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Synthesis of Pyrazolone Derivatives. XXIV.[1] Reaction of Pyrazolo[3,4-*c*]-[1,5]benzothiazepines with Wohl-Ziegler's Reagents[2]

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An unusual reaction where an allylic methylene is converted into an ethyl ester by means of Wohl-Ziegler's reagents is presented: The reaction of 4-acetyl-1-methyl-2-phenyl-1,2,3,10-tetrahydro-4*H*-pyrazolo[3,4-*c*][1,5]benzothiazepin-3-one (**7**) with N-bromosuccinimide or N-bromoacetamide in commercial (ethanol-containing) chloroform gave ethyl 3-acetyl-5'-oxo-1'-phenyl-spiro[benzothiazoline-2,4'-[2]pyrazoline]-3'-carboxylate (**8**).

Similarly ethyl 3,5'-dioxo-1'-phenyl-spiro[benzo[*b*]thiophene-2(3*H*), 4'-[2]pyrazoline]-3'-carboxylate (**11**) was obtained from 1-methyl-2-phenyl-1,2,3,10-tetrahydro-4*H*-pyrazolo-[3,4-*c*][1] benzothiepin-3,4-dione (**10**).

We synthesized earlier 1-methyl-2-phenyl-1,2,3,10-tetrahydro-4*H*-pyrazolo[3,4-*c*][1,5]-benzothiazepin-3-one[4] (**1**) and 1-methyl-2-phenyl-1,2,3,10-tetrahydro-4*H*-pyrazolo[3,4-*c*][1]-benzothiepin-3,4-dione[5] (**10**), examples of new heterotricyclic ring systems, in order to study their reactivity; the unusual reduction of **10** with sodium borohydride was subsequently described.[6] We now wish to report on the reaction of **1** and 4-acetyl-1-methyl-2-phenyl-1,2,3,10-tetrahydro-4*H*-pyrazolo[3,4-*c*][1,5]benzothiazepin-3-one (**7**) with Wohl-Ziegler's reagents in commercial chloroform.

Attempted allylic bromination of **1** with N-bromosuccinimide in commercial chloroform gave 7-bromo-1-methyl-2-phenyl-1,2,3,10-tetrahydro-4*H*-pyrazolo[3,4-*c*][1,5]benzothiazepin-3-one (**2**) whose elementary analysis agreed with the formula, $C_{17}H_{14}ON_3BrS$. Its infrared (IR) spectrum represented a secondary amine at 3200 cm^{-1}. As the compounds (**2**) was scarcely soluble in solvent, it was converted to 7-bromo-4-(N,N-dimethylglycyl)-1-methyl-2-phenyl-1,2,3,10-tetrahydro-4*H*-pyrazolo[3,4-*c*][1,5]benzothiazepin-3-one (**4**) which was soluble in deuteriochloroform. Its nuclear magnetic resonance (NMR) spectrum represented an allylic methylene resonance at δ 3.83 ppm (2H, singlet), which denied the allylically brominated structure. Observation of the only eight aromatic protons at δ 7.20—7.90 ppm indicated that a bromine atom was substituted on an aromatic ring. Comparison of the NMR spectrum with that of 4-(N,N-dimethylglycyl)-1-methyl-2-phenyl-1,2,3,10-tetrahydro-4*H*-pyrazolo[3,4-*c*][1,5]-benzothiazepin-3-one (**6**) clearly supported the above facts: both spectra gave the same pattern except for the aromatic field.

Considering *ortho* and *para* directing affinity of amino group, structures whose bromine atoms were substituted on 2' (or 6'), 4', 5 or 7-position were considered. However, in the NMR spectrum of **4**, one aromatic proton (δ 7.87 ppm, 1H, doublet, J=1 Hz) at the lowest field suggested *para* coupling, and was assigned as the proton at the 8-position between the sulfur and the bromine atom at 7-position. It is known that the bromination of phenothiazine which is structurally related to **1**, occurs initially at the *para* position to the amino group.[7] Similar

1) Part XXIII: I. Ito and S. Nagai, *Chem. Pharm. Bull.* (Tokyo), **22**, 2796 (1974).
2) This work was presented at the Tokai Branch Meeting of Pharmaceutical Society of Japan, November, 17, 1973.
3) Location: *Tanabe-dori, Mizuho-ku, Nagoya.*
4) I. Ito, T. Ueda, and N. Oda, *Chem. Pharm. Bull.* (Tokyo), **18**, 2058 (1970).
5) I. Ito and T. Ueda, *Chem. Pharm. Bull.* (Tokyo), **18**, 1994 (1970).
6) I. Ito and T. Ueda, *Tetrahedron*, **30**, 1027 (1974).
7) A.R. Katritzky and A.J. Boulton, *Advances in Heterocyclic Chemistry*, **9**, 321 (1968).

