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Reactions of Enamino Ketones and an Enamino Ester with Some Electrophiles

MASAFUMI YOSHIMOTO, TETSUO HIRAOKA and YUKICHI KISHIDA

Central Research Laboratories, Sankyo Co., Ltd.[1]

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Based upon our finding[2] of a novel active site in enamino carbonyl compounds, the details were investigated using some active electrophiles. 1-Phenyl-3-N-pyrrolidinyl-2-buten-1-one (Va) reacted with *p*-nitrobenzaldehyde in acidic or basic media to afford 1-phenyl-3-N-pyrrolidinyl-5-hydroxy-5-*p*-nitrophenyl-2-penten-1-one (VI) as the result of IVd-type reaction. The reaction of enamino ketones Va, 4-N-pyrrolidinyl-3-penten-2-one (Vd) and an enamino ester, 1-methoxycarbonyl-2-N-pyrrolidinyl-propene (Vc) with 4-ethoxymethylene-2-phenyl-2-oxazolin-5-one (VIII) gave the corresponding enamino azlactone derivatives (IXa, IXb, IXc), respectively. The reaction of Va and Vb with dichloroketene also afforded IV-d type reaction products, 1,1-dichloro-4-N-pyrrolidinyl-6-phenyl-3-hexene-2,6-dione (XIIa) and 1,1-dichloro-4-N-pyrrolidinyl-3-heptene-2,6-dione (XIIb), respectively. But Vc reacted with dichloroketene to give the ordinary IVb type reaction product. Methanesulfonyl chloride reacted with Vb to yield the cyclic sulfone XIV, which would be produced *via* sulfonylated intermediate XVII as the result of IVd-type reaction.

In the preceding paper,[2] we reported on the formation of some biphenyl derivatives by the cyclization reaction of conjugated diynones with the addition of pyrrolidine or morpholine. Considering the mechanistic pathway of this reaction, the cyclization was assumed to proceed *via* an equilibrium mixture (IIa, IIb) to the product (III).

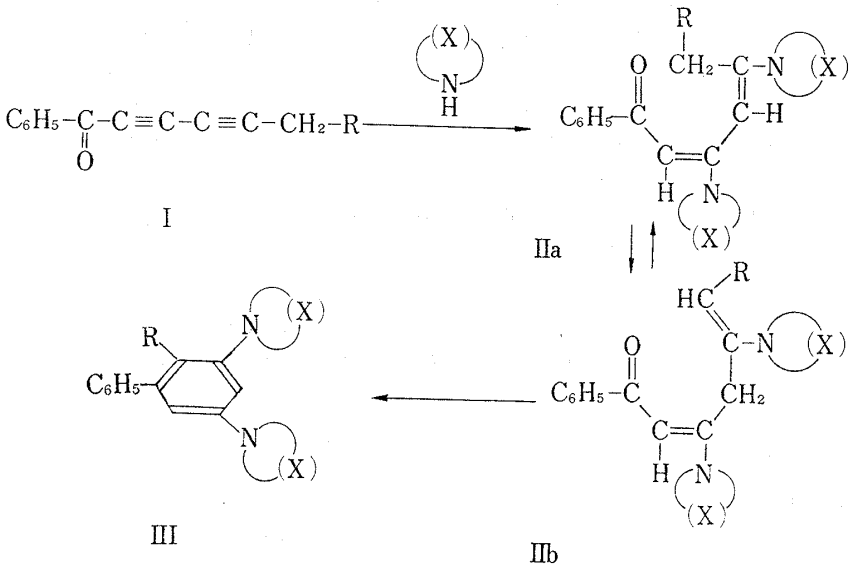
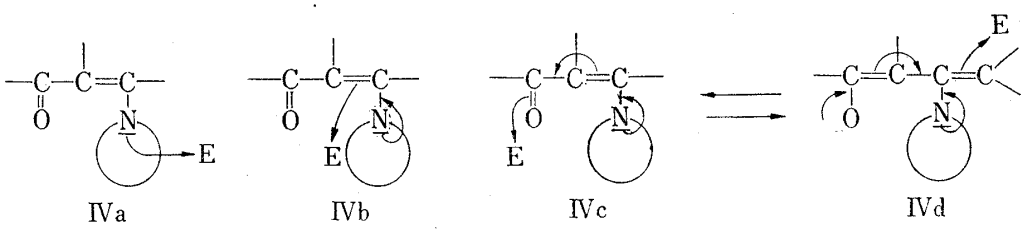


Chart 1

1) Location: *2–58, 1-chome, Hiromachi, Shinagawa-ku, Tokyo.*
2) Y. Kishida, T. Hiraoka and M. Yoshimoto, *Chem. Pharm. Bull.* (Tokyo), **17**, 2126 (1969).

As the continuation and extension of this intramolecular nucleophilic reaction of enamino ketones we attempted to conduct some intermolecular reactions of simple conjugated enamino carbonyl compounds with some electrophiles.

There have been many reports about the reactions of enamino carbonyl compounds with electrophiles.[3] Most of them deals with the reactions based on the nucleophilicity of nitrogen (IVa)[4] or β-carbon to the nitrogen (IVb),[5] the ordinary active site of enamine, or carbonyl oxygen (IVc).[6] However we have discovered that γ-carbon to the carbonyl (IVd) still can exert the nucleophilicity in the presence of accelerating reagents of the enolization. We have noticed two examples in which α-carbon initiated intermolecular nucleophilic reaction accompanying the reaction by γ-carbon,[7] one example of intramolecular nucleophilic attack by γ-carbon towards an allenic moiety[8] to form six-membered ring in an enamine system conjugated with strong electron attracting group, *i.e.* –CO–, $-SO_2-$, and two instances of the selective nucleophilic reaction involving only γ-carbon.



IVa IVb IVc IVd

E : electrophile

Chart 2

One of the two instances was a reaction of 1-morpholinocyclohexene-2-carboxanilide with phenyl isocyanate. Morpholine enamine of cyclohexanone, on reaction with one or two equivalents of phenyl isocyanate, gave 1-morpholinocyclohexene-2-monocarboxanilide and 2,6-dicarboxanilide respectively.[9] Another was a reaction of the same enamine as mentioned above with benzoyl chloride, giving only very poor yield (1.5%) of dibenzoyl derivative.[10]

These electrophilic addition and substitution, being subject to stereoelectronic control,[11] would be assumed to be very reasonable reactions in cyclic enamines and therefore the selective nucleophilic reaction occurred only at γ-carbon of acylic enamino carbonyl compounds constitutes itself as the first instance as far as we know in literatures.

