Synthesis of New Thiazolium Betaines and the Ring Expansion Reaction *via* 1,4-Dipolar Cycloaddition

Dong Chan Kim, Dong Jin Kim, Sang Woo Park, and Kyung Ho Yoo*

Division of Applied Sciences, Korea Institute of Science and Technology, Seoul 131-650, Korea

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The 1,4-dipolar cycloaddition of 3-phenyl-7-[*N*-phenyl(carbamoyl)]-5,6-dihydroimidazo[2,1-*b*]thiazolium betaine (**7d**) with a series of aliphatic alkylating agents such as ethyl bromoacetate, α-chloroacetone, and ethyl 4-chloroacetoacetate gave a variety of new ring-expanded cycloadducts **10a-c** instead of ring transformation compounds **9**. This result was derived from the difference of reactivity between *N*- and *S*-alkylations of thiazolium betaines **7a,d**. The advantage of our method is to prepare the triheterocyclic compounds **10a-c** of complicated structure using reactive thiazolium betaine **7d** in a one-pot without isolation of intermediates. Treatment of *N*-bridged thiazolo compounds **1a-c** with benzoyl isothiocyanate led to new thiazolium betaines **2a-c**, which were reacted with methyl iodide to afford the *S*-alkylated quaternary ammonium salts **3a-c**. Synthesis of new 2-iminothiazolinium betaines **5a,b** also was carried out.

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The betaines are highly reactive organic compounds. They have the strong nucleophilicity owing to the presence of the carbanion. The dipole nature of betaines is more evident in their cycloaddition reactions with dienophile reagents [1,2]. Complicated heterocyclic structures, difficult to prepare using other synthetic methods, were obtained in this way. The spreading of the negative charge assures an increased stability for the anionic part, directly influencing the overall stability of the compound. Many examples were known and it may be concluded that the localization of the negative charge is much more important in determining the betaine stability, as comparison with the spreading of the positive charge.

We have been interested in the *N*-bridged thiazolium betaines [3,4] because of their high reactivities and interesting reaction behavior. Thus, we reported on the various kinds of ring transformation reactions [5,6] and dipolar cycloadditions [7,8] of these betaines.

We now wish to describe our results on the synthesis and the reaction of new thiazolium betaines. Subsequently we report here on the synthesis of triheterocyclic cycloadducts containing ring-expanded thiazine *via* 1,4-dipolar cycloaddition.

Thiazolo compounds **1** [9-11], isolated as the hydrobromide or hydrochloride, were prepared by reacting of cyclic thioureas with α-haloketone or α-haloester by following the general procedure reported previously. The free bases of the hydrobromide salts have also been isolated after neutralizing the aqueous solution either with potassium carbonate or sodium hydroxide. The thiazolo compounds are used as anesthetics, fungistatics, bacteriostatics, antimalarials, antidepressants and for several other biological properties like thyroid hypertrophy and cardiac activity. The cyclic thioureas as starting material were prepared by methods described in the literatures [12-14].

N-Bridged thiazolo compounds **1** are used as strong nucleophiles because of the nonbonding electrons of nitrogen atom at 7-, 8- or 9-position. Thus, a nucleophilic attack on various electrophiles containing electron deficient carbon center due to great electronegativity of heteroatoms O, N, S resulted in the formation of corresponding betaines. Reinvestigation of alkylation of 3-phenyl-5,6-dihydroimidazo[2,1-*b*]thiazole (**1a**) has shown that methylation occurs exclusively at the 7-position [15].

New betaines **2a-c** including the *N*-benzoyl(thiocarbamoyl) moiety were easily prepared from reaction of *N*-bridged thiazolo compounds **1a-c** with benzoyl isothiocyanate in acetone at room temperature, respectively. These betaines are stabilized by a series of resonance structures [16].

Completion of the reaction was detected from the formation of a white precipitate because most betaine compounds were insoluble in common organic solvents. The reaction was carried out in aprotic solvents such as acetone, acetonitrile in order to prevent the dissociation of synthesized betaine in protic solvents. A remarkable down field shift of vinylic proton on the ^{1}H nmr spectra of **2a-c** also corroborated the betaine structure (Table 1).

The reactivity of betaines **2a-c** was achieved by reaction with methyl iodide in acetone or acetonitrile. These betaines reacted with methyl iodide providing the *S*-alkylated quaternary ammonium salts **3a-c**. Lack of absorption of in the region 2050-2070 cm^{-1} on the infrared spectra of **3a-c** shows the absence of benzoyl isothiocyanate thereby suggesting the alkylated structure. In this reaction *S*-alkylation in comparison with *N*-alkylation occurred very exclusively because of the difference of nucleophilicity. The synthetic pathway to **2** and **3** is illustrated in Scheme 1.