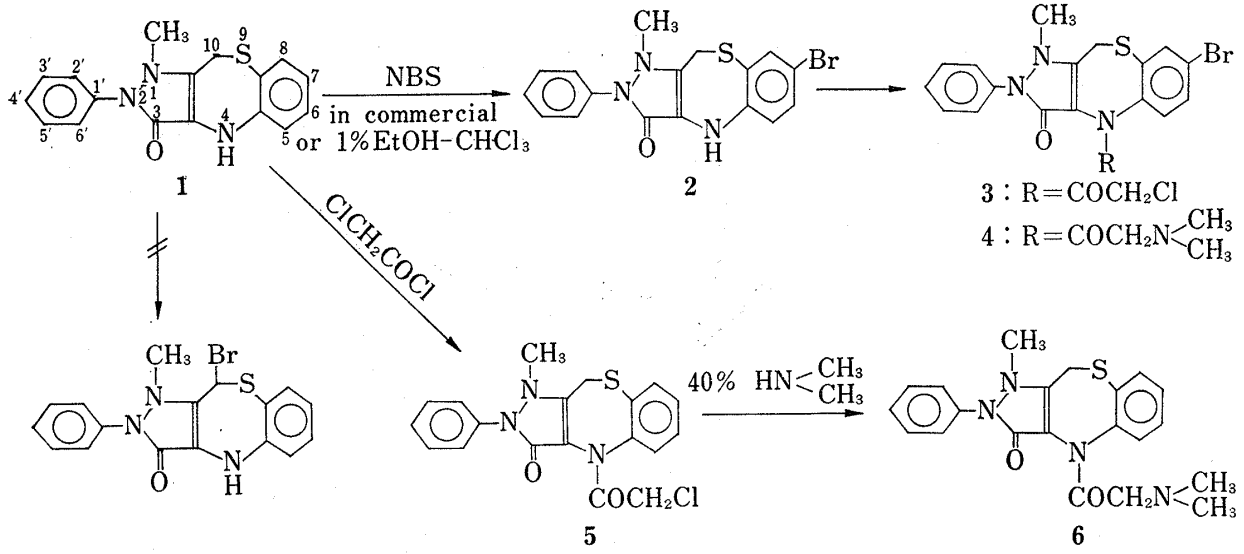

Chart 1

reaction of 2,3-dimethyl-1-phenyl-3-pyrazolin-5-one,[8] 4-bromo-2,3-dimethyl-1-phenyl-3- pyrazolin-5-one,[9] or 1-phenyl-2,3,4-trimethyl-3-pyrazolin-5-one[9] with N-bromosuccinimide did not give the compounds whose bromine atoms were substituted on N-phenyl ring.

From the above observations the compound obtained by the reaction of **1** with N-bromosuccinimide was concluded to be the structure (**2**). Reaction of **1** with N-bromosuccinimide in absolute chloroform also gave **2**.

Since the bromination of **1** yielded **2**, **1** was converted to the corresponding acetyl derivative (**7**), and the reaction of **7** with N-bromosuccinimide in commercial chloroform solution was carried out. A new non-halogenated compound (**8**) was obtained. Its IR and NMR spectra indicated the presence of an ethyl ester group. Furthermore its NMR spectrum did not show any signal attributable to an allylic methylene and only one methyl group (either N-methyl or C-methyl) was observed at δ 2.45 ppm. Its elementary analysis established the presence of four oxygen atoms, and the molecular ion peak (*m/e*: 395) in the mass spectrum gave the formula of $C_{20}H_{17}O_4N_3S$. Since the fragment ion peak (*m/e*: 43) in the mass spectrum suggested the presence of acetyl group, and the peak at δ 2.45 ppm could be assigned to C-methyl of an acetyl group by consideration of the chemical shift, the new compound obtained by the reaction of **7** with N-bromosuccinimide is assumed to be ethyl 3-acetyl-5′-oxo-1′-phenyl-spiro[benzothiazoline-2,4′-[2]pyrazoline-3′-carboxylate (**8**). Its ultraviolet (UV) absorption [λ_{max}^{EtOH} mμ (log ε): 248 (4.41), 311 (3.86)] was similar to that of ethyl 4,4-diallyl-5-oxo-1-phenyl-2-pyrazoline-3-carboxylate[10] [λ_{max}^{EtOH} mμ (log ε): 249 (4.17), 316 (3.58)]. This indicated that the N-methyl group was eliminated during the course of the reaction. Further investigation on this point was carried out as follows. Compound (**10**) which is structurally related to **7** and has only N-methyl group was reacted with N-bromosuccinimide in commercial chloroform solution. The NMR spectrum of the resulting compound (**11**) did not show any signal attributable to an N-methyl group. Elementary analysis, IR, and UV spectra characterized the structure of **11** as ethyl 3,5′-dioxo-1′-phenyl-spiro[benzo[*b*]thiophene-2 (3*H*), 4′-[2]pyrazoline]-3′-carboxylate.