Reaction of 1-phenyl-3-N-pyrrolidinyl-2-buten-1-one (Va) with *p*-nitrobenzaldehyde catalyzed by acidic or basic media afforded 1-phenyl-3-N-pyrrolidinyl-5-hydroxy-5-*p*-nitrophenyl-

3) General discussions: *a*) N.J. Leonard and J.A. Adamick, *J. Am. Chem. Soc.*, **81**, 595 (1959); A.I. Meyers, A.H. Reine and R. Gault, *J. Org. Chem.*, **34**, 698 (1969); *b*) "Enamines: Synthesis, Structure, and Reactions," ed. by A.G. Cook, Marcel Dekker, New York and London, 1969.

4) C.A. Grob and H.J. Wilkens, *Helv. Chim. Acta*, **50**, 725 (1967).

5) J. Goerdeler and U. Keuser, *Chem. Ber.*, **97**, 2209 (1964); G.H. Alt and A.J. Speziale, *J. Org. Chem.*, **29**, 798 (1964).

6) G.H. Alt and A.J. Speziale, *J. Org. Chem.*, **29**, 794 (1964); *idem*, *ibid.*, **30**, 1407 (1965); Z. Valenta, P. Deslongchamps, R.A. Ellison and K. Wiesner, *J. Am. Chem. Soc.*, **86**, 2533 (1964); A.I. Meyers, A.H. Reine and R. Gault, *Tetrahedron Letters*, **1967**, 4049.

7) R.B. Rao, U.P. Singh and G.V. Bhide, *Tetrahedron Letters*, **1967**, 719; O. Tsuge, M. Tashiro and T. Inaba, Abstract of Papers, 21st Annual Meeting of Chemical Society of Japan, Osaka, April, 1968, p. 1846.

8) L. Skattebøl, B. Boulette and S. Solomon, *J. Org. Chem.*, **33**, 548 (1968).

9) G.A. Berchtold, *J. Org. Chem.*, **26**, 3043 (1961); R. Fusco, G. Bianchetti and S. Rossi, *Gazz. Chim. Ital.*, **91**, 825 (1961).

10) G. Opitz and E. Tempel, *Ann.*, **699**, 74 (1966).

11) G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz and R. R. Terrell, *J. Am. Chem. Soc.*, **85**, 207 (1963).

2-penten-1-one (VI), mp 158.5°, which was assumed to be brought about by the nucleophilic attack of γ-carbon (IVd), but any other products which might be given by the reaction at α-carbon (IVb) or oxygen (IVc) were neither isolated nor detected by thin-layer chromatography (TLC). The structural assignment of VI was based on the following data. The infrared (IR) spectrum of VI showed absorption bands at 3280 (–OH), 1604, 1545—1515 (enamino ketone moiety), 1578 and 1348 ($-NO_2$). Absorption maxima in the ultraviolet (UV) spectrum appeared at 244 mμ (log ε=4.053) and 341 (4.432). The nuclear magnetic resonance (NMR) spectrum consisted of a pair of doubletting doublets, *i.e.*, 6.25 (1H, dd, J_1=13.5 Hz, J_2=3.6 Hz) and 7.02 ppm (1H, dd, J_1=13.5 Hz, J_2=10.5 Hz) assignable to $-CH_2-$, a multiplet centered at 5.13 ppm (–CH–OH), and a doublet at 7.03 ascribable to the chelating OH probably with pyrrolidinyl nitrogen to form a six-membered ring, in addition to peaks of pyrrolidine ring protons (8H) and aromatic protons (9H).

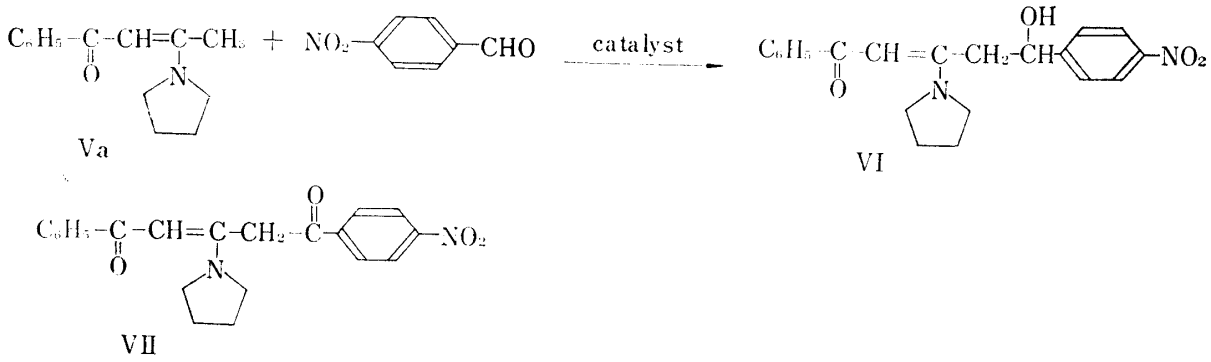


Chart 3

Table I. Catalysts and Yields in the Formation of VI

Catalyst (amount)	Temperature (°C)	Time (hr)	Yield (%)	Solvent
p-TsOH (trace)	80—90	5.0	10	EtOH–benzene (4:1)
NaOEt (1 eq.)	25—30	2.5	30	EtOH
Et_3N (1 eq.)	50—60	40	50	$CHCl_3$
DABCO[a] (trace)	80—90	4.0	30	EtOH

a) 1,4-diazabicyclooctane

The oxidation of VI by activated manganese dioxide in chloroform afforded 1-phenyl-3-N-pyrrolidinyl-5-*p*-nitrophenyl-2-pentene-1,5-dione (VII), mp 156°, which indicated the reasonable spectroscopic data. The absorption maxima in the UV spectrum of VII appeared at 240 mμ (log ε=4.051) and 345 (4.431), and the IR spectrum showed another carbonyl group (1675 cm^{-1}) in place of hydroxy group. The NMR spectrum exhibited broad singlet peaks at 5.03 (2H, $-CH_2-$) and 5.72 ppm (1H, –CH=C) in addition to pyrrolidine protons (8H) and aromatic protons (9H). The other enamines with conjugated carbonyl groups (Vb, Vc) did not react with *p*-nitrobenzaldehyde under the mild catalysis of equimolar triethylamine, recovering unchanged Vb or Vc.

