

Studies in Heterocyclics. VI.¹⁾ Synthesis of Thiazolo-Benzo-Triazepines

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2-Imino-3-(*o*-aminoaryl)-4-thiazolines (II) gave thiazolo-benzo-triazepines(I) on condensation with various aliphatic carboxylic acids. Both *N*-acyl(III) and *N,N'*-diacyl derivatives(IV) were isolated, and the mono-acyl derivatives(III) were also cyclized to thiazolo-benzo-triazepines.

In continuation of our study on the synthesis of bridgehead seven membered heterocyclic systems, we report herewith the synthesis of a new ring system, *i.e.*, thiazolo[2,3-*d*][1,3,5]benzo-triazepines. Thiazolo-benzo-triazepines (Ia–d; Table 2) have been synthesized according to Scheme 1.

2-Imino-3-(*o*-aminoaryl)-4-thiazolines(II) were synthesized according to the scheme described earlier.²⁾ The stoichiometric quantities of II and requisite carboxylic acid when refluxed in toluene gave thiazolo-benzo-triazepines(I) in one step. In a number of attempts to achieve the synthesis of I by refluxing II and excess carboxylic acids (RCOOH; R=H, CH₃, C₂H₅) in the presence of acetic anhydride, the diacyl derivatives (IV; Table 1) were formed. The characteristic features of IR spectra of these diacyl derivatives are the presence of >NH and >C=O at 3330 and 1635 cm⁻¹ in IV (R₁=R₂=R=H); at 3270 and 1660 cm⁻¹ in IV (R₁=R₂=H; R=CH₃); at 3350 and 1665 cm⁻¹ in IV (R₁=R₂=H; R=C₂H₅). The structure of IV (R₁=R₂=H, R=CH₃) was also supported by its NMR spectrum (100 MHz; CDCl₃) which

shows a singlet at δ 2.14 (3H; CH₃-C(=O)-NH); a singlet at δ 2.30 (3H, CH₃-C(=O)-N=), one H amidic proton at δ 8.60 and aromatic multiplet at δ 6.71–7.96 for C₆H₅-C=CH- and -NH-C₆H₄-N-. These diacyl derivatives did

not give I as suggested by Kanaoka *et al.*³⁾

When stoichiometric quantities of the carboxylic acid and II along with polyphosphate ester (PPE) in chloroform were refluxed, only mono acyl derivatives (III) were obtained. The IR spectrum of III (R₁=R₂=H; R=CH₃) showed the characteristics >C=NH; >C=O vibrations at 3260 and 1650 cm⁻¹, respectively. The NMR spectrum (100 MHz; CDCl₃) also gave a singlet at δ 2.15 (3H; CH₃CO); a multiplet between δ 6.2–7.92 (10H; C₆H₅-C=CH- and -N-C₆H₄-N-); and a singlet at δ 6.50 (1H; >C=NH). These monoacyl derivatives are cyclized to I on refluxing in toluene. Moreover III are acylated to IV on heating with excess of carboxylic acids and acetic anhydride.

Experimental

The melting points are uncorrected. Microanalysis was carried out by the Microanalytical Service, CSIRO, Australia. IR spectra were run in KBr wafers on a Perkin-Elmer Infracord-137 spectrophotometer, and NMR spectra were recorded on a Varian HA-100 spectrometer.

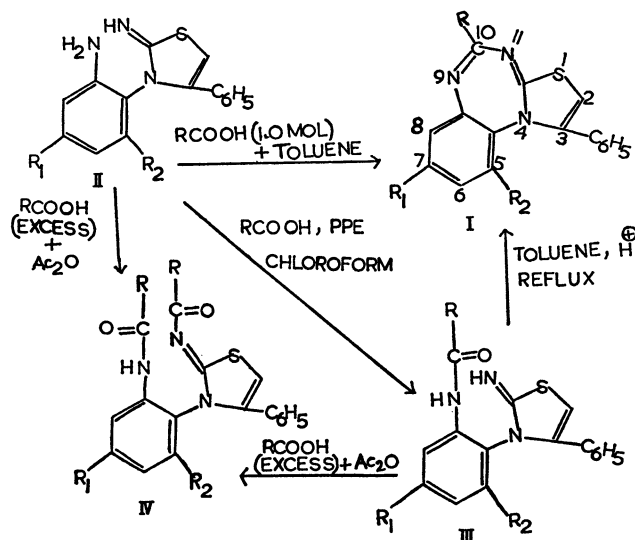
2-Acylimino-3-(*o*-acetylaminophenyl)-4-phenyl-4-thiazolines (IV). 3-(*o*-Aminophenyl)-2-imino-4-phenyl-4-thiazoline (2.67 g; 0.01 mol), acetic acid (10 ml) and acetic anhydride (10 ml) were heated under reflux for 3 h. The clear solution thus obtained was evaporated to dryness under reduced pressure and the solid so obtained was recrystallized from ethanol to afford IV (R₁=R₂=R=CH₃).

