Synthesis of Thiazolotriazepinones

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The synthesis of 4,5-dihydro-7-phenylthiazolo[2,3-*c*][1,2,4]triazepin-3(2*H*)-one (**4**) from 2-propenoic acid 2-(4-phenyl-2-thiazolyl)hydrazide (**14**), is reported. A synthesis of **4** which was reported earlier by Mahajan, Sondhi and Ralhan (9), from 3-chloropropanoic acid 2-(4-phenyl-2-thiazolyl)hydrazide (**3**), is erroneous. We were able to cyclize **3** to 1-(4-phenyl-2-thiazolyl)-3-pyrazolidinone (**5**). The cyclizations of **14** to **4** and **3** to **5** are consistent with the Baldwin Rules for Ring Closure.

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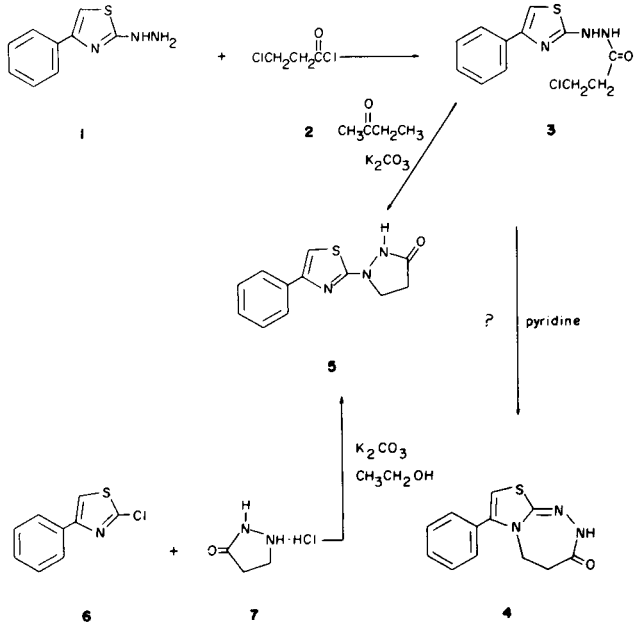
Synthetic design of triazepines and annellated triazepines requires a consideration of other cyclization reactions which may result from acyclic precursors. Thus, if competitive five- or six-membered ring closures can be envisioned, these more favorable cyclizations usually result. We have reinvestigated several literature reports describing triazepine systems which proved to be, instead, quinazolinediones (1), quinazolinones (2), benzimidazoles (3), an imidazoline (3) and oxadiazoles (4). Other investigators have also reinvestigated reported triazepines and reassigned the structures as azetidinediones (5), oxadiazoles (6), pyrazolotriazoles (7) and pyrazolonaphthotriazines (8).

A report by Mahajan, Sondhi and Ralhan (9) describes the synthesis of thiazolotriazepine **4** and five additional phenyl-substituted analogs. These compounds were prepared as shown for **4** in Scheme I. Acylation of 2-hydrazino-4-phenylthiazole (**1**) with 3-chloropropionyl chloride (**2**) gave hydrazide **3**, which then was reported to cyclize in pyridine at room temperature to thiazolotriazepine **4**. After examining this report, we had two concerns. First, we felt that compound **5**, 1-(4-phenyl-2-thiazolyl)-3-pyrazolidinone, was an alternate cyclization product which could have resulted from **3**, which should have been considered by Mahajan, *et al.* (9). Our second concern was that the conditions described for the cyclization of **3** to **4** were surprisingly mild.

Scheme I



We first prepared an authentic sample of compound **5**. Treatment of 2-chloro-4-phenylthiazole (**6**) with 3-pyrazolidinone hydrochloride (**7**) and potassium carbonate in ethanol at reflux gave pyrazolidinone **5**, which displayed a melting point of 113°. This melting point did not coincide with the melting point of 173° reported for **4** by Mahajan, *et al.* (9).

We next decided to repeat the procedure for the preparation of **4** as reported by Mahajan, *et al.* (9). Treatment of **4** with pyridine under a variety of conditions, *i.e.* undistilled pyridine, pyridine freshly distilled from calcium hydride, wet pyridine, pyridine dried over potassium hydroxide, and pyridine at elevated temperature, led only to recovery of unchanged **4**. We were, however, able to cyclize **3** to pyrazolidinone **5** using potassium carbonate in 2-butanone (at reflux). Thus, we found that under conditions which *would* effect the cyclization of **3**, we isolated **5** rather than thiazolotriazepinone **4**.