As the second electrophilic reagent for enaminoketones 2-phenyl-4-ethoxymethylene-2-oxazolin-5-one (VIII) was chosen. The reaction of 1-phenyl-3-N-pyrrolidinyl-2-buten-1-one (Va), 4-N-pyrrolidinyl-3-penten-2-one (Vb) and 1-methoxycarbonyl-2-N-pyrrolidinyl propene (Vc) with VIII catalyzed by one equivalent triethylamine in anhydrous benzene afforded the corresponding enamino azlactone derivatives (IXa, IXb, IXc), respectively. The UV spectra were reproduced in Fig. 1, which exhibited the maintenance of azlactone rings and extension

of the conjugated system with the azlactone moiety. The broad singlets of methylenes (IXa: 4.35, IXb: 3.78, IXc: 3.64 ppm) in NMR exhibited that vicinal carbons to the methylene carbon bore no proton. These data indicated the deconjugation of the original conjugated carbonyls with the enamine double bond. Complicated NMR signals of olefinic protons (see Experimental) suggested that each of the products, IX (a, b and c) consisted of two geome-

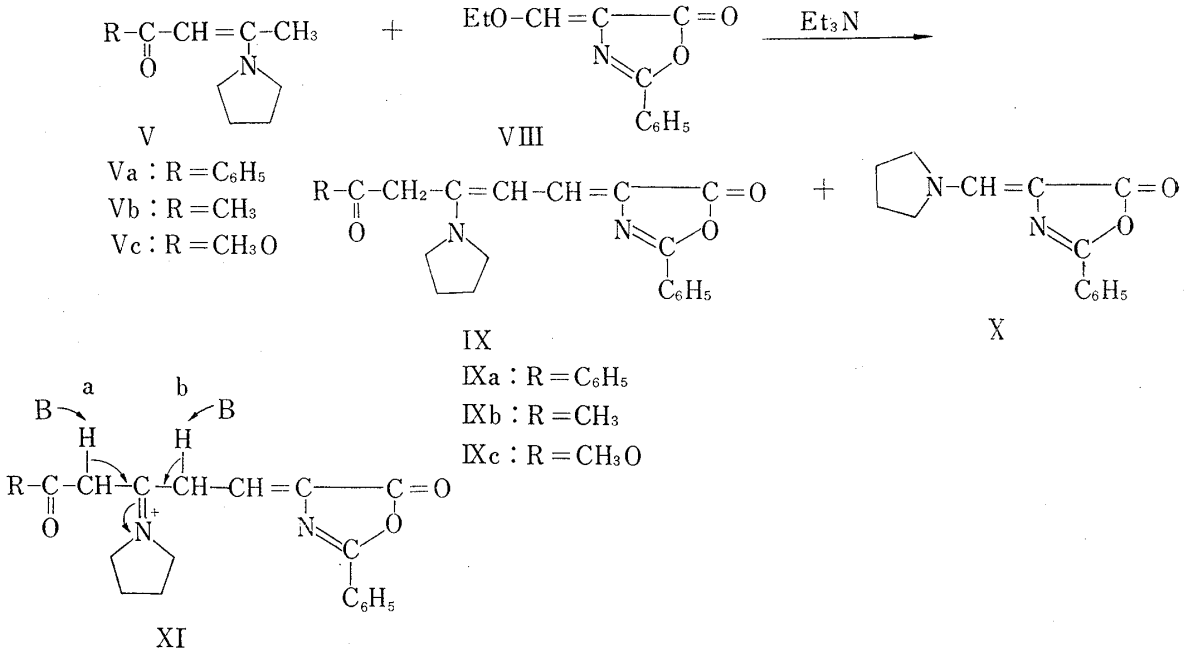


Chart 4

trical isomers in the ratio of *ca.* 7:3. Of course the presence of two carbon-carbon double bonds makes the existence of four geometrical isomers possible, but the products (IXa, IXb and IXc) isolated were crystalline mixtures consisting of the two isomers. We elucidated the structure of 2-phenyl-4(3-N-pyrrolidinyl-4-carbomethoxy-2-butenyliden)-2-oxazolin-5-one by nuclear Overhauser effects (NOE) using the degassed sample (Chart 5, Table II). The increase of the integrated intensity in the signals of olefinic protons, which locate at the *cis* position to the pyrrolidine ring, on irradiation of the pyrrolidine α-methylenes was described in our previous report.[2] A possible mechanistic pathway for the formation of IX from V and VIII would be assumed as follows. The enamino ketones (Va, Vb) and the enamino ester (Vc) would be initially converted to the IVd-type compounds by triethylamine. Of course the equilibrium between IVa, IVb, IVc and IVd would exist, and their competitive nucleophilic reactions with VIII would be able to ensue, but only IVd type would have enough nucleophilicity to complete the reaction to IX. Then the ethoxy

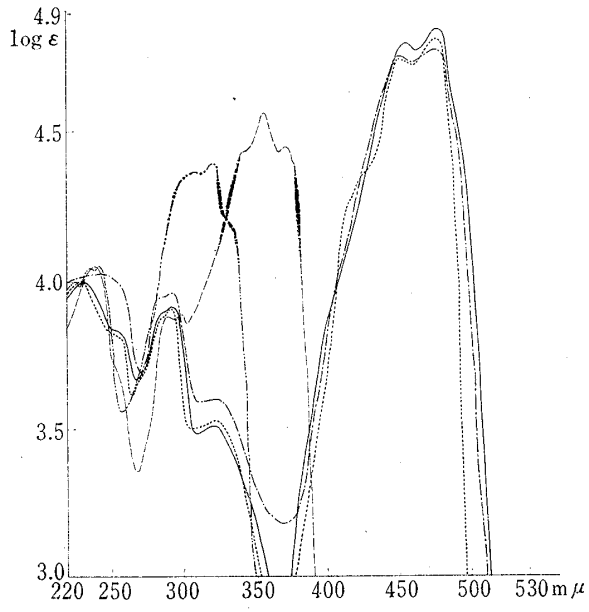
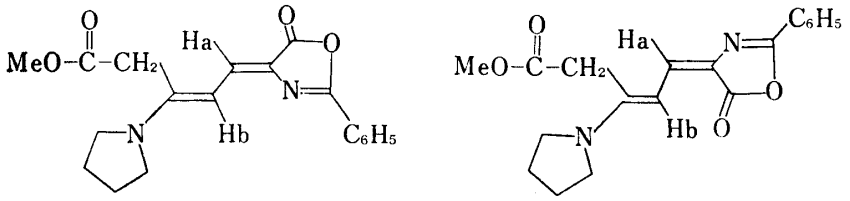