Appropriately substituted 2-imino-4-thiazolinium-betaines **5** were obtained in 64 and 57% yields by treatment of 2-imino-4-thiazolines **4** with phenyl isothiocyanate, respectively. At this time the reaction didn't lead to the *s*-triazine **6** containing fused spiro ring system as

Table 1

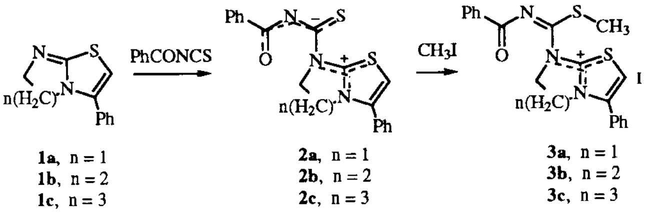
Synthetic Data of Thiazolium Betaines **2a-c**

Product	n	Yield [a] (%)	mp [b] (°C)	IR (KBr) [c] ν (cm^{-1})	^{1}H NMR [d] (TMS) δ ppm	Molecular Formula (MW)	Analysis (%) Calcd.	Found
2a	1	78	162-163.5	2070, 1690, 1530, 1450, 1385, 1320	4.73 (s, 4H, 2NCH$_2$), 7.13 (s, 1H, =CH), 7.25-8.13 (m, 10H, 2ArH)	$C_{19}H_{15}N_3OS_2$ (365.47)	C: 62.42 H: 4.14 N: 11.50	62.20 4.10 11.40
2b	2	87	193.5-194.5	2055, 1675, 1580, 1280, 1215	2.00-2.60 (m, 2H, CH$_2$), 3.80-4.50 (m, 4H, 2NCH$_2$), 7.70 (s, 1H, =CH), 7.36-8.10 (m, 10H, 2ArH)	$C_{20}H_{17}N_3OS_2$ (379.49)	C: 63.28 H: 4.52 N: 11.07	63.10 4.53 11.10
2c	3	90	189-190.5	2050, 1690, 1500, 1455, 1340, 1270	1.27-2.47 (m, 4H, 2CH$_2$), 3.67-4.66 (m, 4H, 2NCH$_2$), 6.92-7.80 (m, 10H, 2ArH), 7.88 (s, 1H, =CH)	$C_{21}H_{19}N_3OS_2$ (393.52)	C: 64.07 H: 4.87 N: 10.68	63.80 4.90 10.50

[a] Yield of isolated compounds. [b] Melting points were determined on a Thomas-Hoover capillary melting point apparatus and were uncorrected. [c] The ir spectra were recorded on a Perkin-Elmer Model 267 spectrophotometer. [d] The nmr spectra were obtained on a JEOL JNM-PMX 60_{SI}.

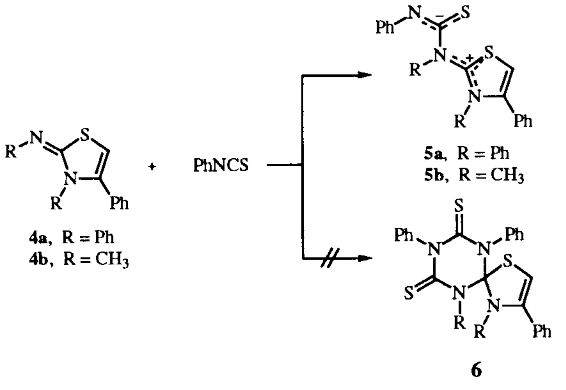
shown in Scheme 2. The betaines **5** possessing a 1,4-dipole didn't undergo subsequent cyclization with another molecule of phenyl isothiocyanate to yield a 1:2 cycloadduct **6**, although an excess of phenyl isothiocyanate was added. The starting materials **4a,b** were synthesized from *N,N*-disubstituted-thioureas [17,18] by the literature methods [19,20].

Scheme 1



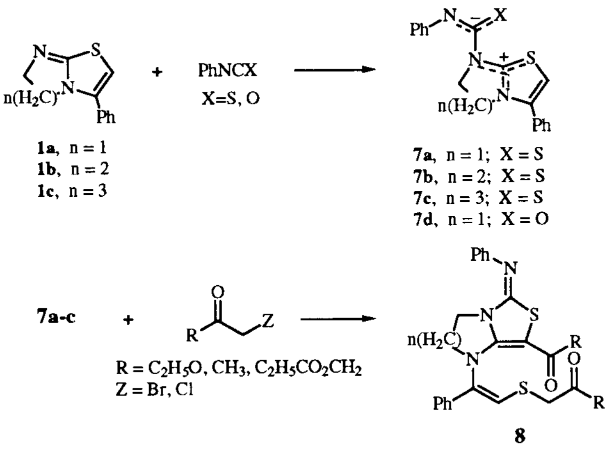
In 1976 it was reported [5] that the ring transformation reaction of bicyclic zwitterionic thiazoles with phenacyl bromide afforded the new bicyclic thiazoles by the ring opening and the renewed cyclization. These molecular structures were solved by X-ray crystallograpy and their reaction mechanisms were identified.