Although the above experimental observations supported our assignment of structure **8**, the final structural proof was provided by synthesizing 5′-oxo-1′-phenyl-spiro[benzothiazoline-2,4′-[2]pyrazoline]-3′-carboxylic acid (**14**) by the unequivocal route as shown in Chart 3.

8) L. Knorr, *Chem. Ber.*, **17**, 546 (1884).
9) L. Knorr, *Ann. Chem.*, **238**, 137 (1887).
10) S. Ono, O. Otani, K. Kato, M. Hori, and H. Fujimura, The 93rd Annual Meeting of Pharmaceutical Society of Japan, Tokyo, April, 1973, Abstracts of Papers, II, P. 96.

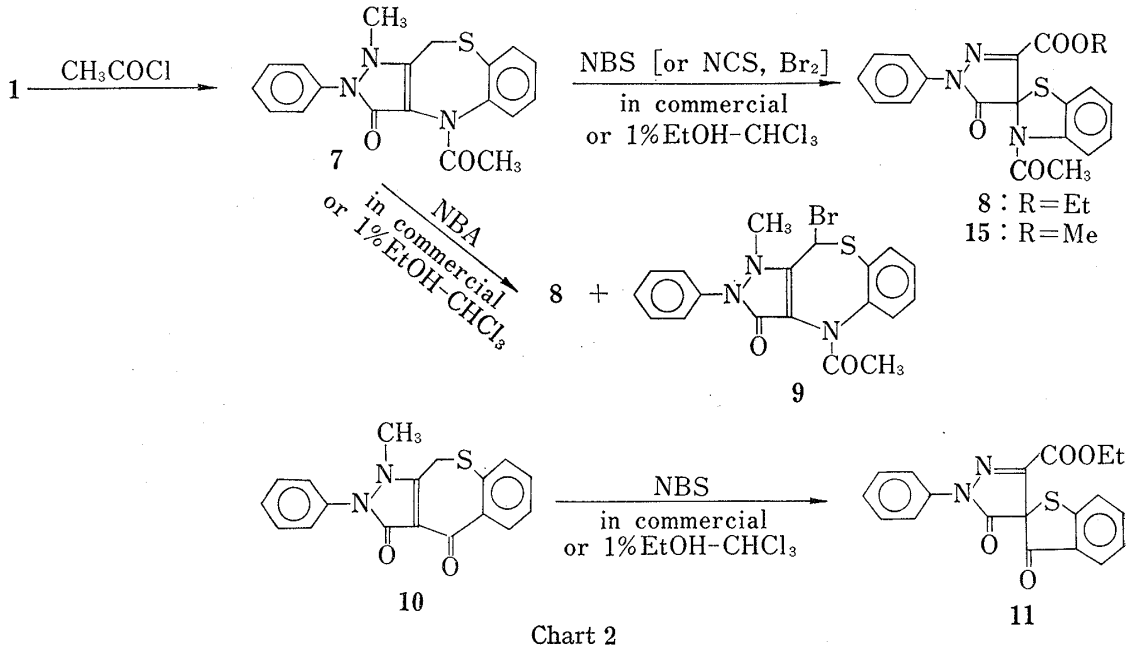

Chart 2

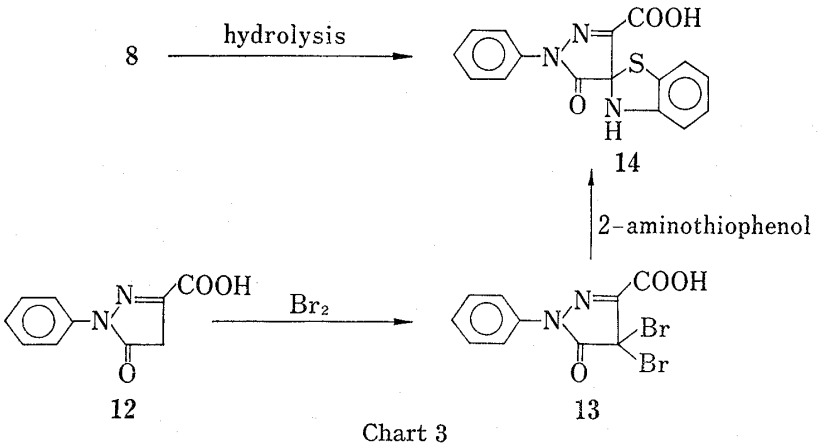

Chart 3

Bromination of 5-oxo-1-phenyl-2-pyrazoline-3-carboxylic acid[11] (**12**) gave 4,4-dibromo-5-oxo-1-phenyl-2-pyrazoline-3-carboxylic acid (**13**). Elementary analysis and IR spectrum confirmed its structure. Knorr, *et al.* synthesized similarly 4,4-dibromo-3-methyl-1-phenyl-2-pyrazolin-5-one[12] from 3-methyl-1-phenyl-2-pyrazolin-5-one. The reaction of **13** with 2-aminothiophenol gave **14** which was identical with the compound derived from **8**. However, attempts to approach **8** from **14** were unsuccessful, and other routes to synthesize **8** are now under investigation.

The reaction of **7** with other Wohl-Ziegler's reagents was then examined under the same conditions, and it was determined that N-chlorosuccinimide, N-bromoacetamide or bromine also gave ethyl ester (**8**). When N-bromoacetamide was used a trace of 4-acetyl-10-bromo-1-methyl-2-phenyl-1,2,3,10-tetrahydro-4*H*-pyrazolo[3,4-*c*][1,5]benzothiazepin-3-one (**9**) was