In the preparation of hydrazide **3**, employing excess 3-chloropropionyl chloride according to the procedure of Mahajan, *et al.* (9), we also isolated a diacylated product to which we assign structure **8** (Scheme II), rather than structure **9**, which is the other possible product of diacylation. (Compound **8** was also isolated unchanged after treatment with pyridine at room temperature for 30 minutes.) This assignment is made on the basis of spectral evidence. Table I lists the ultraviolet maxima and extinction coefficients for **8** and related compounds which were prepared in this study. The ultraviolet spectra of these compounds, with the exception of compounds **8** and **6**, displayed very noticeable changes when hydrochloric acid was added to the sample solutions. We feel that protonation of the imino nitrogen of **8** should not give rise to a change in its

Scheme II

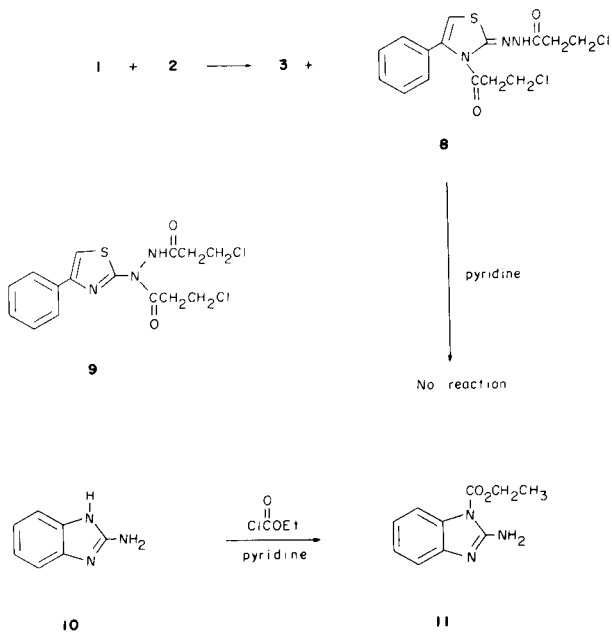


Table I

Ultraviolet Spectra of Thiazoles

Compound	Solvent: Methanol λ max (mμ) (Σ max)	Solvent: Methanol and Hydrogen Chloride λ max (mμ) (Σ max)
1	231 (22,200) 263 (8,900) 278 (7,800)	220 (15,300) 269 (12,500)
3	230 (23,600) 262 (9,900) 278 (9,200)	265 (16,200)
5	239 (21,400) 265 (14,400)	228 (15,100) 285 (16,800)
6	256 (13,500)	255 (13,500)
8	230 (21,800) 265 (16,900)	230 (20,000) 265 (16,400)
14	230 (25,100) 262 (10,500) 278 (10,200)	265 (16,800)
4	234 (22,500) 261 (10,500) 278 (8,500)	232 (19,300) 265 (14,200)
15 (a)	234 (18,600) 261 (9,850) 280 (8,700)	232 (23,300) 265 (14,600)

(a) The compound was not completely in solution until addition of hydrochloric acid.

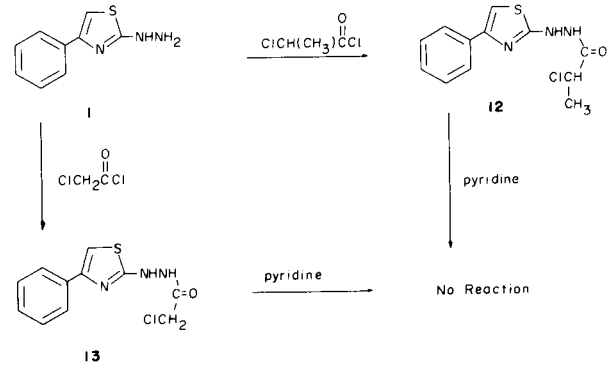
spectrum, since the imino nitrogen is not directly attached to the styrene chromophore. However, protonation of the thiazole nitrogen of **9**, which is an integral part of the phenylthiazole chromophore, should effect a change in the ultraviolet spectrum.

The infrared spectrum of the diacylated material is also consistent with structure **8**. Acylhydrazine **3** displays a carbonyl band at 1680 cm^{-1}, whereas **8** displays carbonyl bands at 1690 and 1720 cm^{-1}. We conclude that the second acyl group of **8** is contributing the 1720 cm^{-1} band, which is a resonable position for an *N*-acyl carbonyl frequency, since 1-acetylimidazole displays a carbonyl band at 1725 cm^{-1} (10). An acceptable infrared model compound for **9** may be 1,2-diacetylmethylhydrazine, which we reported (11), previously, which displays a carbonyl band at 1670 cm^{-1}. This frequency is significantly lower than the 1720 cm^{-1} carbonyl frequency observed for **8**.