Scheme 2



For a similar purpose we had synthesized previously many biheterocyclic compounds **8** *via* such ring transformation reaction by treatment of thiazolium betaines **7a-c** having *N*-phenyl(thiocarbamoyl) moiety with various alkylating agents [5,6]. In this case α-haloketone, α-haloester, and χ-haloketoester such as α-chloroacetone, ethyl bromoacetate, and ethyl 4-chloroacetoacetate were used as the alkylating agents (Scheme 3).

Scheme 3

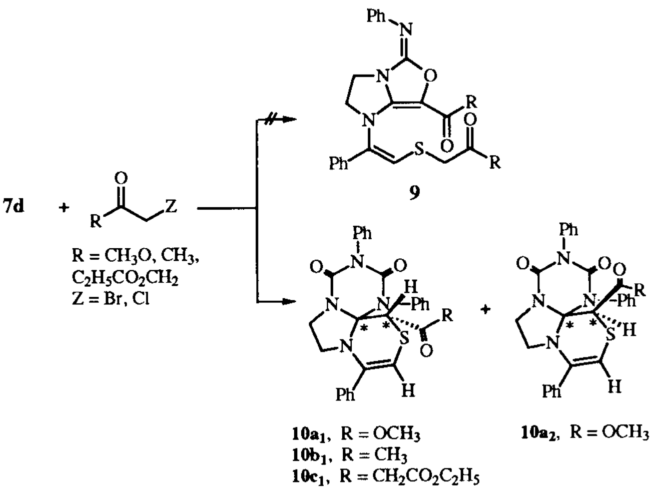


The 1,4-dipolar cycloaddition reaction gives rise to the formation of six-membered ring adducts [21,22]. In isocyanates both the C=N and the C=O double bond can participate in polar cycloaddition reactions, but usually reaction products resulting from addition across the C=N double bond are isolated [23,24].

In our previous report [7a], the reaction mechanism and structure of cycloadducts *via* 1,4-dipolar cycloaddition were described. On the other hand, it was found that one isomer of the cycloadducts was converted into the other in the reaction mixture under thermal condition [7b]. This phenomenon suggests that these stereoisomeric cycloadducts should be the thermodynamically and kinetically controlled products, respectively.

In the present work, new ring-expanded triheterocyclic compounds (12*RS*,13*SR*)- and (12*SR*,13*SR*)-12-methoxycarbonyl-2,4-dioxo-1,3,9-triphenyl-6,7-dihydro-12*H*-thiazino[3',4';2,3]imidazo[1,2-*a*][1,3,5]triazines **$10a_1$,a_2** *via* 1,4-dipolar cycloaddition instead of ring transformation compounds **9** were prepared as a mixture of isomers by treatment of 3-phenyl-7-[*N*-phenyl(carbamoyl)]-5,6-dihydroimidazo[2,1-*b*]thiazolium betaine (**7d**) with methyl bromoacetate. Similarly, treatment of **7d** with a series of aliphatic alkylating agents such as α-chloroacetone and ethyl 4-chloroacetoacetate led to (12*RS*,13*SR*)-12-acetyl-2,4-dioxo-1,3,9-triphenyl-6,7-dihydro-12*H*-thiazino[3',4';2,3]-imidazo[1,2-*a*][1,3,5]triazine (**$10b_1$**) and (12*RS*,13*SR*)-12-ethoxycarbonylacetyl-2,4-dioxo-1,3,9-triphenyl-6,7-dihydro-12*H*-thiazino[3',4';2,3]imidazo[1,2-*a*][1,3,5]triazine (**$10c_1$**) as a single diastereomer, respectively (Scheme 4).

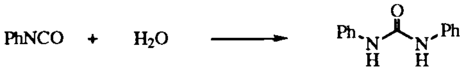
Scheme 4



In competition of the nucleophilicity of *N*-phenyl(carbamoyl) and *N*-phenyl(thiocarbamoyl) moieties of thiazolium betaines **7a** and **7d**, in case of **7a** *S*-alkylation have priority over *N*-alkylation, but **7d** undergoes *N*-alkylation than *O*-alkylation.

Interestingly, in case that the substituent R was methoxy group having strong electron donating property, the kinetically controlled product **$10a_2$** was predominantly obtained over the thermodynamically controlled product **$10a_1$**. The ^1H nmr spectrum of **10a** showed an *ca.* 1:2 mixture of component for **$10a_1$** and **$10a_2$**. However, when R was a methyl or a methylene ester group having a weak electron donating effect, the thermodynamically controlled product **$10b_1$** or **$10c_1$** only was obtained. No diastereomer of **$10b_1$** or **$10c_1$** was found. Phenyl isocyanate isolated during the reaction, except for participation in a 1,4-dipolar cycloaddition, reacted with a little water in the acetone affording a small amount of *N*,*N*-diphenylurea (**14**) as shown in Scheme 5.