obtained in addition to **8**. The structure of **9** was confirmed by elementary analysis, IR and NMR spectra. Since the yield of **9** was very small amount, further investigation could not be carried out. That bromine in commercial chloroform solution converted **7** to ethyl ester (**8**) seemed to be attributable to the small amount of ethanol contained in commercial chloroform as a stabiliser. To support this conclusion the reaction of **7** with bromine in methanol-con-

11) W. Wislicenus, *Chem. Ber.*, **19**, 3225 (1886).
12) L. Knorr and P. Duden, *Chem. Ber.*, **25**, 759 (1892).

taining chloroform was carried out. The expected methyl ester (**15**) was obtained, whose structure was confirmed by elementary analysis, IR spectrum, and mass spectrum [*m/e*: 381 (M^+)].

The reaction of **7** in purified (*i.e.*, ethanol-free) chloroform solution or in dichloromethane resulted in the formation of a resinous oil which could not be purified. Attempts to obtain a good yield of **8** were unsuccessful(Table I). Petracek, *et al.*[13] found that the allylic methylene of β-carotene was converted into ketone by means of N-bromosuccinimide in chloroform solution in the presence of 1% ethanol, and they suggested the presence of ethanol would initially cause conversion to the diethoxy grouping followed by the formation of a carbonyl from this ketal.

It is also said that free bromine is produced from N-bromosuccinimide in the presence of ethanol in chloroform.[14] Thus the reaction mechanism of the synthesis of **8** from **7** appears to proceed by ionic reaction according to Chart 4.