Chemical evidence also exists for *endo*-acylation (ring acylation) of ambident, amidine-like nucleophiles such as **3**, rather than *exo*-acylation. Acylation of 2-aminobenzimidazole (**10**) with ethyl chloroformate in pyridine gives 2-amino-1*H*-benzimidazole-1-carboxylic acid ethyl ester (**11**), rather than the isomeric 2-benzimidazolylcarbamic acid ethyl ester (3,12,13).

To further assess the conditions of cyclization employed by Mahajan, *et al.* (9), we prepared 2-chloropropanoic acid 2-(4-phenyl-2-thiazolyl)hydrazide (**12**) and chloroacetic acid 2-(4-phenyl-2-thiazoloyl)hydrazide (**13**) from **1** and 2-chloropropionyl chloride and chloroacetyl chloride, respectively, as shown in Scheme III. Neither **12** or **13** underwent cyclization to thiazolotriazinones when treated with pyridine at room temperature for 30 minutes. We felt that 6-membered (triazinone) ring closure would be more favorable than 7-membered (triazepinone) ring closure, and we were curious to see whether pyridine would effect these more favorable ring closures. We were also trying to rule out the possibility, by preparing **12**, that Mahajan, *et al.* (9), had inadvertently used 2-chloropropionyl chloride rather than 3-chloropropionyl chloride in their syntheses.

Scheme III



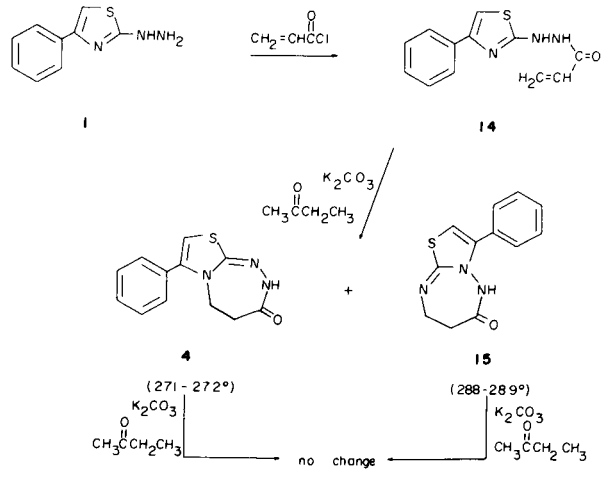
Turning back to the cyclization which we were able to effect with hydrazide **3** to produce pyrazolidinone **5**, we felt that this was, indeed, a predictable result. From a consideration of entropy of activation for cyclization, the 5-membered closure is favored with respect to a 7-membered closure (14). In similar ring closure reactions involving intramolecular alkylation which produced rings of from three to seven members, five-membered ring closures proceeded in highest yields (15-18).

In order to prepare thiazolotriazepinone **4**, we concluded that a precursor other than **3** was necessary. From an examination of the Baldwin Rules for Ring Closure (19-21), it appeared that an *endo-trigonal* closure would be ideal, since *5-endo-trigonal* closures are disfavored processes (20) and *7-endo-trigonal* closures are favored processes (19,22). Accordingly, we prepared 2-propenoic acid 2-(4-phenyl-2-thiazolyl)hydrazide (**14**) from **1** and acryloyl chloride. Cyclization of **14** with potassium carbonate in 2-butanone gave *no detectable* **5** (by tlc), the product which would result from unpredicted *5-endo-trigonal* closure. The products of this cyclization, resulting from *7-endo-trigonal* closures, were 4,5-dihydro-7-phenylthiazolo[2,3-*c*][1,2,4]triazepin-3(2*H*)-one (**4**), and 7,8-dihydro-3-phenylthiazolo[3,2-*b*][1,2,4]triazepin-6(5*H*)-one (**15**), as shown in Scheme IV. The melting point reported for **4** (173°) by Mahajan, *et al.* (9), was vastly different from the melting ponts which we observed for either **4** (271-272°) or **15** (288-289°). The isomeric thiazolotriazepinones **4** and **15** were cleanly separated, albeit painstakingly, by silica gel column chromatography.