Scheme 5



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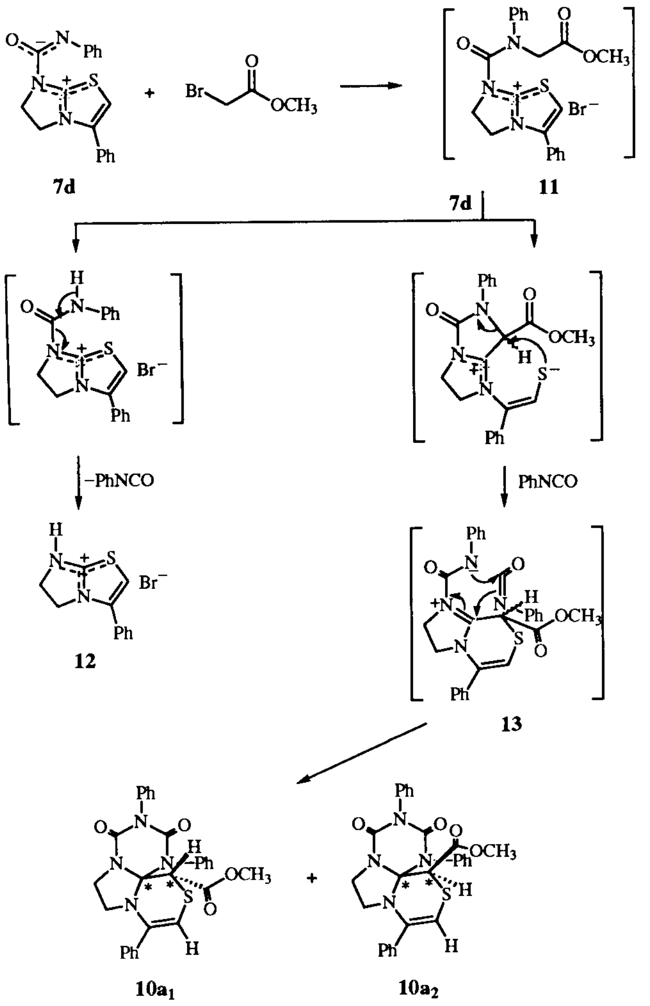
3-Phenyl-5,6-dihydroimidazo[2,1-*b*]thiazole (**1a**) was reacted with phenyl isocyanate in acetone at room temperature to give the betaine **7d** as a white solid [3,4].

On determining the structure of diastereomeric cycloadducts, long range W-coupling [25] by zig-zag arrangement of C-H and C-C bonds becomes an important factor. The existence of W-coupling on the ^1H nmr spectrum of **10a** manifested that H-10 (d, 1H, $J_{10,12} = 1.6$ Hz, vinylic, δ 4.83) and H-12 (d, 1H, $J_{12,10} = 1.6$ Hz, methine, δ 4.73) of **$10a_1$** had the coplanar arrangement. On the other hand, the singlets of **$10a_2$** at δ 5.02 and δ 3.58 suggested that they did not have coplanarity. The ^{13}C nmr spectrum of **10a** also provides the additional evidences for the structure elucidation of diastereomeric cycloadducts. Namely, the characteristic absorptions at δ 167.8 and 168.6 ($COOCH_3$), δ 88.4 and 96.4 (vinylic-C), δ 41.7 and 50.0 (methine-C) showed the consistence with above assignment. The presence of carbonyl groups was observed by infrared spectrum. And the base peak [274 (M^+-2PhNCO)] of ms spectrum proved that phenyl isocyanate was easily fallen apart. Based on all the spectral data, it was concluded that **$10a_1$** is in relation of diastereomer with **$10a_2$**. The assignments of **$10b_1$** and **$10c_1$** were fully characterized in an analogous manner described above.

