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(10) See J. B. Stothers, "Carbon-13 NMR Spectroscopy", Academic Press, New York, N.Y., 1972.
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Heterocycles from *N*-Ethoxycarbonylthioamides and Dinucleophilic Reagents. 2. Five-Membered Rings Containing Two Heteroatoms at 1,3 Positions

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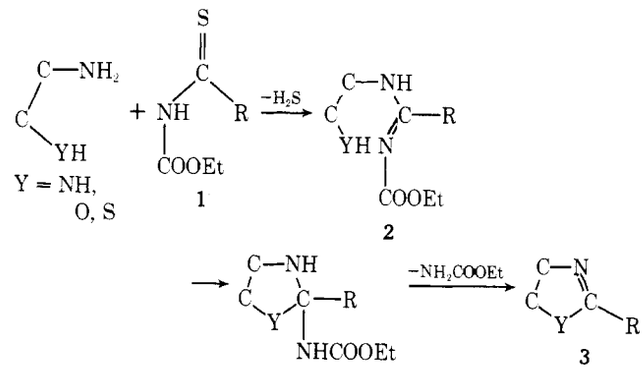
The reaction of *N*-ethoxycarbonylthioamides (1) with 1,2-diamines, amino alcohols, or aminomercaptans yields five-membered heterocyclic rings containing the thiocarbonyl carbon atom of 1 flanked by the two heteroatoms of the dinucleophilic reagent.

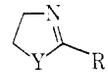
A recent study has shown that *N*-ethoxycarbonylthioamides (1) react with reagents possessing two adjacent nucleophilic sites (NH_2, NHR, OH) at both thiocarbonyl and carbonyl groups to form five-membered, carbonyl-containing heterocyclic rings. Thus reactions with hydrazines and hydroxylamines yield dihydro-1,2,4-triazolones and 1,2,4-oxadiazolones, respectively.[1] In view of these results, it was of interest to investigate the behavior of 1 toward reagents containing two nucleophilic groups separated by two or more positions. Were these reactions to proceed in the same manner as the previous ones, seven-membered or larger rings would be the anticipated products. A related study, however, has revealed that *S*-methyl derivatives of carbamates obtained by addition of alcohols to alkoxycarbonyl isothiocyanates react with 1,2- and 1,3-dinucleophilic reagents without participation of the ester group. Such reactions involving aliphatic 1,2- or 1,3-diamines result in formation of 2-alkoxycarbonyl derivatives of cyclic guanidines, whereas those with *o*-phenylenediamine lead to *N*-alkoxycarbonyl-2-aminobenzimidazoles.[2] On the other hand, it has long been known that primary thioamides react with ethylenediamine to form 2-substituted 4,5-dihydrothiazoles with elimination of H_2S and NH_3.[3]

Our investigation has shown that reactions of *N*-ethoxycarbonylthioamides (1) with 1,2-dinucleophilic reagents H_2NCCYH (Y = NH, O, S), in refluxing ethanol or tetrahydrofuran, proceed in complete analogy with the behavior of primary thioamides. The ester group is neither attacked by the reagent nor retained as side chain of the heterocyclic product. Instead, it is found in the reaction by-product, ethyl carbamate. On the basis of previous experience,[1] initial interaction between the thiocarbonyl of 1 and amino group of the reagent would be expected to result in elimination of H_2S and formation of a substituted amidine (2) as an intermediate. It now appears that this is followed by intramolecular addition of the second nucleophilic group YH to the C=N of 2 and elimination of ethyl carbamate. A five-membered, heterocyclic ring (3) is thus formed which is made up of the N–C–C–Y chain of the reagent and the thiocarbonyl carbon atom of 1.



This is a general reaction that *N*-ethoxycarbonylthioamides (1) undergo upon treatment with substances containing two primary amino, or a primary amino and a hydroxyl or mercapto groups on adjacent carbon atoms. Thus, treatment of 1 with 1,2-diaminoethane, 2-aminoethanol, and 2-aminoethanethiol yields 2-substituted 4,5-dihydroimidazoles (4), -oxazoles (5), and -thiazoles (6), respectively. Similarly, reactions with *o*-phenylenediamine, *o*-aminophenol, and *o*-aminothiophenol lead to 2-substituted benzimidazoles (7), benzoxazoles (8), and benzothiazoles (9) (Scheme I).