Fig. 1. UV Spectra of Azlactone Derivatives

——: VIII ——: IXa
……: IXb ——: IXc
——: X



IXc-A IXc-B

Chart 5

Table II. Nuclear Overhauser Effects of IXc-A and IXc-B

		Irradiation of pyrrolidine a-CH_2– (3.54)[a]	Irradiation of –CO–CH_2– (3.65)
IXc-A	Δ integ. of Ha (7.24)	$<+10\%$	$+31\%$
	Δ integ. of Hb (6.01)	$+41\%$	$<+5\%$
IXc-B[b]	Δ integ. of Hb (6.52)	$+35\%$	$<+10\%$

a) δppm in $CDCl_3$
b) The signal of Ha in IXc-B was assigned by NMDR irradiating at 6.5 ppm (Hb) and the NOE of its peaks (7.42, d, $J=13$ Hz) could not be measured because of overlapping with the aromatic region.

group of VIII would be eliminated in usual manner[12] according to addition-elimination mechanism.[13] An assumed intermediate, XI plays the key role for the reason why the enamine double bond of IX migrated from the original system (V) and why the double bond of Va was maintained intact in the case of forming VI. The iminium compound (XI) would be led to IX by arrows of a route and the preference of a or b route would depend on either the acidity of methylene protons of the both sides of the iminium carbon or the product stability of IX and its double bond isomer.

A by-product, X was isolated in all three cases, but it is a question why pyrrolidine was eliminated from V or IX and attacked VIII.

Ketenes have also served as electrophilic reagent for enamines[14] and as the third electrophilic reagent in this study dichloroketene[15] was chosen. Reaction of enaminoketone (Va, Vb) with dichloroketene, which was generated *in situ* by adding dichloroacetyl chloride into a mixture of V, DABCO and dry THF, afforded XII (the dichloroacetyl derivatives of V). The structural assignments of 1,1-dichloro-4-N-pyrrolidinyl-6-phenyl-3-hexene-2,6-dione (XIIa) and 1,1-dichloro-4-N-pyrrolidinyl-3-heptene-2,6-dione (XIIb) were based on the following spectroscopic data. The UV spectrum of XIIa, which showed absorption maxima at 242 mμ (log ε=4.179) and 332 (4.412), was very reasonable as compared with the spectrum of original enamino ketone (Va), whose maxima appeared at 243 (4.051) and 341 (4.432). The IR spectra of both XIIa and Va exhibited very similar bands at 1500—1700 cm^{-1} region except for the dichloroacetyl absorption (1690 cm^{-1}). The extinction of methyl group and appearance of methylene group in NMR explained the structure of XIIa decisively. The structure of XIIb was elucidated analogously to XIIa (see Experimental).

12) T. Kaneko, H. Ohizumi and H. Katsura, *Nippon Kagaku Zasshi*, **79**, 91 (1958); I.T. Strukov, *Zhur. Obshchei. Khim.*, **29**, 2359 (1959); *Chem. Abstr.*, **54**, 9889e (1960).
13) H. Behringer and H. Taul, *Chem. Ber.*, **90**, 1398 (1957).
14) *a*) G.A. Berchtold, G.I. Harvey and G.E. Wilson, *J. Org. Chem.*, **26**, 4776 (1961); *b*) R.H. Hasek and J.C. Martin, *J. Org. Chem.*, **28**, 1468 (1963).
15) L.F. Fieser and M. Fieser, "Reagents for Organic Synthesis," John Wiley & Sons, Inc., 1968, p. 221.

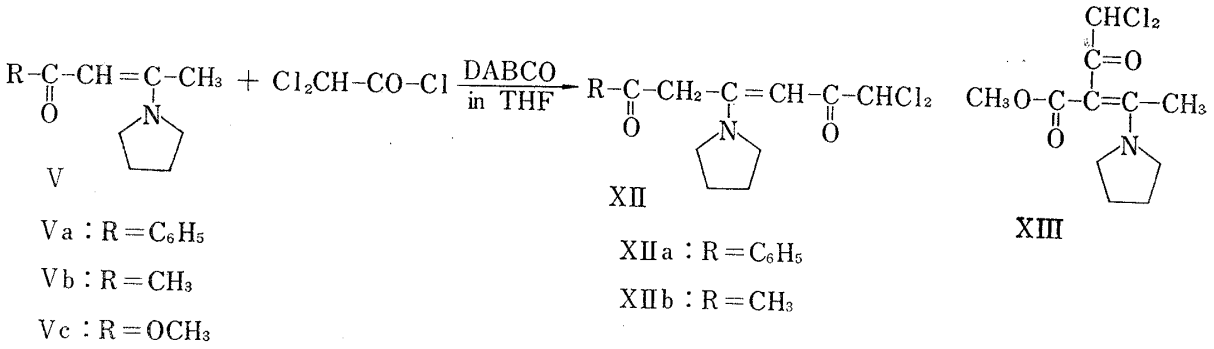


Chart 6

The product from Vc and dichloroketene, however, appeared to be very different from the aforementioned two products. The maintenance of C-methyl group and disappearance of olefinic proton showed the ordinary C-acylation product (IVb in Chart 2), 1,1-dichloro-3-methoxycarbonyl-4-N-pyrrolidinyl-3-penten-2-one (XIII). The IR, UV, and NMR spectra were very reasonable for the structure, XIII.

The fourth electrophilic reagent was sulfene. The reactions of sulfenes with enamines have been extensively investigated,[3b] and some enamino ketones have been found to undergo 1,4-cycloaddition reaction with sulfene prepared from methanesulfonyl chloride.[16,17] However, the enamino ketone, Vb reacted with methanesulfonyl chloride to give a different type of product, which would be the identical substance with that reported by Opitz and Tempel referring to the physical constants.[16a] But the substance has been left for the structure study by them probably because of the very complicated spectral data, which can hardly be interpreted, and it was really different from the ordinary cycloaddition product.