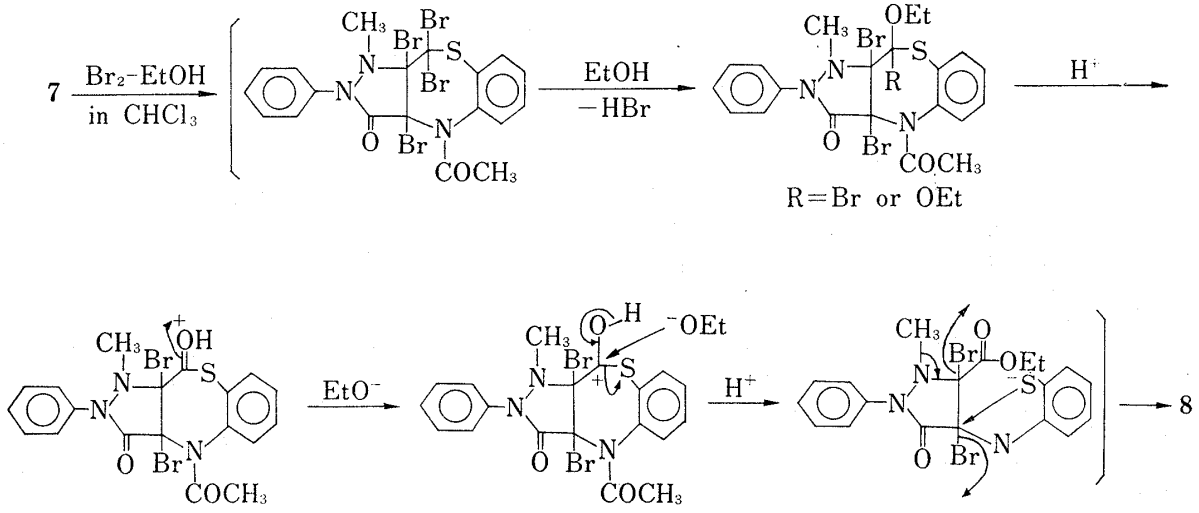

Chart 4

Table I. Yields of Ethyl 2-Acetyl-5′-oxo-1′-phenyl-spiro[benzothiazoline-2,4′-[2]pyrazoline]-3′-carboxylate (**8**) in the Reaction of 4-Acetyl-1-methyl-2-phenyl-1,2,3,10-tetrahydro-4*H*-pyrazolo[3,4-*c*][1,5]benzothiazepin-3-one (**7**) with N-Bromosuccinimide (NBS) in Various Conditions

Compound (**7**) (mg)	Solvent	NBS (mg)	Yield (mg)	Refluxed time (h)
351(0.001 mol)	0.2% EtOH–$CHCl_3$ (40 ml)	712(0.004 mol)	—	3
351(0.001 mol)	0.2% EtOH–$CHCl_3$ (40 ml)	712(0.004 mol)	trace	5
351(0.001 mol)	0.5% EtOH–$CHCl_3$ (40 ml)	356(0.002 mol)	16.2(4.1%)	5
351(0.001 mol)	0.5% EtOH–$CHCl_3$ (40 ml)	712(0.004 mol)	17.6(4.5%)	2
351(0.001 mol)	0.5% EtOH–$CHCl_3$ (40 ml)	712(0.004 mol)	39.5(10.0%)	5
351(0.001 mol)	1% EtOH–$CHCl_3$ (40 ml)	178(0.001 mol)	trace	3
351(0.001 mol)	1% EtOH–$CHCl_3$ (40 ml)	356(0.002 mol)	18.5(4.7%)	5
351(0.001 mol)	1% EtOH–$CHCl_3$ (40 ml)	712(0.004 mol)	42.7(10.8%)	5
351(0.001 mol)	1% EtOH–$CHCl_3$ (40 ml)	1068(0.006 mol)	20.1(5.1%)	8
351(0.001 mol)	1% EtOH–$CHCl_3$ (40 ml)	712(0.004 mol)	26.1(6.6%)	3
351(0.001 mol)	2% EtOH–$CHCl_3$ (40 ml)	356(0.002 mol)	4.0(1.0%)	5
351(0.001 mol)	2% EtOH–$CHCl_3$ (40 ml)	712(0.004 mol)	5.6(1.4%)	5
351(0.001 mol)	5% EtOH–$CHCl_3$ (40 ml)	356(0.002 mol)	trace	5
351(0.001 mol)	5% EtOH–$CHCl_3$ (40 ml)	712(0.004 mol)	trace	5
351(0.001 mol)	EtOH (40 ml)	712(0.004 mol)	—	5

13) F.J. Petracek and L. Zechmeister, *J. Am. Chem. Soc.*, **78**, 1427 (1956).
14) L. Horner and E.H. Winkelmann, *Angew. Chemie*, **71**, 349 (1959).

Experimental[15]

7-Bromo-1-methyl-2-phenyl-1,2,3,10-tetrahydro-4*H*-pyrazolo[3,4-*c*][1,5]benzothiazepin-3-one (2)——N-Bromosuccinimide (3 g) was added to a solution of **1** (3.1 g) in commercial $CHCl_3$ (40 ml), and the mixture was refluxed for 1 hr. After cooling, the resulting crystals were collected by filtration and washed with water. Yield 3.3 g (85%). One part of this material was recrystallized from large amount of EtOH to provide analytical sample as scales, mp 226—228°. IR ν_{max}^{KBr} cm^{-1}: 3200 (–NH–), 1650 (–N–CO–). *Anal.* Calcd. for $C_{17}H_{14}ON_3BrS$: C, 52.59; H, 3.63; N, 10.82. Found: C, 52.46; H, 3.54; N, 10.57.