In addition to displaying similar elution behavior, compounds **4** and **15** were very similar spectrally. The nmr and ultraviolet (see Table I) spectra were almost superimposable. The mass spectra were also very similar, but the subtle differences allowed us to differentiate the structures with confidence. A fragmentation pathway observed for **4**, and also for hydrazides **3**, **5** and **14**, but *not* for **15**, is shown in Scheme V. We postulate that McLafferty rearrangement of **4** leads to hydrazide **14**, which also results from McLafferty rearrangement of **5** (followed by tautomerism) and elimination of hydrogen chloride from **3**. Thus, we feel that structure **14** is a mass spectral focal point for structures **3**, **4** and **5**. Cleavage of the thiazole ring of **14** as shown in Scheme V, with the charge capable of going with either fragment, produces the ions at m/e 116 and 129.

Thiazolotriazepinone **4** is the predicted product from the cyclization of **14**, and the production of the isomeric thiazolotriazepinone **15** required explanation. Dimroth rearrangements, sometimes referred to as disguised Dimroth or Dimroth-like rearrangements, are well-documented in the literature and have been observed in fused ring systems similar to **4** (23-33). We recognized that thiazolotriazepinone **15** was formally a Dimroth-rearranged product of **4** (and *vice versa*). However, when we

Scheme IV

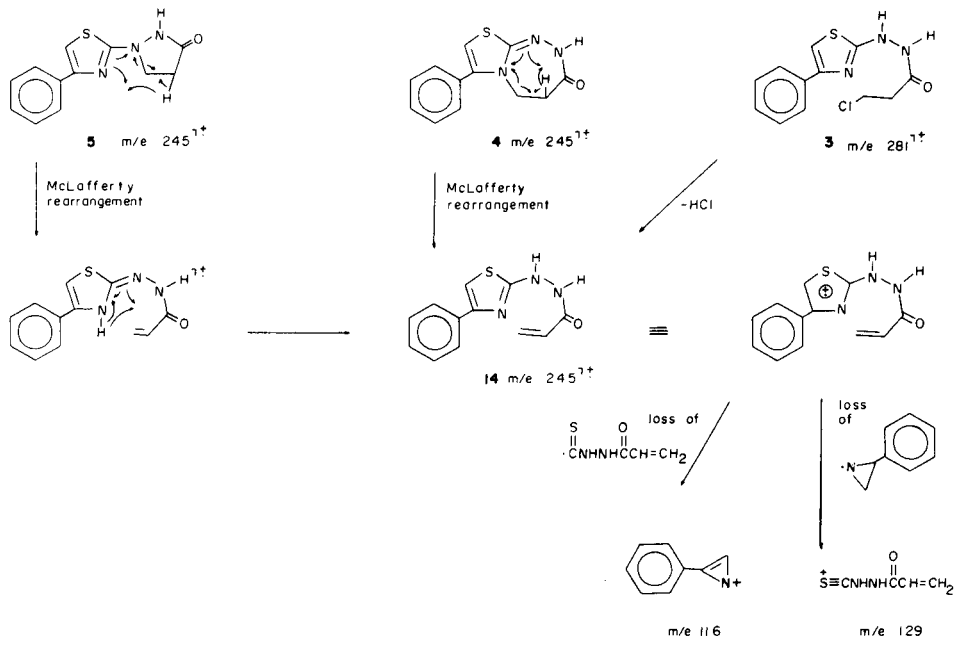


separately subjected both **15** and **4** to the exact reaction conditions which were employed in producing them from **14**, no interconversion occurred (34). Thus, we conclude that **14** undergoes partial Dimroth rearrangement to intermediate **19** prior to cyclization to **15**, as shown in Scheme VI. We envision the rearrangement to proceed through **16**, a tautomer of **14**, which undergoes hydration of the carbon-carbon thiazole double bond to give intermediate **17**. Rupture of hemiaminal **17** as shown produces ketone **18**, which recloses in the manner shown to give intermediate **19**. Internal Michael addition, again by a favored *7-endo-trigonal* process, produces thiazolotriazepinone **15**.

