) Ethanol

These compounds were obtained by heating an intimate mixture of *o*-aminothiophenol with cinnamic or acrylic acids **2**[3] at 170°. The 2,3-dihydro[1,5]benzothiazepin-4(5H)-ones (**3a-3i**) were isolated in 66-78% yield. Acetylation of these compounds with acetic anhydride in acetic acid at 60° led to 5-acetyl-2,3-dihydro [1,5]benzothiazepin-4(5H)-ones (**4a-4i**). The structure of these benzothiazepines was confirmed by NMR spectra.

EXPERIMENTAL SECTION

Melting points were determined on a Kofler WME type apparatus and were uncorrected. IR spectra were recorded as KBr pellets on a Philips P. U. spectrometer. ^1H NMR spectra were obtained on a Varian EM 390 spectrometer at 90 MHz in DMSO-d_6 with TMS as an internal reference and chemical shifts are expressed as δ (ppm). The thienylacrylic and cinnamic acids were prepared according to the literature method.[9]

TABLE 2. 5-Acetyl-2,3-dihydro[1,5]benzothiazepin-4-ones

Cmpd.	Yield (%)	mp.[a] (°C)	Time (hrs)	IR (cm^{-1})	^1H NMR (δ) ppm
4a	77	131	1	1710, 1700	8.40, 7.46, 7.30 (Ar, H), 4.96 (1H, CH), 2.76 (2H, CH_2), 2.58 (3H, CH_3).
4b	70	150	1	1710, 1700	7.95, 7.30, 6.90 (Ar, H), 4.92 (1H, CH), 2.41 (2H, CH_2), 2.41 (3H,$COCH_3$).
4c	69	141	1	1715, 1700	7.46, 7.03 (Ar, H), 4.86 (1H, CH), 2.73 (2H, CH_2), 2.56 (3H, $COCH_3$).
4d	78	120	1	1710, 1700	7.20, 6.06, 5.80 (Ar, H), 4.73 (1H, CH), 2.56 (2H, CH_2), 2.38 (3H, $COCH_3$).
4e	85	112	1	1715, 1710	7.40, 7.13(Ar, H), 5.10 (1H, CH), 2.90 (2H, CH_2), 2.60 (3H, $COCH_3$).
4f	76	132	0.5	1710, 1700	7.43, 6.56 (Ar, H), 5.06 (1H, CH), 2.86 (2H, CH_2), 2.36 (3H, CH_3), 2.60 (3H, $COCH_3$).
4g	80	149	1	1710, 1695	7.40, 6.93, 6.63 (Ar, H), 5.10 (1H, CH), 2.96 (2H, CH_2), 2.53 (3H, $COCH_3$).
4h	74	127	1.3	1710, 1700	7.40, 7.16, 6.70 (Ar, H), 4.90 (1H, CH), 2.80 (2H, CH_2), 2.66 (3H, $COCH_3$).
4i	69	130	1	1710, 1700	7.40, 7.10 (Ar, H), 3.76 (1H, CH), 2.50 (2H, CH_2), 1.50 (8H, $(CH_2)_4$), 0.96 (3H, CH_3), 2.68 (3H, $COCH_3$).

a) Crystallized from diethyl ether .

2,3-Dihydro-2-(3-pyridyl)[1,5]benzothiazepin-4(5H)-one (3a). General Procedure.- A viscous mixture of equimolar amounts (0.1 mol) of **1** and of 3-(3-pyridyl)acrylic acid (**2**) was heated with stirring for 6 hrs at 170°. The residue was triturated at 5° with 100 mL ethanol. The resulting crystals were collected and recrystallized from acetonitrile to give 17 g (66%) of **3a**. The data for the products are summarized in the Table 1 .

5-Acetyl-2,3-dihydro-2-(3-pyridyl)[1,5]benzothiazepin-4-one (4a). General Procedure.- A solution of 5 g (0.0195 mol) of 2,3-dihydro-2-(3-pyridyl)[1,5]benzothiazepin-4-one (**3a**) in 10 mL of acetic anhydride and 15 mL of acetic acid was heated for 1 hr at 60°. After dilution with water and cooling at 5°, white crystals deposited. The solid was collected and crystallized from diethyl ether to give 4.50 g (77%) of **4a**. The data for products **4b-4i** are summarized in the Table 2.

TABLE 3. Elemental Analysis Data of Compounds **3** and **4**.

Cmpd.	Elemental Analysis Data					
	C		H		N	
	Calcd.	Found	Calcd.	Found	Calcd.	Found
3a	65.62	65.60	4.72	4.70	10.93	10.97
3b	60.00	60.00	4.03	4.06	9.33	9.35
3c	65.91	65.96	4.42	4.50	5.12	5.20
3d	63.67	63.70	4.52	4.55	5.71	5.80
3e	59.77	59.81	4.24	4.31	5.36	5.42
3f	61.09	61.12	4.76	4.80	5.09	5.10
3g	48.15	48.22	3.10	3.15	4.31	4.45
3h	59.77	59.82	4.24	4.30	5.36	5.38
3i	67.44	67.52	7.68	7.71	5.62	5.58
4a	64.42	64.50	4.73	4.80	9.39	9.45
4b	59.65	59.75	4.12	4.20	8.18	8.22
4c	64.74	64.82	4.47	4.48	4.44	4.50
4d	62.71	62.76	4.56	4.60	4.88	4.92
4e	59.40	59.47	4.32	4.40	4.62	4.72
4f	60.56	60.70	4.77	4.80	4.41	4.52
4g	47.12	47.22	3.16	3.20	3.66	3.76
4h	59.40	59.62	4.32	4.34	4.62	4.80
4i	65.95	66.10	7.27	7.32	4.81	4.94

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