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

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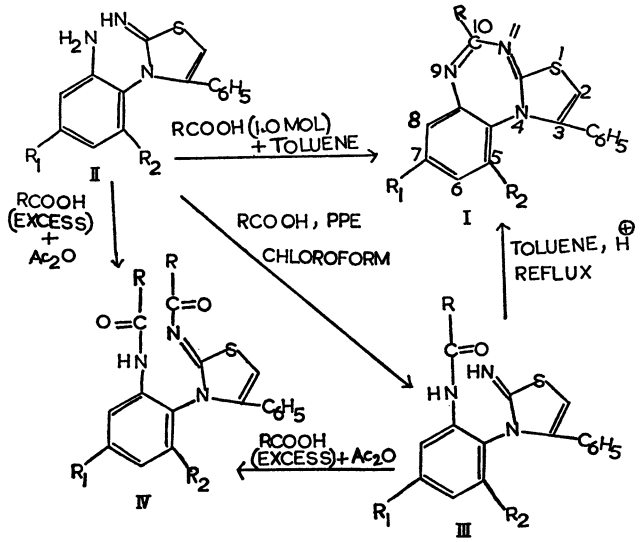
(Received October 21, 1975)

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 stochiometric 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, CH_3, C_2H_5) 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 ($R_1=R_2=R=H$); at 3270 and 1660 cm^{-1} in IV ($R_1=R_2=H$; $R=CH_3$); at 3350 and 1665 cm^{-1} in IV ($R_1=R_2=H$; $R=C_2H_5$). The structure of IV ($R_1=R_2=H$, $R=CH_3$) was also supported by its NMR spectrum (100 MHz; $CDCl_3$) which shows a singlet at δ 2.14 (3H; CH_3–C(=O)–NH); a singlet at δ 2.30 (3H, CH_3–C(=O)–N=), one H amidic proton at δ 8.60 and aromatic multiplet at δ 6.71—7.96 for C_6H_5–C=CH– and –NH–(C$_6$H$_4$)–N<. These diacyl drivatives did not give I as suggested by Kanaoka *et al.*[3]



(a) $R_1=H$, $R_2=H$, $R=H$, CH_3, C_2H_5
(b) $R_1=CH_3$, $R_2=H$, $R=H$, CH_3, C_2H_5
(c) $R_1=OCH_3$, $R_2=H$, $R=H$, CH_3, C_2H_5
(d) $R_1=H$, $R_2=CH_3$, $R=H$, CH_3, C_2H_5

Scheme 1.

When stoichiometric quantitaties 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 ($R_1=R_2=H$; $R=CH_3$) showed the characteristics >C=NH; >C=O vibrations at 3260 and 1650 cm^{-1}, respectively. The NMR spectrum (100 MHz; $CDCl_3$) also gave a singlet at δ 2.15 (3H; CH_3CO); a multiplet between δ 6.2—7.92 (10H; C_6H_5–C=CH– and –N–C_6H_4–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-acylamino-substituted phenyl)-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 ($R_1=R_2=R=CH_3$).

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); ($R_1=R_2=H$, $R=CH_3$). 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 $C_{17}H_{15}N_3SO$: C, 66.02; H, 4.85; N, 13.59%).

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

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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_2H_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_2H_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_2H_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_2H_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_2H_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_2H_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_2H_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_2H_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 $C_{19}H_{17}N_3SO_2$: 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 ($R_1=R_2=H$, $R=CH_3$). Yield 0.35 g (60%), mp 241 °C (Found C, 70.30; H, 4.52; N, 14.31%. Calcd for $C_{17}H_{13}N_3S$: 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 ($R_1=R_2=H$; $R=CH_3$), yield 0.42 g (74%); mp 241 °C.

I ($R_1=R_2=H$; $R=CH_3$) 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 ($R_1=R_2=H$; $R=CH_3$) 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 ($R_1=R_2=R=H$) and ($R_1=R_2=H$; $R=C_2H_5$) also show the absence of >C=O and >N-H bands. NMR spectra of Ia ($R_1=R_2=H$; $R=H$) and ($R_1=R_2=H$; $R=CH_3$) show the absence of protons due to amino acid >C=NH functions.

References

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