7-Bromo-4-chloroacetyl-1-methyl-2-phenyl-1,2,3,10-tetrahydro-4*H*-pyrazolo[3,4-*c*][1,5]benzothiazepin-3-one (3)——A mixture of **2** (2 g) and chloroacetyl chloride (10 ml) was refluxed on an oil-bath for 1 hr until a clear solution was obtained. The excess chloroacetyl chloride was distilled. The residue was washed with saturated $NaHCO_3$ solution and extracted with $CHCl_3$. The extract was washed with water and dried over Na_2SO_4. Evaporation of $CHCl_3$ gave crystalline powder, mp 261—262°, Yield 2.1 g (87.5%). IR ν_{max}^{KBr} cm^{-1}: 1690, 1650 (C=O). *Anal.* Calcd. for $C_{19}H_{15}O_2N_3SBrCl$: C, 49.10; H, 3.25; N, 9.04. Found: C, 49.01; H, 3.46; N, 9.17.

7-Bromo-4-(N,N-dimethylglycyl)-1-methyl-2-phenyl-1,2,3,10-tetrahydro-4*H*-pyrazolo[3,4-*c*][1,5]benzothiazepin-3-one (4)——A mixture of **3** (1 g), 40% dimethylamine aqueous solution (10 ml), and benzene (50 ml) was refluxed on a water-bath until clear solution was obtained. Solvent was distilled and saturated $NaHCO_3$ was added to the residue. The mixture was extracted with $CHCl_3$. The extract was washed with water and dried over Na_2SO_4. $CHCl_3$ was distilled to give an oil, which was crystallized by addition of a small amount of ether. Recrystallization from EtOH gave colorless prisms of mp 183—185°, yield 0.9 g (88.5%). IR ν_{max}^{KBr} cm^{-1}: 1690, 1650 (C=O). NMR (JNM-MH-100) $\delta_{ppm}^{CDCl_3}$: 2.36 (6H, singlet, $-N(CH_3)_2$), 3.02 (3H, singlet, $N-CH_3$), 3.60 (2H, singlet, $-COCH_2-$), 3.83 (2H, singlet, $-CH_2-S-$), 7.20—7.60 (7H, multiplet, aromatic protons), 7.87 (1H, doublet, $J=1$ Hz, aromatic proton). *Anal.* Calcd. for $C_{21}H_{21}O_2N_4SBr$: C, 53.28; H, 4.47; N, 11.84. Found: C, 53.22; H, 4.68; N, 11.66.

4-Chloroacetyl-1-methyl-2-phenyl-1,2,3,10-tetrahydro-4*H*-pyrazolo[3,4-*c*][1,5]benzothiazepin-3-one(5)——The reaction of **1** (309 mg) and chloroacetylchloride (10 ml) was carried out by the same procedure as described in the synthesis of **3**. Yield 316 mg (82.1%), mp 201—202°. IR ν_{max}^{KBr} cm^{-1}: 1690, 1650 (C=O). *Anal.* Calcd. for $C_{19}H_{16}O_2N_3SCl$: C, 59.14; H, 4.18; N, 10.89. Found: C, 59.06; H, 3.96; N, 10.56.

4-(N,N-Dimethylglycyl)-1-methyl-2-phenyl-1,2,3,10-tetrahydro-4*H*-pyrazolo[3,4-*c*][1,5]benzothiazepin-3-one (6)——The reaction of **5** (385 mg, 0.001 mole) with 40% dimethylamine aqueous solution (3 ml) in benzene (10 ml) was carried out by the same procedure as described in the synthesis of **4**. Yield 350 mg (88.6%). Recrystallization from benzene gave colorless prisms of mp 179—180°. IR ν_{max}^{KBr} cm^{-1}: 1690, 1650 (C=O). NMR $\delta_{ppm}^{CDCl_3}$: 2.35 (6H, singlet, $-N(CH_3)_2$), 2.95 (3H, singlet, $N-CH_3$), 3.56 (2H, singlet, $-COCH_2-$), 3.75 (2H, singlet, $-CH_2-S-$), 7.00—7.50 (9H, multiplet, aromatic protons). *Anal.* Calcd. for $C_{21}H_{22}O_2N_4S$: C, 63.94; H, 5.62; N, 14.20. Found: C, 63.74; H, 5.64; N, 13.97.

4-Acetyl-1-methyl-2-phenyl-1,2,3,10-tetrahydro-4*H*-pyrazolo[3,4-*c*][1,5]benzothiazepin-3-one (7)——A mixture of **1** (5 g) and acetyl chloride (20 ml) was refluxed on an oil-bath for 1 hr to obtain a clear solution. Excess acetyl chloride was distilled, and saturated $NaHCO_3$ solution was added to the residue, which was extracted with $CHCl_3$. The extract was washed with water and dried over Na_2SO_4. Distillation of $CHCl_3$ gave an oil which was crystallized by addition of ether. Recrystallization from EtOH gave colorless prisms of mp 199—200°, Yield 5.1 g (89.8%). IR ν_{max}^{KBr} cm^{-1}: 1680, 1660 (shoulder) (C=O). NMR $\delta_{ppm}^{CDCl_3}$: 2.33 (3H, singlet, $-COCH_3$), 3.00 (3H, singlet, $N-CH_3$), 3.80 (2H, singlet, $-CH_2-S-$), 7.41—7.90 (9H, multiplet, aromatic protons). *Anal.* Calcd. for $C_{19}H_{17}O_2N_3S$: C, 64.94; H, 4.88; N, 11.96. Found: C, 64.89; H, 4.80; N, 11.90.