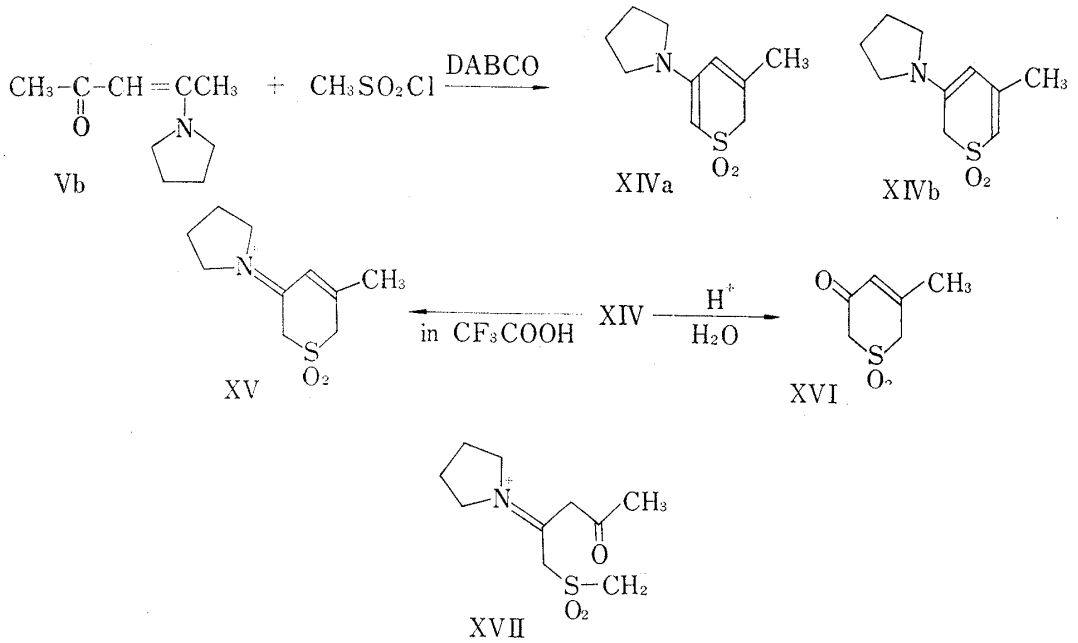
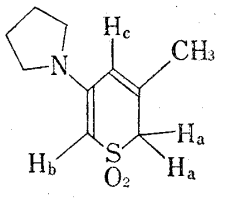


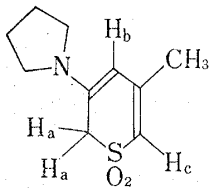
Chart 7

16) *a*) G. Opitz and E. Tempel, *Ann.*, **699**, 68 (1966); *b*) *Idem*, *Angew. Chem. Intern. Ed. Engl.*, **3**, 754 (1964); *Angew. Chem.*, **76**, 922 (1964).
17) A. Gandini, P. Schenone and G. Bignardi, *Monatsh.*, **98**, 1518 (1967).

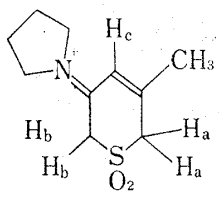
Table III. NMR Data of XIV and XV



XIVa



XIVb



XV

	XIVa	XIVb	XV
Ha	3.38 (1.4H)	4.01 (0.6H)	4.38[a] (2H)
Hb	4.90 (0.7H)	4.68 (0.3H)	4.75 (2H)
Hc	6.33 (0.7H)	5.75 (0.3H)	6.98 (1H)
CH_3	2.0 (3H)[a]		2.47[b] (3H)

The spectrum of XIV was obtained in DMSO-d_6 and that of XV in CF_3COOH. Chemical shifts: δppm (integrated intensities) were tabulated.
a) Overlapped with the α-methylene peaks of the corresponding pyrrolidine ring.
b) Overlapped with the β-methylene peaks of the corresponding pyrrolidine ring.

From our point of view for seeking the possibility of the expected IV-d type reaction, the product was very interesting. The elemental analysis indicated that one mole of water was lost from a 1:1 adduct of Vb and sulfene. The intricate NMR spectrum showed a marked resemblance to the product from di-2-propynyl sulfone and piperidine,[8] which would be produced by intramolecular nucleophilic attack of an intermediate enamine on the allenic moiety. The mixture of two double bond isomers consisted of 3-methyl-5-N-pyrrolidinyl-2H-thiopyran 1,1-dioxide (XIVa) and 5-methyl-3-N-pyrrolidinyl-2H-thiopyran 1,1-dioxide (XIVb) in the ratio of 7:3 in DMSO-d_6 at 30° and it was never separated by ordinary methods (fractional recrystallization, TLC). A possible explanation would be that XIVa and XIVb are in equilibrium. The NMR measurement in trifluoroacetic acid indicated that the mixture had been converted to a sole protonated compound (XV). Acid catalyzed hydrolysis of XIV afforded also only one cyclic sulfone (XVI), whose identity was obtained in every respect by the literature.[8] A probable mechanistic route to XIV from Vb and sulfene appears to be the one proceeding *via* an intermediate XVII, IV-d type species.

Experimental[18]

Reactants——Enamino ketones Vb[3] and an enamino ester Vc[19] were synthesized according to published procedures, as was 4-ethoxymethylene-2-phenyl-2-oxazolin-5-one.[20] Other electrophiles, *p*-nitrobenzaldehyde, dichloroacetyl chloride and methanesulfonyl chloride were obtained commercially.

1-Phenyl-3-N-pyrrolidinyl-2-buten-3-one (Va)——To a solution of benzoylacetone[21] (17.4 g, 0.100 mole) in 100 ml of AcOEt was added pyrrolidine (7.35 g, 0.103 mole) with 50 ml of AcOEt at room temperature (r.t.) under stirring. The mixture was allowed to stand overnight. Precipitated crystals were washed

18) All melting points were uncorrected. NMR spectra were obtained in the specified solvents on a Varian A-60 and HA-100 spectrometer with tetramethylsilane as an internal standard.
19) R.B. Rao, U.P. Singh and G.V. Bhide, *Tetrahedron Letters*, **1967**, 719. The sample used in our experiments exhibited to consist exclusively of *cis*-2-N-pyrrolidinyl crotonate by NOE measurement: irradiation of α-methylene peaks of pyrrolidine ring (6.7 ppm) increased the integrated intensity of olefinic proton (5.54 ppm) by 37%.
20) T. Kaneko, K. Oizumi and H. Katsura, *Nippon Kagaku Zasshi*, **79**, 91 (1958).
21) Prepared by the methods of following references: S.C. Chatterji and B.N. Ghosh, *J. Chem. Soc.*, **113**, 446 (1918), L. Claisen, *Chem. Ber.*, **38**, 695 (1905).