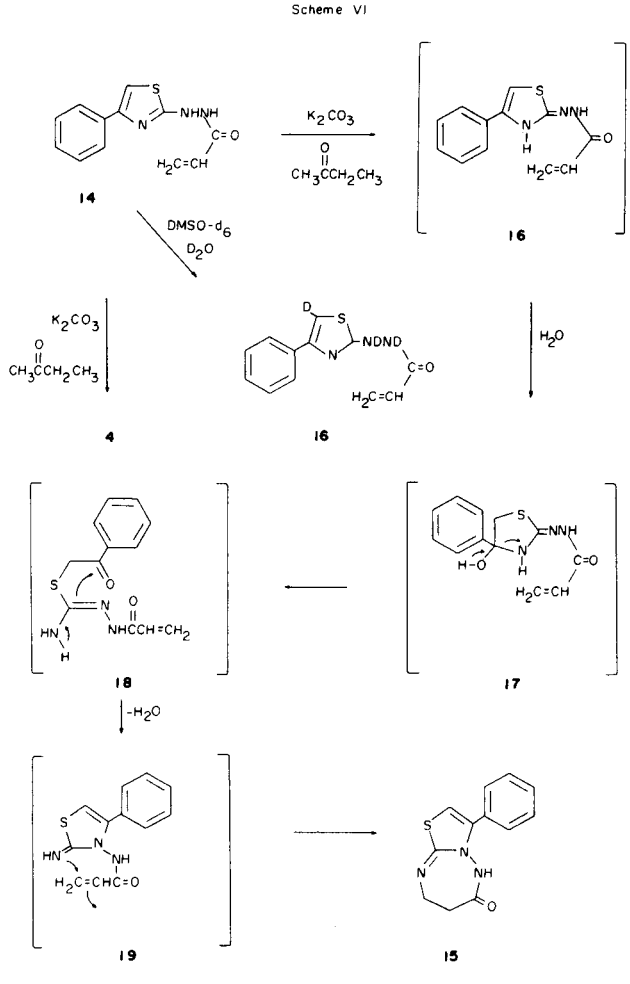
The key step in the mechanism shown in Scheme VI is the hydration of the double bond. In a separate experiment, we showed that this hydration did occur. After recording the nmr spectrum of **14** in dimethylsulfoxide-d_6, we added deuterium oxide and again recorded the spectrum. Exchange of both protons on nitrogen had taken place. When we recorded the spectrum again after 48 hours, the thiazole ring hydrogen had also exchanged. This exchange necessarily results from reversible hydration of the thiazole carbon-carbon double bond with deuterium oxide.

We also found that the thiazole ring protons of both **4** and **15** underwent exchange in dimethylsulfoxide-d_6 (plus deuteriochloroform, with **4**) and deuterium oxide. However, these exchanges appeared to be slower than the corresponding exchange with **14**, since neither exchange was complete in 48 hours. With thiazolotriazepinone **4**, exchange of the thiazole ring hydrogen was 40% complete after 24 hours and 65% complete after 48 hours.

Scheme V



Scheme VI



In summary, we were unable to repeat the preparation of thiazolotriazepinone **4** from hydrazide **3** as reported by Mahajan, Sondhi and Ralhan (9). Using the conditions described by these authors (pyridine, room temperature), we only recovered unchanged **3**. Employing conditions that would effect the cyclization of **3** (potassium carbonate, 2-butanone at reflux), we obtained pyrazolidinone **5**, as predicted, rather than **4**. When we used an appropriate starting material for the preparation of **4**, *i.e.*, hydrazide **14**, we did produce thiazolotriazepinone **4** and the isomeric thiazolotriazepinone **15**, both of which were completely characterized. The melting point of either **4** or **15** is *ca.* 100° higher than reported by Mahajan, *et al.* (9), for **4**. We conclude that Mahajan, *et al.* (9) *did not* prepare thiazolotriazepinone **4** as they report, and we are unable to determine what new compound, if any, they obtained from hydrazide **3** and pyridine.

EXPERIMENTAL

All melting points are uncorrected. The ir spectra were recorded with either a Beckman Model 4240 or a Perkin-Elmer Model 727B spectrophotometer, uv spectra with a Hewlett-Packard Model 8450A UV/vis spectrophotometer, nmr spectra with Varian EM-360A and Perkin-Elmer R-32 (90 MHz) spectrometers, and mass spectra with a Finnigan gc/ms Model 4023 (electron impact and chemical ionization) mass spectrometer. Combustion analysis for C, H and N were performed by Dow Analytical Laboratories, Midland, MI.

Treatment of 2-Hydrazino-4-phenylthiazole (**1**) with 3-Chloropropionyl Chloride (**2**).