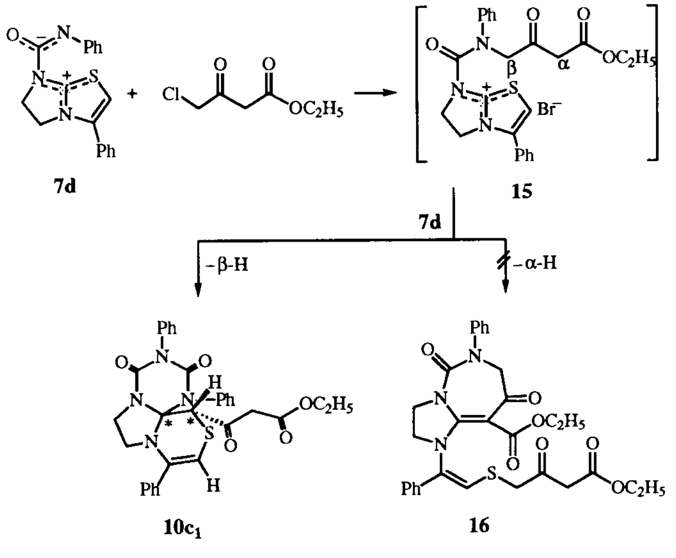
First, *N*-alkylation by thiazolium betaine **7d** occurred to afford the *N*-alkylated intermediate **11**. Then, the unreacted thiazolium betaine **7d** as a base deprotonated the acidic methylene proton adjacent to carbonyl of **11** to generate the carbanion. During the reaction, imidazo[2,1-*b*]thiazole hydrobromide salt **12** precipitated as a white solid. Simultaneously, thiazole ring opening by bridgehead carbon attack of the carbanion followed by the attack of the sulfido anion to the methine carbon yielded the key intermediate **13** possessing a ring-expanded thiazine ring and reactive 1,4-dipole. Subsequent 1,4-dipolar cycloaddition of 1,4-dipole with phenyl isocyanate as a dienophile led to a stereoisomeric mixture of cycloadducts **$10a_1$,a_2** containing a triazine ring. Many examples of 1,4-dipolar cycloadditions to give the six-membered ring 2:1 adduct were known [26,27]. All of these reactions occurred in one-pot. The cycloadducts **$10a_1$** and **$10a_2$** so produced were separated by column chromatography (silica-gel, hexane/ethyl acetate = 3/2).

In case of ethyl 4-chloroacetoacetate as the alkylating



agent, 1,4-dipolar cycloadduct **10c$_1$** was obtained by the deprotonation of β-H instead of ring transformation compound **16** by the elimination of α-H at *N*-alkylated intermediate **15** as depicted in Scheme 6. This result means that the 1,4-dipolar cycloaddition is more reactive than ring transformation reaction and formation of a 6-membered ring is more favorable than that of 7-membered ring.

Scheme 6



The ^{1}H nmr spectrum of **10c$_1$** showed the AB system [δ 3.42 (d, 1H, A portion of AB, J_{AB} = 15.4 Hz), δ 4.20 (d, 1H, B portion of AB, J_{BA} = 15.4 Hz)] of methylene protons between carbonyl groups. Because of the rigidity of the larger ring system on the molecular shape, the methylene protons become non-equivalent.

EXPERIMENTAL

Melting points were determined on a Thomas-Hoover capillary melting point apparatus and were uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 267 spectrophotometer or Analect FX-6160 FT-IR spectrometer as potassium bromide pellets. The ^{1}H nmr and ^{13}C nmr were obtained on a JEOL JNM-PMX 60$_{SI}$ or 300 MHz Gemini Varian nmr spectrometer using tetramethylenesilane as the reference. Multiplicity was simplified as follows: s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet. Elemental analyses were performed with Perkin-Elmer Model 240C elemental analyzer. Mass spectra were determined on a Hewlett-Packard model 5988A GC-Mass spectrometer. Column chromatography was carried out using silica gel (230-400 mesh).

General Procedure for the Preparaton of Thiazolium Betaines **2a-c**.

In a round-bottom flask equipped with a dropping funnel, a drying calcium chloride tube, and a magnetic stirring bar, the appropriate thiazolo compound **1a-c** (4.95 mmoles) was dissolved in 50 ml of acetone. To this solution equimolar amounts of benzoyl isothiocyanate (0.81 g) in 10 ml of acetone was added dropwise and the reaction mixture was stirred for 30 minutes at room temperature. The resulting solution was concentrated and the residue was collected by filtration, washed with cold acetone to afford the corresponding betaine as a pale yellow solid.

General Procedure for the Preparaton of *S*-Alkylated Compounds **3a-c**.

To a solution of the appropriate thiazolium betaines **2a-c** (1.37 mmoles) dissolved in hot acetone was gradually added methyl iodide (0.195 g, 1.37 mmoles) in 10 ml of acetone and the resulting mixture was allowed to reflux for 1 hour. The solution was concentrated and washed with cold acetone to afford the *S*-alkylated compound as a white solid.

7-[*C*-Methylthio-*N*-benzoylforimidoyl]-3-phenyl-5,6-dihydroimidazo[2,1-*b*]thiazolium Iodide (**3a**).

This compound was obtained using 7-[*N*-benzoyl(thiocarbamoyl)]-3-phenyl-5,6-dihydroimidazo[2,1-*b*]thiazolium betaine (**2a**) in a yield of 0.41 g (59%), mp 204-205.5° dec; ir (potassium bromide): ν 1680 (C=O), 1535, 1420, 1390, 1340 cm^{-1}; ^{1}H nmr (dimethyl sulfoxide-d$_6$): δ 3.28 (s, 3H, CH$_3$), 4.90 (s, 4H, 2NCH$_2$), 7.50-8.00 (m, 10H, 2ArH), 7.80 (s, 1H, =CH).