All the other derivatives using formic acid and propionic acid (IVa–d) were prepared following a procedure similar to that described above. Yield, mp, and microanalytical data are reported in Table 1.

3-(*o*-Acetamidophenyl)-2-imino-4-phenyl-4-thiazoline (III); (R₁=R₂=H, R=CH₃). 3-(*o*-Aminophenyl)-2-imino-4-phenyl-4-thiazoline (0.534 g; 0.002 mol), acetic acid (0.12 g; 0.002 mol); polyphosphate ester (3.0 g) and chloroform (20 ml) were heated under reflux for 2 h. The solvent was removed under reduced pressure and the residue was treated with aqueous sodium hydrogencarbonate. The solid obtained was filtered, washed with water, air dried and recrystallized from THF/Pet. ether (bp 80–100 °C); yield 0.43 g. (70%), mp 153 °C (Found: C, 65.98; H, 4.64; N, 13.45%. Calcd for C₁₇H₁₅N₃SO: C, 66.02; H, 4.85; N, 13.59%).

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2-Acetylimino-3-(*o*-acetamidophenyl)-4-phenyl-4-thiazoline (IVa)



- (a) R₁ = H, R₂ = H, R = H, CH₃, C₂H₅
 (b) R₁ = CH₃, R₂ = H, R = H, CH₃, C₂H₅
 (c) R₁ = OCH₃, R₂ = H, R = H, CH₃, C₂H₅
 (d) R₁ = H, R₂ = CH₃, R = H, CH₃, C₂H₅

Scheme 1.

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TABLE 1. PHYSICAL CONSTANTS OF IV

Sr. No.	Substituents			Yield %	Mp °C	Found %				Calcd %			
	R	R ₁	R ₂			C	H	N	S	C	H	N	S
IVa	H	H	H	77	203	63.11	4.02	13.20	—	63.15	4.02	13.00	—
	CH ₃	H	H	80	223	64.66	5.00	11.70	—	64.95	4.84	11.96	—
	C ₂ H ₅	H	H	80	213	66.09	5.40	11.01	—	66.49	5.54	11.08	—
IVb	H	CH ₃	H	70	191	—	—	12.26	9.31	—	—	12.46	9.49
	CH ₃	CH ₃	H	82	220	65.59	5.35	11.35	—	65.75	5.20	11.50	—
	C ₂ H ₅	CH ₃	H	84	215	—	—	—	8.38	—	—	—	8.14
IVc	H	OCH ₃	H	72	184	61.30	4.19	11.68	—	61.18	4.24	11.90	—
	CH ₃	OCH ₃	H	80	212	—	—	—	8.41	—	—	—	8.39
	C ₂ H ₅	OCH ₃	H	76	206	—	—	10.09	—	—	—	10.26	—
IVd	H	H	CH ₃	76	205	64.23	4.36	12.28	—	64.09	4.45	12.46	—
	CH ₃	H	CH ₃	78	228	65.99	5.31	11.31	—	65.75	5.20	11.50	—
	C ₂ H ₅	H	CH ₃	75	232	—	—	10.82	8.30	—	—	10.68	8.14

All the compounds (IVa—d) were crystallized from ethanol.