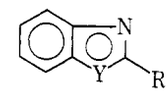
Table I.[a] 4,5-Dihydroimidazoles (4), -oxazoles (5), and -thiazoles (6)



Registry no.	Y	R	Yield,[b] %	Mp (bp), °C
59-98-3	NH	$PhCH_2$[c,d]	51[e]	66–67[f,g]
13623-58-0	NH	4-MeC_6H_4[h]	97[i]	181.5–183[j,k]
6302-84-7	NH	4-$MeOC_6H_4$[c]	85[l]	137–139[m,n]
60705-30-8	NH	2-Pyrrolyl[h]	84[l]	212–213[o]
45753-18-2	NH	2-Thienyl[c]	87[l]	175–177[p]
10431-98-8	O	Et[d,h]	50[q]	(124–126)[r]
10200-70-1	O	4-MeC_6H_4[c]	85[l]	72–73.5[s,t]
13676-94-3	O	4-$MeOC_6H_4$[c]	90[l]	62.5–63.5[f,u]
60705-31-9	O	2-Pyrrolyl[h]	73[l]	165–166[o]
60705-32-0	O	2-Thienyl[c]	39[v]	58–60[w]
13084-31-6	S	4-MeC_6H_4 [x]	90[y]	41.5–42.5[z,aa]
2519-93-9	S	4-$MeOC_6H_4$[x]	93[y]	53.5–54.5[s,bb]
60705-33-1	S	2-Pyrrolyl[x]	66[y]	93–95[o]
60705-34-2	S	2-Thienyl[x]	94[y]	40.5–41.5[w]

[a] Satisfactory analytical data (±0.3% for C, H, N) were reported for all new compounds listed in this table. [b] Crude or partially purified material with melting point lower than that of the pure compound by 1–10 °C. [c] Reaction run in THF. [d] Equimolar amounts of reactants used. [e] A cold solution of the reaction residue in absolute Et_2O was saturated with dry HCl and the precipitated hydrochloride salt was recrystallized from MeOH–Et_2O and then treated with NaOH–H_2O. Extraction of the resulting mixture with Et_2O followed by evaporation of the dried ($MgSO_4$) ethereal solution yielded the product. [f] Recrystallized from petroleum ether (bp 35–60 °C). [g] Lit. mp 66–68 °C: P. Oxley and W. F. Short, *J. Chem. Soc.*, 497 (1947). [h] Reaction run in EtOH. [i] The reaction residue was washed with cold Et_2O. [j] Sublimed. [k] Lit. mp 183 °C: A. J. Hill and S. R. Aspinall, *J. Am. Chem. Soc.*, 61, 822 (1939). [l] The reaction residue was washed with cold water. [m] Recrystallized from EtOAc–petroleum ether (bp 60–75 °C). [n] Lit. mp 140 °C: ref in *g*. [o] Recrystallized from H_2O. [p] Recrystallized from benzene. [q] A petroleum ether (bp 35–60 °C) extract of the reaction residue was evaporated and the new residue was distilled. [r] Lit. bp 129–130 °C: W. Seeliger and W. Thier, *Justus Liebigs Ann. Chem.*, 698, 158 (1966). [s] Recrystallized from hexane. [t] Lit. mp 67–68 °C: ref in *r*. [u] Lit. mp 63 °C: P. Rehländer, *Chem. Ber.*, 27, 2154 (1894). [v] Following washing with cold water, the reaction residue was boiled with two 100-ml portions of petroleum ether (bp 30–65 °C) and the decanted solution was chilled in dry ice–acetone to yield the product. [w] Recrystallized from pentane. [x] Reaction run in MeOH with MeONa used to liberate $HSCH_2CH_2NH_2$ from its hydrochloride salt. [y] The reaction residue was washed with cold, dilute NaOH–H_2O and then with cold water. [z] Recrystallized from EtOH–H_2O. [aa] Lit. mp 42.5–43.5 °C: Y. Iwakura, A. Nabeya, and T. Nishiguchi, *J. Org. Chem.*, 32, 2362 (1967). [bb] Lit. mp 54.5 °C: ref in *u*.