A solution of 3.82 g (20.0 mmoles) of **1** (9) in 75 ml of tetrahydrofuran was added, with stirring over a 30-minute period, to 20 ml of 3-chloropropionyl chloride at 0°. The resulting mixture (solid was present) was stirred for an additional 30 minutes and poured onto crushed ice. The white solid was collected, washed with water and air-dried to yield 5.30 g of white solid, which showed two spots on tlc (silica gel; 9:1::chloroform:methanol). The solid was crystallized from methanol and four crops were collected. Crops 1 and 3, which were predominantly the higher R_f spot by tlc, were recrystallized from ethanol-water to yield pure 3-chloropropanoic acid [3-(3-chloro-1-oxopropyl)-4-phenyl-2(3*H*)-thiazolylidene]hydrazide (**8**), mp 176.5-177°; ir (potassium bromide): 3335 (NH), 1720 (C=O), 1690 (C=O) cm^{-1}; nmr (dimethylsulfoxide-d_6): δ 11.40 (s, 1H, NH), 8.14-7.73 (m, 3H, 2 phenyl protons and thiazole proton, s, at 7.77), 7.67-7.27 (m, 3H, phenyl protons), 4.27-3.83 (m, 4H, both CH_2Cl groups), 3.60-2.97 (m, 4H, both $COCH_2$ groups); ms: (70 eV, chemical ionization, methane) m/e (relative intensity) 372 (4, $M^+ + 1$), 336 (20, with one Cl), 300 (14), 282 (s, with one Cl), 246 (15), 231 (40), 203 (24), 177 (21), 135 (25), 108 (100, with one Cl).

Anal. Calcd. for $C_{15}H_{15}Cl_2N_3O_2S$: C, 48.39; H, 4.06; N, 11.29. Found: C, 48.26; H, 4.10; N, 11.47.

Crops 2 and 4, which were predominantly the lower R_f spot by tlc, were recrystallized from ethanol-water to give pure 3-chloropropanoic acid 2-(4-phenyl-2-thiazolyl)hydrazide (**3**), mp 179-184°; ir (potassium bromide): 3400-2500 (broad NH), 1680 (C=O) cm^{-1}; nmr (deuteriochloroform and dimethylsulfoxide-d_6): δ 10.20 (s, 1H, NH), 7.88-7.70 (m, 2H, phenyl protons), 7.50-7.20 (m, 3H, phenyl protons), 6.87 (s, 1H, thiazole proton), 3.81 (t, J = 7 Hz, 2H, CH_2Cl), 2.70 (t, J = 7 Hz, 2H, $COCH_2$); ms:(70 eV, electron impact): m/e (relative intensity): 281 (14), 246 (32), 245 (100), 217 (24), 191 (27), 190 (17), 176 (3), 174 (8), 161 (35), 135 (7), 134 (19), 192 (9), 116 (3), 102 (74), 91 (20), 89 (15).

Anal. Calcd. for $C_{11}H_{10}ClN_3OS$: C, 49.34; H, 3.76; N, 15.69. Found: C, 49.34; H, 3.75; N, 15.97.

When the acylation of **1** was performed with a stoichiometric amount of 3-chloropropionyl chloride (**2**), diacylation was not observed.

Preparation of 1-(4-Phenyl-2-thiazolyl)-3-pyrazolidinone (**5**). A. From 2-Chloro-4-phenylthiazole (**6**) and 3-Pyrazolidinone Hydrochloride (**7**).

To a solution of 4.19 g (20.0 mmoles) of **6** (35) in 100 ml of ethanol was added 6.90 g (0.500 mole) of potassium carbonate and 2.45 g (20.0 mmoles) of **7** (Pfaltz and Bauer). The mixture was heated at reflux for 42 hours and concentrated. The residue was partitioned between water and methylene chloride. The organic phase was dried (sodium sulfate) and concentrated to leave 2.50 g (51%) of crude **5**. Trituration with ether gave a solid which was collected and air-dried to yield pure **5**, mp 113°; ir (Nujol): 1735 (C=O) cm^{-1}; nmr (deuteriochloroform): δ 9.11 (broad s, 1H, NH), 7.84-7.45 (m, 2H, phenyl protons), 7.45-7.04 (m, 3H, phenyl protons), 6.77 (s, 1H, thiazolyl proton), 4.18 (t, J = 7.5 Hz, 2H, protons at 5-position), 2.57 (t, J = 7.5 Hz, 2H, protons at 4-position); ms: (70 eV, electron impact) m/e (relative intensity) 245 (100, molecular ion), 217 (26), 191 (2), 190 (4), 176 (3), 174 (3), 161 (36), 135 (3), 134 (15), 129 (7), 116 (3), 102 (83), 91 (7), 89 (9).