TABLE 2. PHYSICAL CONSTANTS OF I

Sr. No.	Substituents			Yield %	Mp °C	Found %			Calcd %		
	R	R ₁	R ₂			C	H	N	C	H	N
Ia	H	H	H	73	245	59.65	3.87	14.84	59.31	3.97	15.16
	CH ₃	H	H	74	241	70.25	4.32	14.03	70.10	4.47	14.43
	C ₂ H ₅	H	H	80	238	70.64	4.63	13.55	70.81	4.91	13.77
Ib	H	CH ₃	H	65	236	70.01	4.26	14.31	70.00	4.46	14.43
	CH ₃	CH ₃	H	68	234	70.76	4.72	13.56	70.81	4.91	13.77
	C ₂ H ₅	CH ₃	H	72	230	71.51	5.23	13.25	71.47	5.32	13.16
Ic	H	OCH ₃	H	60	214	66.25	4.35	13.71	66.46	4.23	13.68
	CH ₃	OCH ₃	H	58	216	67.17	4.52	13.10	67.28	4.67	13.08
	C ₂ H ₅	OCH ₃	H	76	212	68.10	5.10	12.32	68.05	5.07	12.53
Id	H	H	CH ₃	62	176	70.20	4.25	14.32	70.10	4.46	14.43
	CH ₃	H	CH ₃	62	175	70.75	4.80	13.87	70.81	4.91	13.71
	C ₂ H ₅	H	CH ₃	68	172	71.36	5.31	13.21	71.47	5.32	13.16

All the compounds (Ia—d) were crystallized from toluene.

from 3-(*o*-Acetamidophenyl)-2-imino-4-phenyl-4-thiazoline (IIIa). 3-(*o*-Acetamidophenyl)-2-imino-4-phenyl-4-thiazoline (IIIa) (0.618 g; 0.002 mol), acetic acid (10 ml) and acetic anhydride (10 ml) were heated under reflux for 2 h. The solution obtained was evaporated to dryness under reduced pressure and the solid residue obtained was recrystallized from ethanol, mp 223 °C, yield 0.500 g. (70%) (Found: C, 64.62; H, 5.13; N, 11.66%. Calcd for C₁₉H₁₇N₃SO₂: C, 64.95; H, 4.84; N, 11.96%).

The identity of the compound was confirmed by undepressed mixture mp with the authentic sample obtained by the alternative route described above.

3-Phenyl-(10-substituted)-thiazolo[2,3-d][1,5,3]benzotriazepines (Ia—d).

(i) III to I: 3-(*o*-Acetamidophenyl)-2-imino-4-phenyl-4-thiazoline (0.618 g; 0.002 mol) was refluxed in toluene (20 ml) with a drop of acetic acid for 3 h. The solvent was removed under reduced pressure and the solid residue obtained was recrystallized from toluene to afford I (R₁=R₂=H, R=CH₃). Yield 0.35 g (60%), mp 241 °C (Found: C, 70.30; H, 4.52; N, 14.31%. Calcd for C₁₇H₁₃N₃S: C, 70.10, H, 4.47; N, 14.43%).

(ii) II to I: 3-(*o*-Aminophenyl)-2-imino-4-phenyl-4-thiazoline (0.543 g; 0.002 mol), acetic acid (0.12 g; 0.002 mol) were refluxed in toluene (20 ml) for 3 h. After removal of the solvent under reduced pressure, the solid obtained was

recrystallized from toluene to afford I (R₁=R₂=H; R=CH₃), yield 0.42 g (74%); mp 241 °C.

I (R₁=R₂=H; R=CH₃) obtained from routes (i) and (ii) was identical since its mixed mp was underpressed and superimposable IR spectra were obtained.

All the other derivatives of (Ia—d) were prepared by means of method (ii). The yield, mp and microanalytical data are reported in Table 2.

Salient features of IR spectrum of I (R₁=R₂=H; R=CH₃) are the absence of original bands at 3260 and 1650 cm⁻¹ due to >C=NH and >C=O functions and the presence of >C=N vibrations at 1610 cm⁻¹. Other derivatives of Ia (R₁=R₂=R=H) and (R₁=R₂=H; R=C₂H₅) also show the absence of >C=O and >N-H bands. NMR spectra of Ia (R₁=R₂=H; R=H) and (R₁=R₂=H; R=CH₃) show the absence of protons due to amino acid >C=NH functions.

References

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