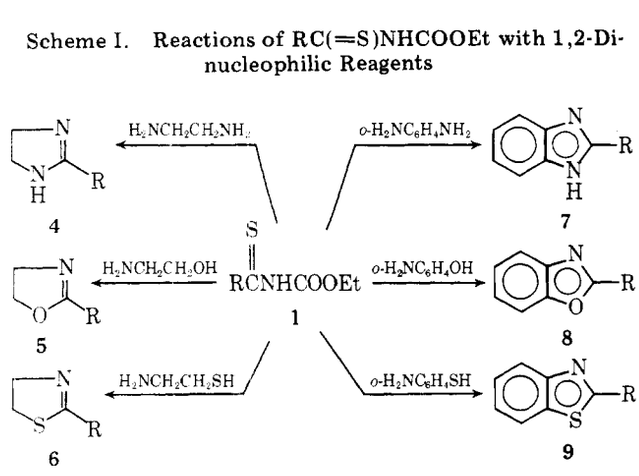
Table II.[a] Benzimidazoles (7), Benzoxazoles (8), and Benzothiazoles (9)



Registry no.	Y	R	Yield,[b] %	Mp (bp), °C
1848-84-6	NH	Et[c,d]	88[e]	172–174[f,g]
120-03-6	NH	4-MeC_6H_4 [c,d]	85[h]	275–276[i,j]
2620-81-7	NH	4-$MeOC_6H_4$[k]	80[l]	226–227[i,m]
3878-23-7	NH	2-Pyrrolyl[c]	92[e]	274–275[n]
3878-18-0	NH	2-Thienyl[k]	95[e]	332–334[i,o]
835-71-2	O	4-MeC_6H_4[c]	90[l]	114–114.5[n,p]
838-34-6	O	4-$MeOC_6H_4$[k]	93[l]	99.5–101[i,q]
54584-08-6	O	2-Pyrrolyl[c]	71[l]	149–149.5[n]
23999-63-5	O	2-Thienyl[k]	75[l]	103–105[n,r]
936-77-6	S	Et[d,k]	46[s]	(129–130, 18 Torr)[t]
16112-21-3	S	4-MeC_6H_4[k]	95[l]	85–86[i,u]
6265-92-5	S	4-$MeOC_6H_4$[k]	83[l]	121–122[n,v]
54584-09-7	S	2-Pyrrolyl[c]	67[h]	158–160[n]
34243-38-4	S	2-Thienyl[k]	92[l]	98–100[n,w]

[a] Satisfactory analytical data (±0.3% for C, H, N) were reported for all new compounds listed in this table. [b] Crude or partially purified material with melting point lower than that of the pure compound by 1–10 °C. [c] Reaction run in EtOH. [d] Equimolar amounts of reactants used. [e] The reaction residue was washed with water. [f] Recrystallized from water. [g] Lit. mp 172 °C: E. L. Hölljes, Jr., and E. C. Wagner, *J. Org. Chem.*, 9, 31 (1944). [h] The reaction mixture was concentrated to a small volume, chilled, and filtered to yield the product. [i] Recrystallized from EtOH. [j] Lit. mp 266–269 °C: ref in *g*. [k] Reaction run in THF. [l] The reaction residue was washed with cold, dilute NaOH–H_2O and then with water. [m] Lit. mp 227 °C: T. Bacchetti and A. Alemagna, *Atti Accad. Naz. Lincei, Rend., Cl. Sci. Fis. Mat. Nat.* 28, 824 (1960); *Chem Abstr.*, 56, 7304*f* (1962). [n] Recrystallized from EtOH–H_2O. [o] Lit. mp 334 °C: W. Ried and P. Stahlhofen, *Chem. Ber.*, 90, 815 (1957). [p] Lit. mp 114 °C: ref in *g*. [q] Lit. mp 100–101 °C: K. Nakagawa, H. Onoue, and J. Sugita, *Chem. Pharm. Bull.*, 12, 1135 (1964). [r] Lit. mp 104.5 °C: R. Royer, G. Colin, P. Demerseman, S. Combrisson, and A. Gheutin, *Bull. Soc. Chim. Fr.*, 2785 (1969). [s] The reaction residue was chromatographed on an alumina column using petroleum ether (bp 60–75 °C) as eluent and the crude product was distilled under reduced pressure. [t] Lit. bp 132 °C (18 Torr): V. G. Brudz, D. A. Drapkina, V. A. Inshakova, and I. P. Plitina, *Metody Poluch. Khim. Reakt. Prep.*, 178 (1967); *Chem. Abstr.*, 71, 30387q (1969). [u] Lit. mp 86 °C: A. I. Kiprianov, I. K. Ushenko, and A. L. Gershun, *J. Gen. Chem. USSR (Engl. Transl.)*, 14, 865 (1944). [v] Lit. mp 121 °C: F. S. Babichev, L. A. Kirpianova, and T. A. Dashevskaya, *Ukr. Khim. Zh.*, 32, 706 (1966); *Chem. Abstr.*, 65, 13682*a* (1966). [w] Lit. mp 98.5–100 °C: R. E. Atkinson and P. R. H. Speakman, *J. Chem. Soc. B*, 2077 (1971).