Anal. Calcd. for $C_{12}H_{11}N_3OS$: C, 58.77; H, 4.52; N, 17.13. Found: C, 58.70; H, 4.52; N, 17.16.

B. From **3**.

A slurry of 0.5 g (1.77 mmoles) of **3**, 0.5 g of potassium carbonate and 30 ml of 2-butanone was heated at reflux for 3 hours. The purple mixture was cooled, concentrated and partitioned between water and chloroform. The aqueous phase was acidified with dilute hydrochloric acid. The resulting cloudy aqueous phase was extracted with chloroform and the organic extracts were dried (sodium sulfate) and concentrated. The residue was extracted with three portions of ether and the ether was evaporated to leave 0.120 g (28%) of **5**, mp 109-111°. Spectral data (ir and nmr) for this sample of **5** were identical to those of the material prepared in Part A.

2-Chloropropanoic Acid 2-(4-Phenyl-2-thiazolyl)hydrazide (**12**).

To a solution of 5.73 g (30.0 mmoles) of **1** in 50 ml of tetrahydrofuran was added 3.81 g (30.0 mmoles) of 2-chloropropionyl chloride in 10 ml of tetrahydrofuran. A precipitate formed immediately, and the mixture was stirred for 30 minutes. Addition of water gave a solution, which was concentrated to a slurry. The precipitate was collected, air-dried and recrystallized from ethanol to afford 5.40 g (64%) of **12**, mp 178-179°; ir (potassium bromide): 3350-2600, with spike at 3250 (NH), 1675 (C=O) cm^{-1}; nmr (dimethylsulfoxide-d_6): δ 10.70 (s, 1H, NH, deuterium oxide-exchangeable), 9.60 (broad s, 1H, NH, deuterium oxide-exchangeable), 8.00-7.65 (m, 2H, phenyl protons), 7.55-7.15 (m, 4H, 3 phenyl protons and thiazole proton, s, at 7.24), 4.59 (q, J = 6 Hz, 1H, CHCl), 1.60 (d, J = 6 Hz, 3H, CH_3); ms: (70 eV, electron impact) m/e 281 (molecular ion).

Anal. Calcd. for $C_{12}H_{12}ClN_3OS$: C, 51.15; H, 4.29; N, 14.91. Found: C, 50.96; H, 4.36; N, 14.96.

Chloroacetic Acid 2-(4-Phenyl-2-thiazolyl)hydrazide (**13**).

To a solution of 1.50 g (7.85 mmoles) of **1** in 25 ml of tetrahydrofuran was added 1.00 g (88.5 mmoles) of chloroacetyl chloride in 10 ml of tetrahydrofuran. A precipitate formed immediately. After 30 minutes of stirring, the white solid was collected, washed with water and air-dried to yield 2.00 g (95%) of **13**; mp 173-174° (ethanol); ir (potassium bromide): 3400-2600, with spike at 3195 (NH), 1680 (C=O) cm^{-1}; nmr (dimethylsulfoxide-d_6): δ 10.56 (s, 1H, NH, deuterium oxide-exchangeable), 9.60 (s, 1H, NH, deuterium oxide exchangeable), 7.97-7.64 (m, 2H, phenyl protons), 7.53-7.15 (m, 4H, 3 phenyl protons and thiazole proton, s, at 7.25), 4.17 (s, 2H, CH_2); ms: (70 eV, electron impact) m/e 267 (molecular ion).

Anal. Calcd. for $C_{11}H_{10}ClON_3S$: C, 49.34; H, 3.76; N, 15.69. Found: C, 49.34; H, 3.75; N, 15.97.

2-Propenoic Acid 2-(4-Phenyl-2-thiazolyl)hydrazide (**14**).