with AcOEt and dried in vacuum. Recrystallization from EtOH afforded colorless prisms of mp 164—165°. Yield, 20.3 g (94.7%). *Anal.* Calcd. for $C_{14}H_{17}ON$: C, 78.10; H, 7.96; N, 6.51. Found: C, 77.85; H, 8.00; N, 6.70. UV λ_{max}^{EtOH} mμ (log ε): 243 (4.051), 341 (4.432). IR ν_{max}^{Nujol} cm^{-1}: 1600, 1565, 1530. NMR δ ppm in $CDCl_3$: 8.00—7.70, 7.50—7.25 (5H, multiplet, $C_6\underline{H}_5$), 5.60 (1H, singlet, $-C\underline{H}$=C–), 3.62—3.18 (4H, multiplet, $-C\underline{H}_2$–N–$C\underline{H}_2$–), 2.65 (3H, singlet, $-C\underline{H}_3$), 2.12—1.82 (4H, multiplet, β-methylenes of pyrrolidine ring).

1-Phenyl-3-N-pyrrolidinyl-5-hydroxy-5-*p*-nitrophenyl-2-penten-1-one (VI)——A 1:1 mixture of 1-phenyl-3-N-pyrrolidinyl-2-buten-1-one (Va) and *p*-nitrobenzaldehyde in the specified solvents was treated with the diverse catalysts (Table I). Removal of the solvent gave the solid mixture of Va and VI, which was separated by fractional crystallization from EtOH. The pure VI, mp 158°, was given as neeldes. *Anal.* Calcd. for $C_{21}H_{22}O_4N_2$: C, 68.83; H, 6.05; N, 7.65. Found: C, 68.80; H, 6.03; N, 7.55. UV λ_{max}^{EtOH} mμ (log ε): 252 (4.146), 344 (4.350), λ_{sh} mμ (log ε): 270 (4.076). IR ν_{max}^{Nujol} cm^{-1}: 3280 (–OH), 1605, 1573, 1520—1540. NMR δ ppm in $CDCl_3$: 8.22 (2H, doublet, J=8.5 Hz, *o*-protons to $-NO_2$ on the nitrobenzene group), 7.72 (2H, J=8.5 Hz, *m*-protons to $-NO_2$), 8.7—8.0 (5H, multiplet, $-C_6\underline{H}_5$), 5.82 (1H, broad singlet, $\underline{H}$–C=C), 5.18 (1H, dd, J_1=3.2 Hz, J_3=10.0 Hz, $\underline{H}$–C–O), 3.77 (1H, dd, J_2=13.0 Hz, J_3=10.0 Hz, one proton of $-CH_2$–), 2.93 (1H, dd, J_1=3.2 Hz, J_2=13.0 Hz, another proton of $-CH_2$–), 3.7—3.3 (4H, multiplet, α-methylenes on the pyrrolidine ring), 2.2—1.8 (4H, multiplet, β-methylenes on the pyrrolidine ring).

1-Phenyl-3-N-pyrrolidinyl-5-*p*-nitrophenyl-2-pentene-1,5-dione (VII)——To a mixture of VI (1.83 g, 5.00 mmole) and purified $CHCl_3$ (150 ml) was added activated manganese dioxide (30 g). The mixture was stirred for 12 hr at r.t. The chloroform solution was separated from inorganic mixture through glass-filter, washed with H_2O, dried over Na_2SO_4 and evaporated. The residual solid was collected and recrystallized from $CHCl_3$–EtOH. Pale yellow needles of mp 156° were given. Yield, 1.09 g (30%). *Anal.* Calcd. for $C_{21}H_{20}O_4N_2$: C, 69.21; H, 5.53; H, 7.69. Found: C, 69.54; H, 5.47; N, 7.85. UV λ_{max}^{EtOH} mμ (log ε): 247 (4.301), 272 (4.210), 368 (4.161). IR ν_{max}^{Nujol} cm^{-1}: 1675, 1615, 1590, 1522. NMR δ ppm in $CDCl_3$: 8.3—7.3 (9H, multiplet, aromatic protons), 5.27 (1H, broad singlet, H$\underline{C}$=C), 5.03 (2H, broad singlet, $-C\underline{H}_2$–), 3.7—3.3 (4H, multiplet, α-methylenes on the pyrrolidine ring), 1.8—2.2 (4H, multiplet, β-methylenes on the pyrrolidine ring).

2-Phenyl-4-(3-N-pyrrolidinyl-5-oxo-5-phenyl-2-pentenyliden)-2-oxazolin-5-one (IXa)——A mixture of 1-phenyl-3-N-pyrrolidinyl-2-buten-1-one (Va) (2.15 g, 10.01 mmole), 2-phenyl-4-ethoxymethylene-2-oxazolin-5-one (VIII) (2.17 g, 10.0 mmole), triethylamine (1.01 g, 10.0 mmole) and dry benzene (20 ml) was heated under reflux for 8 hr and then allowed to stand at room temperature overnight. The precipitated orange needles were collected on a glass filter and washed with benzene. Recrystallization from EtOH or acetone gave orange needles (IXa), mp 196°—197° (decomp.). Yield, 1.2 g (31%). *Anal.* Calcd. for $C_{24}H_{22}O_3N_2$: C, 74.59; H, 5.74; N, 7.25. Found: C, 74.41; H, 5.69; N, 7.14. UV λ_{max}^{EtOH} mμ (log ε): 244 (4.319), 292 (3.962), 325 (3.606), 453 (4.751), 476 (4.783), λ_{sh}^{EtOH}: 285 (3.945). IR ν_{max}^{Nujol} cm^{-1}: 1725, 1682, 1620, 1550. NMR δ ppm in $CDCl_3$: 8.15—7.85, 7.70—7.25 (10H, miltiplet, aromatic protons), 7.30 (0.3H, doublet, J_1=13 Hz) and 6.82 (0.7H, doublet, J_2=13 Hz):olefinic H on the α-carbon from the azlactone ring, 6.63 (0.3H, doublet, J_1=13 Hz) and 6.17 (0.7H, doublet, J_2=13 Hz): olefinic H on the β-carbon from the azlactone ring, 4.35 (2H, signlet, $-CH_2$–), 3.7–3.3 (4H, multiplet, α-methylenes on the pyrrolidine ring), 2.2—1.8 (4H, multiplet, β-methylenes on the pyrrolidine ring).