Scheme I. Reactions of RC(=S)NHCOOEt with 1,2-Dinucleophilic Reagents



The reaction progress is followed easily by testing for evolution of H_2S with lead acetate paper. The time necessary for completion of H_2S evolution (2–48 h) depends on the basicity of the dinucleophilic reagent used, aromatic amines requiring longer reaction times. An excess of reagent and use of tetrahydrofuran (rather than ethanol) as solvent generally result in shorter reaction times. Isolation of the product is very simple, as in most cases the heterocycle is insoluble in water, and ethyl carbamate, the by-product, is soluble. Water-soluble heterocycles are isolated by conventional techniques such as selective extraction, formation of their hydrochloride salts, or column chromatography.

With very good yields in the majority of the cases studied, this reaction allows convenient preparation of several heterocyclic compounds in one step from *N*-ethoxycarbonylthioamides, which are obtainable in one step from ethoxycar-

bonyl isothiocyanate and simple aromatic or heteroaromatic compounds or alkylmagnesium halides.[1,4] It is noteworthy that in contrast to most common synthetic approaches to the same heterocyclic systems,[5] the present method circumvents the use of carboxylic acids or their derivatives as starting materials.

Experimental Section[6]

***N*-Ethoxycarbonylthioamides (1)** were prepared as previously described.[1,4]

General Procedure for Preparation of Compounds 4–9. A solution of 0.010 mol of 1 and 0.012 mol of dinucleophilic reagent in 10 ml of tetrahydrofuran (or 0.010 mol of 1 and 0.020 mol of reagent in 20 ml of ethanol) was refluxed until evolution of H_2S had stopped (2–48 h). Following removal of the solvent by distillation under reduced pressure, the residue was treated as indicated in Tables I and II.

Isolation of Ethyl Carbamate. The residue from the reaction of *N*-ethoxycarbonyl-2-pyrrolethioamide with 2-aminoethanol was treated with water and the resulting mixture was filtered. Extraction with ether of the acidified aqueous filtrate followed by evaporation of the ethereal solution (charcoal, $MgSO_4$) yielded a solid the IR and NMR spectra of which were superimposable on those of authentic ethyl carbamate.

Acknowledgments. Financial support by the Research Corporation, the Research Allocations Committee of the University of new Mexico, and the Department of Chemistry of the University of New Mexico is gratefully acknowledged.

Registry No.—1 (R = $PhCH_2$), 60705-35-3; 1 (R = MeC_6H_4), 57774-66-0; 1 (R = $MeOC_6H_4$), 57774-72-8; 1 (R = 2-pyrrolyl), 37488-43-0; 1 (R = 2-thienyl), 51774-59-5; 1 (R = Et), 59812-12-3; $H_2NCH_2CH_2NH_2$, 107-15-3; $H_2NCH_2CH_2OH$, 141-43-5; $H_2NCH_2CH_2SH$, 60-23-1; *o*-$H_2NC_6N_4NH_2$, 95-54-5; *o*-$H_2NC_6H_4OH$, 95-55-6; *o*-$H_2NC_6H_4SH$, 137-07-5.

Supplementary Material Available. NMR data for all compounds in tables (2 pages). Ordering information is given on any current masthead page.

References and Notes

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(4) E. P. Papadopoulos, *J. Org. Chem.*, **41**, 962 (1976).
(5) R. C. Elderfield, Ed., "Heterocyclic Compounds", Vol. 5, Wiley, New York, N.Y., 1957, pp 239, 274, 377, 420, 507, 679.
(6) Melting points were determined in a Thomas-Hoover apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 337 spectrometer using mineral oil mulls. NMR spectra were obtained on a Varian EM 360 spectrophotometer using solutions in hexadeuteriodimethyl sulfoxide with tetramethylsilane as internal standard.