8-[*C*-Methylthio-*N*-benzoylforimidoyl]-3-phenyl-6,7-dihydro-5*H*-thiazolo[3,2-*a*]pyrimidinium Iodide (**3b**).

This compound was obtained using 8-[*N*-benzoyl(thiocarbamoyl)]-3-phenyl-6,7-dihydro-5*H*-thiazolo[3,2-*a*]pyrimidinium betaine (**2b**) in a yield of 0.57 g (80%), mp >250° dec; ir (potassium bromide): ν 1680 (C=O), 1525, 1450, 1390, 1325, 1280, 1015 cm^{-1}; ^{1}H nmr (dimethyl sulfoxide-d$_6$): δ 2.10-2.47 (m, 2H, CH$_2$), 3.33 (s, 3H, CH$_3$), 3.97-4.40 (m, 4H, 2NCH$_2$), 7.60-8.03 (m, 10H, 2ArH), 7.70 (s, 1H, =CH).

9-[*C*-Methylthio-*N*-benzoylforimidoyl]-3-phenyl-5,6,7,8-tetrahydro-thiazolo[3,2-*a*][1,3]diazepinium Iodide (**3c**).

This compound was obtained using 9-[*N*-benzoyl(thiocarbamoyl)]-3-phenyl-5,6,7,8-tetrahydrothiazolo[3,2-*a*]-[1,3]diazepinium betaine (**2c**) in a yield of 0.48 g (66%), mp 227.5-229° dec; ir (potassium bromide): ν 1700 (C=O), 1505, 1450, 1380, 1350, 1275 cm^{-1}; ^{1}H nmr (dimethyl sulfoxide-d$_6$): δ 1.83-2.37 (m, 4H, 2CH$_2$), 3.33 (s, 3H, CH$_3$), 3.93-4.66 (m, 4H, 2NCH$_2$), 7.40-7.97 (m, 10H, 2ArH), 8.05 (s, 1H, =CH).

3,4-Diphenyl-2-phenylimino-4-thiazoline (**4a**).

N-Bromosuccinimide (3.0 g, 0.8 mole) was dissolved in 100 ml of phenyl methyl ketone. To this solution *N,N*-diphenylthiourea (3.7 g, 0.0162 mole) in 120 ml of phenyl methyl ketone was added with constant stirring. The mixture was allowed to heat for 8 hours at high temperature. When the mixture was cooled in an ice bath, 3,4-diphenyl-2-phenylimino-4-thiazoline hydrobromide (yield 65%, mp 276°) was formed. The hydrobromide salt was dissolved in water and neutralized with 40% sodium hydroxide solution. The resulting free-base was filtered and washed with water to give 2.25 g (42%) of **4a** as a white solid, mp 192-194° dec; ir (potassium bromide): ν 1630, 1595, 1500, 1455, 1370, 1315, 1260 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 6.00 (s, 1H, =CH), 7.27-7.57 (m, 15H, 3ArH).

3-Methyl-2-methyllimino-4-phenyl-4-thiazoline (**4b**).

N,N-Dimethylthiourea (2.0 g, 0.0192 mole) was dissolved in 50 ml of absolute ethanol. To this solution phenacyl bromide (3.82 g) in 40 ml of absolute ethanol was added with constant stirring. The reaction mixture was refluxed for 2 hours. The resulting solution was then concentrated and it solidified. The hydrobromide salt obtained was dissolved in water and a solution of potassium hydroxide was added with cooling. The upper oily layer was separated and the aqueous layer was extracted three times with ether. The combined solution was dried over magnesium sulfate and filtered. The ether was distilled off to give 1.76 g (45%) of **4b** as white crystallines, mp 72-74° (lit [9] 76-77°); ir (potassium bromide): ν 1630, 1455, 1410, 1375, 1170 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 3.00 (s, 3H, NCH$_3$), 3.13 (s, 3H, =NCH$_3$), 6.67 (s, 1H, =CH), 7.28 (s, 5H, ArH).

General Procedure for the Preparation of 2-Imino-4-thiazolinium Betaines **5a,b**.

In 50 ml of acetone the appropriate 2-substituted-imino-4-thiazoline **4a,b** (0.50 g) was charged and dissolved with heating. Equimolar amounts of phenyl isothiocyanate was added dropwise to this solution. The reaction mixture was refluxed for 5 hours, and cooled. The resulting solution was concentrated under reduced pressure and solidified with ethyl ether to afford the corresponding betaine.

3,4-Diphenyl-2-phenylimino-7-[*N*-phenyl(thiocarbamoyl)]-4-thiazolinium Betaine (**5a**).