2-Phenyl-4-(3-N-pyrrolidinyl-5-oxo-2-hexenyliden)-2-oxazolin-5-one (IXb)——A mixture of 4-N-pyrrodinyl-3-penten-2-one (Vb) (6.13 g, 40.0 mmole), VIII (8.69 g, 40.0 mmole), triethylamine (4.05 g, 40.0 mmole) and dry benzene (100 ml) was heated under reflux for 3 hr and then allowed to stand at room temperature overnight. The precipitated orange needles were collected on a glass filter and washed with benzene. Recrystallization from acetone afforded orange needles (IXb), mp 200—201° (decomp.). Yield, 3.8 g (28%). *Anal.* Calcd. for $C_{19}H_{20}O_3N_2 \cdot \frac{2}{3}C_6H_6$ (⅔ equimoler benzene): C, 73.38; H, 6.43; N, 7.44. Found: C, 72.61; H, 6.28; N, 7.36. UV λ_{max}^{EtOH} mμ (log ε): 230 (3.998), 293 (3.910), 324 (3.538), 454 (4.758), 476 (4.821), λ_{sh}^{EtOH} mμ (log ε): 256 (3.810), 286 (3.879). IR ν_{max}^{Nujol} cm^{-1}: 1727, 1615, 1533. NMR δ ppm in $CDCl_3$: 8.15—7.85, 7.55—7.25 (5H, multiplet, $-C_6\underline{H}_5$), 7.33 (4H, singlet, $\frac{2}{3}C_6\underline{H}_6$), 7.18 (0.7 H, doublet, J_1=13.0 Hz, olefinic H on the α-carbon from the azlactone ring), 6.58 (0.3H, singlet, J_2=13.5 Hz) and 6.08 (0.7H, doublet, J_1=13.0 Hz): olefinic H on the β-carbon from the azlactone ring, 3.78 (2H, singlet, $-CH_2$–), 3.68—3.33 (4H, multiplet, o-methylenes on the pyrrolidine ring), 2.27 (3H, singlet, $-CH_3$), 1.27—1.82 (4H, multiplet, β-methylenes on the pyrrolidine ring).

2-Phenyl-4-(3-N-pyrrolidinyl-4-carbomethoxy-2-butenyliden)-2-oxazolin-5-one (IXc)——A mixture of 1-methoxycarbonyl-2-N-pyrrolidinyl-1-propene (Vc) (3.38 g, 20 mmole), VIII (4.34 g, 20 mmole), triethylamine (2.02 g, 20 mmole) and dry benzene (50 ml) was heated under reflux for 10 hr and the solvent was removed under reduced pressure. The crystalline residue was washed with AcOEt and recrystallization from acetone gave orange needles (IXc), mp 171—173° (decomp.). Yield, 3.4 g (50%). *Anal.* Calcd. for $C_{19}H_{20}O_4N_2$: C, 67.04; H, 5.93; N, 8.23. Found: C, 66.86; H, 6.32; N, 7.73. UV λ_{max}^{EtOH} mμ (log ε): 227 (4.013), 293 (3.916), 322 (3.502), 455 (4.804), 477 (4.850), λ_{sh}^{EtOH} mμ (log ε): 256 (3.833), 286 (3.887). IR ν_{max}^{Nujol} cm^{-1}: 1738, 1623, 1537. NMR δ ppm in $CDCl_3$: 8.08—7.87, 7.48—7.33 (5H, multiplet, $-C_6\underline{H}_5$), 7.42 (doublet, J_1=13 Hz, irradiation at 6.5 indicated a singlet peak at 7.42) and 7.23 (0.7H, doublet, J_2=13 Hz): olefinic H on the α-carbon the azlactone ring, 6.53 (0.3H, doublet, J_1=13 Hz), 6.02 (0.7H, doublet, J_2=13 Hz): olefinic H on the β-carbon from the azlactone ring, 3.72 (3H, singlet, $-CH_3$), 3.65 (–CO–CH_2–), 3.69—3.42 (4H, multiplet, α-methylenes on the pyrrolidine ring), 2.09—1.88 (4H, multiplet, β-methylenes on the pyrrolidine ring).

2-Phenyl-4-N-pyrrolidinylmethylene-2-oxazolin-5-one (X) from the Mother Liquor of IX——When IXa, IXb and IXc were synthesized, another product was detected by TLC in the mother liquor in common with the enaminocarbonyl compounds. Fractional recrystallization from acetone gave pale yellow thin plates of X, mp 195°, in the specified yields (IXa: trace, IXb: 11%, IXc: 20%). *Anal.* Calcd. for $C_{14}H_{14}O_2N_2$: C, 69.40; H, 5.83; N, 11.56. Found: C, 69.25; H, 5.82; N, 11.52. UV λ_{max}^{EtOH} mμ (log ε): 241 (4.049), 290 (3.868), 298 (3.878), 356 (4.562), 373 (4.452). IR ν_{max}^{Nujol} cm^{-1}: 1732, 1640, 1600, 1590. NMR δ ppm in $CDCl_3$: (2H, multiplet, *o*-H on the phenyl ring), 7.51—7.29 (4H, multiplet, *m*- and *p*-H on the phenyl ring and an olefinic proton), 4.04 (2H, broad triplet, J=6.5 Hz, -N-C<u>H</u>$_2$-), 3.64 (2H, broad triplet, J=6.5 Hz, -N-C<u>H</u>$_2$-), 2.25—1.78 (4H, multiplet, β-methylenes on the pyrrolidine ring).

An Alternate Synthesis of X from Pyrrolidine and VIII—To a solution of VIII (4.34 g, 20.0 mole) in 80 ml of dry benzene was added pyrrolidine (1.42 g, 20.0 mmole) with 20 ml of dry benzene for 0.5 hr. The resulting mixture was stirred for 2 hr. A crystalline substance so precipitated was recrystallized from acetone to give pale yellow thin plates, which were identified by TLC, mixed melting point test and IR spectrum comparison with an authentic sample obtained from the mother liquor of IX. Yield, 4.2 g (87%).