Solutions (in addition funnels) of 1.91 g (10.0 mmoles) of **1** in 50 ml of tetrahydrofuran and 0.950 g (10.5 mmoles) of acryloyl chloride in 25 ml of tetrahydrofuran were added simultaneously, over a 5-minute period, to a flask containing 400 ml of tetrahydrofuran. A cloudy solution resulted. After 30 minutes of stirring, a white solid was present. After the addition of 400 ml of water, solution resulted. The solution stood for 2 hours in an icebath, and the resulting amber needles were collected and air-dried to yield 1.54 g (63%) of **14**, mp 177-179°; ir (potassium bromide): 3350-2600, with spike at 3260 (NH), 1665 (C=O) cm^{-1}; nmr (dimethylsulfoxide-d_6): δ 10.4 (s, 1H, NH, deuterium oxide-exchangeable), 9.53 (s, 1H, NH, deuterium oxide-exchangeable), 7.96-7.76 (m, 2H, phenyl protons), 7.53-7.20 (m, 4H, 3 phenyl protons and thiazole proton, s, at 7.23), 6.40-6.25 (m, 2H, $CH=CH_2$), 6.89-6.68 (m, 1H, $CH=CH_2$); ms: (70 eV, electron impact) m/e (relative intensity) 245 (75, molecular ion), 191 (71), 190 (100), 176 (7), 174 (10), 161 (2), 135 (24), 134 (52), 129 (8), 116 (2), 102 (27), 91 (62), 89 (15).

Anal. Calcd. for $C_{12}H_{11}N_3OS$: C, 58.75; H, 4.52; N, 17.13. Found: C, 58.80; H, 4.63; N, 17.12.

Treatment of **14** with Potassium Carbonate in 2-Butanone.

A mixture of 1.50 g (6.11 mmoles) of **14**, 1.50 g of potassium carbonate and 90 ml of 2-butanone was heated at reflux for 90 minutes. Tlc (silica gel; 9:1::chloroform:methanol) showed the absence of **14** and no **5**. The mixture was concentrated and the residue was treated with water. The resulting reddish-brown solid was collected (1.6 g), and tlc showed two closely spaced spots at $R_f \cong 0.6$. The solid was dissolved in a minimum volume of choroform and applied to a 175-g column of Silica Gel 60 (EM Reagents, 70-230 mesh) which was slurry-packed in chloroform. Elution was accomplished with 3 ℓ of 1% ethanol in chloroform followed by 1 ℓ of 2% ethanol in chloroform and 3 ℓ of 3% ethanol in chloroform. A total of 66 fractions of *ca.* 100 ml each were collected. Fractions 38-48 were combined and concentrated to leave 0.22 g of solid. Recrystallization from ethanol-water gave pure 4,5-dihydro-7-phenylthiazolo[2,3-c][1,2,4]triazepin-3(2*H*)-one (**4**) as an orange solid, mp 271-272°; ir (potassium

bromide): 3260 and 3210 (NH), 1690, 1680 cm^{-1}; nmr (deuteriochloroform and dimethylsulfoxide-d_6): δ 10.82 (s, 1H, NH, deuterium oxide-exchangeable), 7.97-7.55 (m, 2H, phenyl protons), 7.55-7.05 (m, 3H, phenyl protons), 6.87 (s, 1H, thiazole proton), 4.33-3.85 (m, 2H, NCH_2), 3.15-2.52 (m, 2H, $COCH_2$); ms: (70 eV, electron impact) m/e (relative intensity) 245 (25, molecular ion), 191 (38), 190 (52), 176 (50), 174 (7), 161 (16), 135 (22), 134 (100), 129 (13), 116 (3), 102 (48), 91 (58), 89 (34).

Anal. Calcd. for $C_{12}H_{11}N_3OS$: C, 58.75; H, 4.52; N, 17.13. Found: C, 58.80; H, 4.58; N, 17.13.

Fractions 55-65 were combined and concentrated to leave 0.39 g of solid. The solid was dissolved in tetrahydrofuran and precipitated by the addition of water. Collection and air-drying afforded pure 7,8-dihydro-3-phenylthiazolo[3,2-*b*][1,2,4]triazepin-6(5*H*)-one (**15**) as a white solid; mp 288-289° dec; ir (potassium bromide): 3260 (NH), 1710, 1680 cm^{-1}; nmr (dimethylsulfoxide-d_6): δ10.57 (s, 1H, NH), 8.00-7.75 (m, 2H, phenyl protons), 7.60-7.17 (m, 4H, 3 phenyl protons and thiazole proton, s, at 7.27), 4.30-3.90 (m, 2H, NCH_2), 2.90-2.50 (m, 2H, $COCH_2$); ms: (70 eV, electron impact) m/e (relative intensity) 245 (35, molecular ion), 191 (51), 190 (72), 176 (47), 174 (8), 161 (10), 135 (22), 134 (100), 102 (43), 91 (48), 89 (33).

Anal. Calcd. for $C_{12}H_{11}N_3OS$: C, 58.75; H, 4.52; N, 17.13. Found: C, 58.40; H, 4.59; N, 16.96.

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