Ethyl 3-Acetyl-5′-oxo-1′-phenyl-spiro[benzothiazoline-2,4′-[2]pyrazoline]-3′-carboxylate (8)——**7** (0.5 g) was dissolved in 40 ml of commercial $CHCl_3$ and N-bromosuccinimide (0.5 g) was added in portions under reflux and mechanical stirring. Reflux and stirring were continued for 3 hr. After the reaction, water was added and the $CHCl_3$-layer was separated. The $CHCl_3$-layer was dried over Na_2SO_4 and concentrated to submit to column chromatography on silica gel. From the first $CHCl_3$-eluate yellow crystals were obtained, yield 60 mg (10.7%). Negative Beilstein test. Recrystallization from EtOH gave prisms of mp 155—156°. IR ν_{max}^{KBr} cm^{-1}: 1750, 1280, 1100 (ester). Mass Spectrum *m/e*: 395 (M^+). NMR $\delta_{ppm}^{CDCl_3}$: 1.10 (3H, triplet, $J=6.0$ Hz, $-COOCH_2\underline{CH_3}$), 2.45 (3H, singlet, $-COCH_3$), 2.20 (2H, quartet, $J=6.0$ Hz, $-COO\underline{CH_2}CH_3$), 7.00—7.90 (9H, multiplet, aromatic protons). *Anal.* Calcd. for $C_{20}H_{17}O_4N_3S$: C, 60.75; H, 4.33; N, 10.63; O, 16.18. Found: C, 60.72; H, 4.33; N, 10.58; O, 15.99.

This compound was also obtained by the reaction of **7** with N-chlorosuccinimide.

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15) All the melting points were determined on a Yanagimoto Micro Melting Point apparatus and were not corrected. The IR spectra were measured with a Nihon Bunko Spectroscopic Co. Ltd. Model IR-S. The NMR spectra were measured with a Japan Electron Optics Laboratory Co. JNM-MH-60 spectrometer using tetramethylsilane as internal standard. Mass spectra were evaluated on a Hitachi Mass Spectrometer, Model RMU-6E, equipped with a double forcusing system.

Reaction of 7 with N-Bromoacetamide——**7** (0.5 g) was dissolved in 40 ml of commercial $CHCl_3$ and N-bromoacetamide (0.5 g) was added in portions under reflux and mechanical stirring. After the reaction, the mixture was treated as described in the reaction of **7** with N-bromosuccinimide. By the chromatographic separation, from the first $CHCl_3$-eluate 4-acetyl-10-bromo-1-methyl-2-phenyl-1,2,3,10-tetrahydro-4*H*-pyrazolo[3,4-*c*][1,5]benzothiazepin-3-one (**9**) was obtained. Yield 28 mg (4.6%), mp 163—165°. Positive Beilstein test. IR ν_{max}^{KBr} cm^{-1}: 1710, 1650 (C=O). NMR $\delta_{ppm}^{CDCl_3}$: 1.95 (3H, singlet, $-COCH_3$), 2.65 (3H, singlet, $N-CH_3$), 6.23 (1H, singlet, Br–CH–S–), 7.35—8.20 (9H, multiplet, aromatic protons). *Anal.* Calcd. for $C_{19}H_{16}O_2N_3SBr$: C, 53.03; H, 3.75; N, 9.77. Found: C, 53.32; H, 3.72; N, 9.53. From the second $CHCl_3$-eluate **8** was obtained, yield 56 mg (10.0%).

Reaction of 7 with Bromine——**7** (0.5 g) was dissolved in 30 ml of commercial $CHCl_3$. Bromine (0.3 g) in $CHCl_3$ (5 ml) was added dropwise under reflux. Reflux was continued for 3 hr and treated as for the reaction with N-bromosuccinimide. By the column chromatographic purification 45 mg (8.0%) of **8** was obtained.