1,1-Dichloro-4-N-pyrrolidinyl-6-phenyl-3-hexene-2,6-dione (XIIa)——To a mixture of Va (4.31 g, 20 mmole), DABCO (1.12 g, 10 mmole), and dry THF (150 ml) was added dropwise dichloroacetyl chloride (2.95 g, 20 mmole) with 20 ml of dry THF under vigorous stirring for 1 hr at −5°—+3°. The resulting mixture was stirred for 3 hr at 0°——10° and the precipitated substance was removed. To the filtrate was added 300 ml of ether and the organic mixture was washed with satd. NaCl solution, dried over Na_2SO_4 and evaporated under reduced pressure to give a crystalline substance. Recrystallization from acetone afforded XIIa, mp 145°—146°. Yield, 1.6 g (25%). *Anal.* Calcd. for $C_{16}H_{17}O_2NCl_2$: C, 58.95; H, 5.26; N, 4.29; Cl, 21.66. Found: C, 59.07; H, 5.24; N, 4.46; Cl, 21.91. UV λ_{max}^{EtOH} mμ (log ε): 242 (4.179), 332 (4.412). IR ν_{max}^{Nujol} cm^{-1}: 1690, 1635, 1545, 1536. NMR δ ppm in $CDCl_3$: 8.25—8.05, 7.75—7.50 (5H, multiplet, -C$_6$<u>H</u>$_5$), 5.85 (1H, singlet, <u>H</u>C=C-), 5.50 (1H, singlet, -C<u>H</u>Cl$_2$), 4.93 (2H, singlet, -C<u>H</u>$_2$-).

1,1-Dichloro-4-N-pyrrolidinyl-3-heptene-2,6-dione (XIIb)——To a mixture of Vb (3.06 g, 20.0 mmole), DABCO (1.12 g, 10 mmole) and dry THF (100 ml) was added dropwise dichloroacetyl chloride (2.95 g, 20.0 mmole) in 20 ml of dry THF under vigorous stirring for 1 hr keeping the inner temperature at −5°—+3° in a NaCl–ice bath. The resulting mixture was stirred for 2 hr at −3° and the precipitated substance was removed. To the filtrate was added 200 ml of ether and the organic mixture was washed with satd. NaCl solution, dried over Na_2SO_4 and evaporated under reduced pressure to give a crystalline substance. Recrystallization from acetone afforded XIIb, mp 113°—114°. Yield, 2.4 g (45%). *Anal.* Calcd. for $C_{11}H_{15}O_2NCl_2$: C, 49.97; H, 5.72; N, 5.31; Cl, 26.82. Found: C, 49.21; H, 5.64; N, 5.49; Cl, 26.73. UV λ_{max}^{EtOH} mμ (log ε): 219 (3.512), 331 (4.453). IR ν_{max}^{Nujol} cm^{-1}: 1725, 1630, 1623, 1550, 1530. NMR δ ppm in $CDCl_3$: 5.88 (1H, singlet, <u>H</u>C=C-), 5.40 (1H, singlet, -C<u>H</u>Cl$_2$), 4.27 (2H, singlet, -C<u>H</u>$_2$-), 2.37 (3H, singlet, -C<u>H</u>$_3$).

1,1-Dichloro-3-methoxycarbonyl-4-N-pyrrolidinyl-3-penten-2-one (XIII)——To a mixture of Vc (6.12 g, 36.2 mmole), DABCO (1.12 g, 10.0 mmole), and 75 ml of dry THF was added dropwise dichloroacetyl chloride with 20 ml of dry THF for 40 min at −5°—+3°. The resulting mixture was stirred for 2 hr at −3°. The precipitated substance was removed on a glass filter and the filtrate was diluted with ether. The organic mixture was washed with satd. NaCl solution, dried over Na_2SO_4 and evaporated *in vacuo* to give a crystalline substance. Recrystallization from acetone afforded pure XIII, mp 148—149°. Yield, 2.5 g (45% based on dichloracetyl chloride). *Anal.* Calcd. for $C_{11}H_{15}O_3NCl_2$: C, 47.15; H, 5.36; N, 4.98; Cl, 25.27. Found: C, 47.06; H, 5.39; N, 4.86; Cl, 25.35. UV λ_{max}^{EtOH} mμ (log ε): 269 (4.097), 335 (3.935). IR ν_{max}^{Nujol} cm^{-1}: 3030, 1666, 1607, 1555. NMR δ ppm in $CDCl_3$: 7.47 (1H, singlet, -COC<u>H</u>Cl$_2$), 3.75 (3H, singlet, -OC<u>H</u>$_3$), 4.0—3.4 (4H, multiplet, -C<u>H</u>$_2$-N-C<u>H</u>$_2$-), 2.43 (3H, broad singlet, -CO-C<u>H</u>$_3$), 2.3—1.9 (4H, multiplet, β-methylenes on the pyrrolidine ring).

Reaction of 4-N-Pyrrolidinyl-3-penten-2-one (Vb) with Methanesulfonyl Chloride——To a mixture of Vb, (6.12 g, 40.0 mmole), DABCO (4.48 g, 40.0 mmole) and 100 ml of dry THF was added dropwise methanesulfonyl chloride (4.58 g, 40.0 mmole) with 30 ml of dry THF at r.t. in nitrogen under stirring for 20 hr. After the addition the mixture was stirred for 4 days under the nitrogen gas and then the precipitate was removed. The filtrate was concentrated to give 10.9 g of crystalline substance. Recrystallization from acetone or chloroform afforded colorless prisms, mp 183—185°. Yield, 1.28 g (15%). *Anal.* Calcd. for $C_{10}H_{15}O_2NS$: C, 56.31; H, 7.09; N, 6.57; S, 15.03. Found: C, 56.01; H, 7.10; N, 6.71; S, 15.11. UV λ_{max}^{EtOH} mμ (log ε): 239 (3.894), 328 (3.729). IR ν_{max}^{Nujol} cm^{-1}: 3070 (olefinic proton), 1658, 1550, 1265 (-SO$_2$-), 1103 (-SO$_2$-). NMR (δ ppm in DMSO-d$_6$ at 30°) was shown in Table III.

3-Methyl-5-oxo-Δ^3-dihydrothiopyran 1,1-Dioxide (XVI)——A mixture of 250 mg (1.2 mmole) of the dienamines XIVa and XIVb and 5 ml of 5% H_2SO_4 solution was warmed until a homogeneous solution was obtained. Upon standing the ketone crystallized out and recrystallization from EtOH afforded colorless prisms of mp 118°—119°, whose physical properties were almost identical with those of a reference.[8]

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