Thermolysis and Photolysis of Various *N*-Imidolyliminopyridinium Ylides

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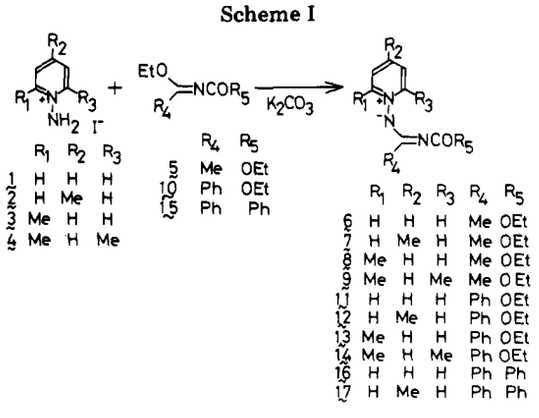
The reactions of pyridinium *N*-imines with some imidates **5**, **10**, and **15** gave the corresponding *N*-imidoyliminopyridinium ylides **6–9**, **11–14**, **16**, and **17** in very good yields. Thermolyses of these *N*-ylides **6–9** and **11–14** in refluxing xylene afforded *s*-triazolo[1,5-*a*]pyridines **18–20**, **23**, **25**, and **27**, pyrazolo[1,5-*a*]pyridines **21**, **22**, **28**, and **29**, and mesoionic compounds **24** and **26**, while thermolyses of *N*-ylides **16** and **17** and photolyses of *N*-ylides **16**, **17**, **11**, and **12** gave the corresponding 1,2,4-oxadiazoles **30** and **31** together with pyridine derivatives in considerable yields. Structural elucidation of these compounds was accomplished mainly by physical and spectral means and partially by their independent syntheses. The formation of pyrazolopyridine derivatives **21**, **22**, **28**, and **29** was confirmed to proceed via isocyanate intermediates.

Pyridinium *N*-ylide acting as an extended dipole is an intriguing molecule in heterocyclic chemistry, and we are especially interested in its reaction leading to polyazabicyclic compounds.[1-3] Recently, a novel 1,6 cyclization has been found in the photolysis of *N*-vinyliminopyridinium ylide.[4] We sought to generalize the 1,6 cyclization, but no such type of reaction could be found in other pyridinium *N*-ylides reported already by us and many investigators.[5-8] Hence, we focused our attention on synthesis of a new class of pyridinium *N*-ylides and we found the 1,6 cyclization in the case of the thermolysis of *N*-imidoyliminopyridinium ylides.[9] In this paper, we wish to report the first synthesis of some *N*-imidoyliminopyridinium ylides and their thermal and photochemical behavior involving the 1,6 cyclization.

Results and Discussion

Preparation of *N*-Imidoyliminopyridinium Ylides 6–9, 11–14, 16 and 17. The title compounds, *N*-imidoyliminopyridinium ylides **6–9**, **11–14**, **16**, and **17**, were synthesized in very good yields by the reactions of 1-aminopyridinium iodides **1–4** with ethyl *N*-ethoxycarbonylacetimidate (**5**), ethyl *N*-ethoxycarbonylbenzimidate (**10**), and ethyl *N*-benzoylbenzimidate (**15**) in the presence of base (Scheme I). All of the *N*-ylides are stable, crystalline compounds and were not apt to cyclize intramolecularly at ordinary conditions. The structures assigned to these *N*-imidoyliminopyridinium ylides

Scheme I



	R_1	R_2	R_3
1	H	H	H
2	H	Me	H
3	Me	H	H
4	Me	H	Me

	R_4	R_5
5	Me	OEt
10	Ph	OEt
15	Ph	Ph

	R_1	R_2	R_3	R_4	R_5
6	H	H	H	Me	OEt
7	H	Me	H	Me	OEt
8	Me	H	H	Me	OEt
9	Me	H	Me	Me	OEt
11	H	H	H	Ph	OEt
12	H	Me	H	Ph	OEt
13	Me	H	H	Ph	OEt
14	Me	H	Me	Ph	OEt
16	H	H	H	Ph	Ph
17	H	Me	H	Ph	Ph