Ethyl 3,5′-Dioxo-1′-phenyl-spiro[benzo[*b*]thiophene-2(3*H*),4′-[2]pyrazoline]-3′-carboxylate (11)——**10** (0.5 g) was dissolved in 40 ml of commercial $CHCl_3$ and N-bromosuccinimide (0.5 g) was added under reflux and stirring. The reaction mixture was treated as for the synthesis of **8**, yield 110 mg (19.4%), mp 168—170°, negative Beilstein test. IR ν_{max}^{KBr} cm^{-1}: 1750, 1700 (C=O). NMR $\delta_{ppm}^{CDCl_3}$: 1.20 (3H, triplet, $J=6.0$ Hz, $-COOCH_2\underline{CH_3}$), 4.25 (2H, quartet, $J=6.0$ Hz, $-COO\underline{CH_2}CH_3$), 7.10—7.80 (9H, multiplet, aromatic protons). *Anal.* Calcd. for $C_{19}H_{14}O_4N_2S$: C, 62.29; H, 3.85; N, 7.65. Found: C, 62.17; H, 3.72; N, 7.48.

4,4-Dibromo-5-oxo-1-phenyl-2-pyrazoline-3-carboxylic Acid (13)——To a solution of 5-oxo-1-phenyl-2-pyrazoline-3-carboxylic acid[8] (2.04 g) in $CHCl_3$ (20 ml) was added a solution of bromine (1.6 g) in $CHCl_3$ (20 ml). The mixture was refluxed for 1 hr. After the reaction, $CHCl_3$ was distilled and the residue was purified by the column chromatography on silica gel. From the first ether eluate yellow crystals, mp 149° (decomp.) was obtained, yield 0.5 g (13.8%). *Anal.* Calcd. for $C_{10}H_6O_3N_2Br_2$: C, 33.18; H, 1.67; N, 7.74; Br, 44.15. Found: C, 33.41; H, 1.89; N, 7.59; Br, 44.11.

5′-Oxo-1′-phenyl-spiro[benzothiazoline-2,4′-[2]pyrazoline]-3′-carboxylate (14)——(i) To a sodium ethoxide solution prepared from Na (46 mg) and EtOH (20 ml), 2-aminothiophenol (125 mg) was added. Then, **13** (362 mg) was dissolved. The mixture was warmed on a water-bath for 30 min. EtOH was distilled and the residue was dissolved in water and insoluble substance was filtered off. The filtrate was neutralized with 10% H_2SO_4 to obtain precipitates, which was collected by filtration. Crude yield 86 mg (26.5%), negative Beilstein test and positive sulfur test. The crude crystals were dissolved in $NaHCO_3$ solution and filtered. The filtrate was neutralized with 10% H_2SO_4 to obtain precipitates. This procedure was repeated for several times to afford analytical sample, mp 170° (decomp.). IR ν_{max}^{KBr} cm^{-1}: 3300—2500 (OH), 1720 (C=O). *Anal.* Calcd. for $C_{16}H_{11}O_3N_3S$: C, 59.07; H, 3.41; N, 12.92. Found: C, 59.35; H, 3.37; N, 12.76.

(ii) **8** (395 mg) was dissolved in 10 ml of ethanolic KOH solution contained 370 mg of KOH and the mixture was heated on a water bath for 30 min. EtOH was distilled and the residue was dissolved in water. Insoluble substance was filtered off and the filtrate was neutralized with 10% H_2SO_4. The precipitates were collected by filtration, and dissolved again in saturated $NaHCO_3$ solution. The solution was filtered and the filtrate was neutralized with 10% H_2SO_4. This procedure was repeated for several times to obtain white crystalline powder, mp 170° (decomp.), yield 108 mg (27.3%).

Methyl 3-Acetyl-5′-oxo-1′-phenyl-spiro[benzothiazoline-2,4′-[2]pyrazoline]-3′-carboxylate (15)——Commercial $CHCl_3$ was purified by elimination of EtOH and 2% MeOH containing-$CHCl_3$ was prepared. **7** (0.5 g) was dissolved in this 2% MeOH containing-$CHCl_3$ (20 ml) and a solution of bromine (0.3 g) in 2% MeOH containing-$CHCl_3$ (5 ml) or N-bromosuccinimide (0.5 g) was added under reflux and stirring. The reaction mixture was treated as for the synthesis of **8**, yield 11 mg, mp 187—188°. IR ν_{max}^{KBr} cm^{-1}: 1760, 1720 (C=O). Mass Spectrum *m/e*: 381 (M^+). *Anal.* Calcd. for $C_{19}H_{15}O_4N_3S$: C, 59.83; H, 3.96; N, 11.02. Found: C, 59.90; H, 4.01; N, 11.13.

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