This compound was obtained using 3,4-diphenyl-2-phenylimino-4-thiazoline (**4a**) in a yield of 0.45 g (64%) as a white solid, mp 168-169.5°; ir (potassium bromide): ν 1615, 1575, 1485, 1360, 1300, 1245 cm^{-1}; ^{1}H nmr (dimethyl sulfoxide-d$_6$): δ 6.17 (s, 1H, =CH), 7.12-7.72 (m, 20H, 4ArH).

3-Methyl-2-methyllimino-4-phenyl-7-[*N*-phenyl(thiocarbamoyl)]-4-thiazolinium Betaine (**5b**).

This compound was obtained using 3-methyl-2-methylimino-4-phenyl-4-thiazoline (**4b**) in a yield of 0.47 g (57%) as a pale yellow solid, mp 167-169°; ir (potassium bromide): ν 1620, 1595, 1495, 1450, 1425, 1375, 1250 cm^{-1}; ^{1}H nmr (dimethyl sulfoxide-d$_6$): δ 3.30 (s, 6H, 2NCH$_3$), 6.21 (s, 1H, =CH), 6.89-7.46 (m, 5H, ArH), 7.50 (s, 5H, ArH).

General Procedure for the Preparation of 1,4-Dipolar Cycloadducts **10a-c**.

To a solution of 5,6-dihydro-3-phenyl-7-[*N*-phenyl(carbamoyl)]imidazo[2,1-*b*]thiazolium betaine (**7d**) (1.01 g, 3.15 mmoles) dissolved by heating in 300 ml of acetone was gradually added the appropriate aliphatic alkylating agent (1.50 mmoles). The reaction mixture was refluxed for 6 hours with constant stirring. Then, the reaction mixture was concentrated under reduced pressure and the hydrobromide salt **12** (mp >250°) formed was filtered off. The solvent was evaporated *in vacuo* and the residue was chromatographed on silica-gel (*n*-hexane/ethyl acetate = 3/2). The combined solutions containing the product were distilled off and the resulting solid was filtered to afford the 1,4-dipolar cycloadducts.

(12*RS*,13*SR*)- and (12*SR*,13*SR*)-12-Methoxycarbonyl-2,4-dioxo-1,3,9-triphenyl-6,7-dihydro-12*H*-thiazino[3',4';2,3]imidazo-[1,2-*a*][1,3,5]triazines **10a$_1$,a$_2$**.

This compound (1:2 mixture of **10a$_1$** and **10a$_2$**) was obtained using methyl bromoacetate as the alkylating agent in a yield of 0.25 g (33%) as a white solid, mp 168.5-169.5° dec; ir (potassium bromide): ν 1725 (C=O), 1710 (C=O), 1675 (C=O), 1490, 1445, 1365, 1335, 1260 cm^{-1}; ^{1}H nmr (300 MHz, deuteriochloroform): δ 2.91-3.02, 3.35-3.49, 3.63-3.98, and 4.05-4.14 (m, 4H, NCH$_2$CH$_2$N), 3.58 and 4.73 (d, 1H, J = 1.6 Hz and s, 1H, CH of mixture, respectively), 3.81 and 3.87 (s, 3H, OCH$_3$ of mixture, respectively), 4.83 and 5.02 (s, 1H and d, 1H, J = 1.6 Hz, =CH of mixture, respectively), 6.83-6.86, 7.15-7.51, and 7.97-7.99 (m, 15H, 3ArH); ^{13}C nmr (75.5 MHz, deuteriochloroform): δ 41.7 (CH), 42.1 (C-6), 42.8 (C-6), 49.2 (C-7), 49.6 (C-7), 50.0 (CH), 52.9 (OCH$_3$), 53.8 (OCH$_3$), 82.9 (C-13), 83.3 (C-13), 88.4 (=CH), 96.4 (=CH), 149.1 (CO), 149.7 (CO), 151.2 (2CO), 167.8 (COOCH$_3$), 168.6 (COOCH$_3$); ms: m/z 274 (M$^+$-2PhNCO, 100).

Anal. Calcd. for $C_{28}H_{24}N_4O_4S$: C, 65.61; H, 4.72; N, 10.93. Found: C, 65.54; H, 4.75; N, 10.87.

(12*RS*,13*SR*)-12-Acetyl-2,4-dioxo-1,3,9-triphenyl-6,7-dihydro-12*H*-thiazino[3',4';2,3]imidazo[1,2-*a*][1,3,5]triazine (**10b$_1$**).

This compound was obtained using α-chloroacetone as the alkylating agent in a yield of 0.28 g (38%) as a white solid, mp 178.5-179.5° dec; ir (potassium bromide): ν 1725 (C=O), 1680 (C=O), 1600, 1495, 1445, 1385, 1360, 1325, 1245 cm^{-1}; ^{1}H nmr (300 MHz, deuteriochloroform): δ 2.43 (s, 3H, CH$_3$), 3.38-3.54

and 3.71-3.93 (m, 4H, NCH_2CH_2N), 4.68 (d, 1H, J = 1.5 Hz, CH), 4.70 (d, 1H, J = 1.5 Hz, = CH), 6.80-6.83 and 7.19-7.52 (m, 15H, 3ArH); ^{13}C nmr (75.5 MHz, deuteriochloroform): δ 30.0 ($\mathit{C}OCH_3$), 43.7 (CH), 47.2 (C-6), 50.4 (C-7), 83.6 (C-13), 86.9 (=CH), 150.2 (CO), 151.7 (CO), 197.9 ($\mathit{C}OCH_3$).

Anal. Calcd. for $C_{28}H_{24}N_4O_3S$: C, 67.72; H, 4.87; N, 11.28. Found: C, 67.73; H, 4.90; N, 11.14.

(12*RS*,13*SR*)-12-Ethoxycarbonylacetyl-2,4-dioxo-1,3,9-triphenyl-6,7-dihydro-12*H*-thiazino[3',4';2,3]imidazo[1,2-*a*]-[1,3,5]triazine (**10c$_1$**).

This compound was obtained using ethyl 4-chloroacetoacetate as the alkylating agent in a yield of 0.13 g (15%), pale yellow solid, mp 104-106° dec; ir (potassium bromide): ν 1720 (C=O), 1675 (C=O), 1490, 1440, 1380, 1320 cm^{-1}; ^1H nmr (300 MHz, deuteriochloroform): δ 1.31-1.25 (t, 3H, CH_3), 3.40-3.54, 3.74-3.80, and 3.90-3.95 (m, 4H, NCH_2CH_2N), 3.42 (d, 1H, A portion of AB, J_{AB} = 15.4 Hz, $COC\mathit{H}_2CO$), 4.13-4.28 (m, 2H, OCH_2), 4.20 (d, 1H, B portion of AB, J_{BA} = 15.4 Hz, $COC\mathit{H}_2CO$), 4.60 (d, 1H, J = 1.2 Hz, CH), 5.12 (d, 1H, J = 1.4 Hz, =CH), 6.81-6.84 and 7.19-7.52 (m, 15H, 3ArH); ^{13}C nmr (75.5 MHz, deuteriochloroform): δ 14.7 ($COOCH_2\mathit{C}H_3$), 43.8 (CH), 46.3 ($CO\mathit{C}H_2CO$), 48.0 (C-6), 50.4 (C-7), 62.6 ($COO\mathit{C}H_2CH_3$), 83.6 (C-13), 86.0 (=CH), 150.2 (CO), 152.1 (CO), 167.7 ($\mathit{C}OOCH_2CH_3$), 191.0 ($\mathit{C}OCH_2CO$).

Anal. Calcd. for $C_{31}H_{28}N_4O_5S$: C, 65.48; H, 4.96; N, 9.85. Found: C, 65.09; H, 5.13; N, 9.43.

5,6-Dihydro-3-phenyl-7-[*N*-phenyl(carbamoyl)]imidazo[2,1-*b*]-thiazolium Betaine (**7d**).

To a solution of 5,6-dihydro-3-phenylimidazo[2,1-*b*]thiazole (**1a**) (2.02 g, 10.0 mmoles) dissolved in 50 ml of acetone was added dropwise phenyl isocyanate (1.19 g, 10.0 mmoles) at room temperature with constant stirring. During the addition, a white precipitate was formed and the reaction mixture was stirred for 30 minutes. The white solid was then collected by filtration and air-dried to give 2.62 g (82%) of **7d**, mp 196.0-197.0°; ir (potassium bromide): ν 1640 (C=O), 1580 cm^{-1}; ^1H nmr (deuteriotrifluoroacetic acid): δ 5.01 (s, 4H, $2NCH_2$), 7.18 (s, 1H, =CH), 7.47 (s, 5H, ArH), 7.68 (s, 5H, ArH).

3-Phenyl-5,6-dihydroimidazo[2,1-*b*]thiazole Hydrobromide (**12**).

This compound was obtained as a white solid, mp >250°; ir (potassium bromide): ν 2975 (R_3NH^+), 1585, 1375, 1285, 1140 cm^{-1}; ^1H nmr (deuterium oxide): δ 4.30 (s, 4H, $2NCH_2$), 6.69 (s, 1H, =CH), 7.46 (s, 10H, 2ArH).

N,*N*-Diphenylurea (**14**).

This compound was obtained as a pale yellow solid, mp 228.0-230.0°; ir (potassium bromide): ν 3240 (NH), 1645 (C=O of amide), 1595, 1550, 1495, 1440, 1315, 1235 cm^{-1}; ^1H nmr (dimethyl sulfoxide-d_6): δ 6.92-7.66 (m, 10H, 2ArH), 8.30 (br, 2H, 2NH).

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