$COOCH_3$), 3.63 (2H, s, Cp–CH_2–S), 3.14 (2H, s, S–CH_2COOR). MS *m/e*: 304 (M^+). **5b**: *Anal.* Calcd. for $C_{15}H_{18}FeO_2S$: C, 56.62; H, 5.70. Found: C, 56.42; H, 5.68. IR ν_{max}^{KBr} cm^{-1}: 3057, 2957 (CH), 1730 (COOR). NMR ($CDCl_3$) δ: 3.64 (2H, s, Cp–CH_2–S), 3.11 (2H, s, S–CH_2COOR). MS *m/e*: 318 (M^+).

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Reaction of Tosylmethyl Isocyanide with Methyl 3-Substituted Propiolates as Acetylenic Michael Acceptors[1)]

HARUO SAIKACHI, TOKUJIRO KITAGAWA, and HIDEAKI SASAKI

Faculty of Pharmaceutical Sciences, Kobe Gakuin University[2)]

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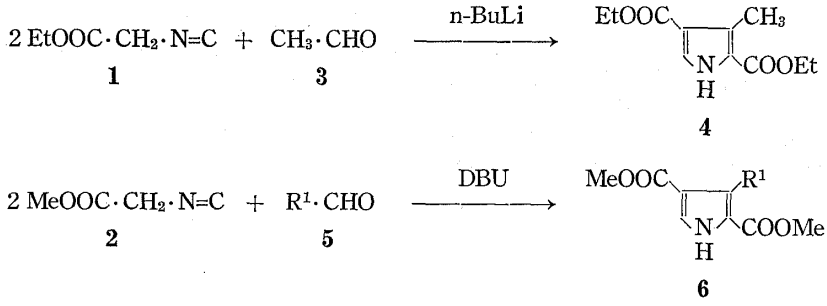
The reaction of tosylmethyl isocyanide (7) with methyl propiolate (**14a**), dimethyl acetylenedicarboxylate (**14b**), methyl 3-(2-furoyl)propiolate (**14c**), and methyl 3-benzoylpropiolate (**14d**) in the presence of an equimolar amount of base at room temperature gave the corresponding 1:2 adducts, *i.e.*, methyl 3-(1-pyrrolyl)acrylate derivatives (**16a**, **16b**, **16c**, and **16d**, respectively) as final products. The temperature dependence of the reaction made it possible to isolate the pyrroles (**15a** and **15b**), postulated as intermediates of the reaction, at low temperature.

Keywords——tosylmethyl isocyanide; α-alkali-metalated isocyanide; Michael addition; acetylenic esters; cycloaddition; 2*H*-azepine; pyrroles; 1:2 adducts; pyrrolylacrylates; acetylenic Michael acceptors

In connection with the synthesis of pyrroles using α-alkali-metalated isocyanides obtained from isocyanides and bases,[3)] it has been reported that the cycloaddition of ethyl isocyanoacetate (**1**) with acetaldehyde (**3**) in the presence of base occurs to form diethyl 3-methylpyrrole-2,4-dicarboxylate (**4**) in 36% yield.[4)] Recently an analogous reaction of methyl isocyanoacetate (**2**) with aliphatic or aromatic aldehydes (**5**) in the presence of 1, 8-diazabicyclo[5,4,0]undec-7-ene (DBU) as a base was reported to give 3-substituted pyrrole-2, 4-dicarboxylic acid esters (**6**).[5)] In an extensive series of papers,[6)] van Leusen and co-workers have maintained that olefinic ketones (**9**), esters (**10**) or nitriles (**11**) which bear an electron-withdrawing substituent are subject to attack by nucleophilic alkali-metalated tosylmethyl isocyanide (TosMIC) (**7**)[7)] and also monosubstituted TosMIC (**8**)[8)] to obtain 3,4-disubstituted pyrroles (**12**), 2,3,4-trisubstituted pyrroles (**13**), and similar compounds.[9)]

1) *a*) Synthesis of Furan Derivatives. LXXXVI; *b*) Part LXXXV: H. Saikachi, T. Kitagawa, H. Sasaki, and A.M. van Leusen, *Chem. Pharm. Bull.* (Tokyo), **27**, 793 (1979).
2) Location: *Ikawadani, Tarumi-ku, Kobe 673, Japan.*
3) *a*) D. Hoppe, *Angew. Chem. Int. Ed. Engl.*, **13**, 789 (1974); *b*) U. Schöllkopf, *ibid.*, **16**, 339 (1977).
4) U. Schöllkopf, F. Gerhart, R. Schröder, and D. Hoppe, *Ann.*, **766**, 116 (1972).
5) M. Suzuki, M. Miyoshi, and K. Matsumoto, *J. Org. Chem.*, **39**, 1980(1974).
6) Leading references: *a*) O.H. Oldenziel, D. van Leusen, and A.M. van Leusen, *J. Org. Chem.*, **42**, 3114 (1977), and references cited therein; *b*) A.M. van Leusen and J. Wildeman, *Synthesis*, **1977**, 501.
7) *a*) A.M. van Leusen, J. Wildeman, and O.H. Oldenziel, *J. Org. Chem.*, **42**, 1153 (1977); *b*) B.E. Hoogenboom, O.H. Oldenziel, and A.M. van Leusen, "Organic Synthesis," Vol. 57, ed. by C.R. Johnson, John Wiley and Sons, Inc., New York, 1977, p. 102.
8) A.M. van Leusen, R.J. Bouma, and O. Possel, *Tetrahedron Lett.*, **1975**, 3487.
9) *a*) A.M. van Leusen, H. Siderius, B.E. Hoogenboom, and D. van Leusen, *Tetrahedron Lett.*, **1972**, 5337; *b*) O. Possel and A.M. van Leusen, *Heterocycles*, **7**, 77 (1977).



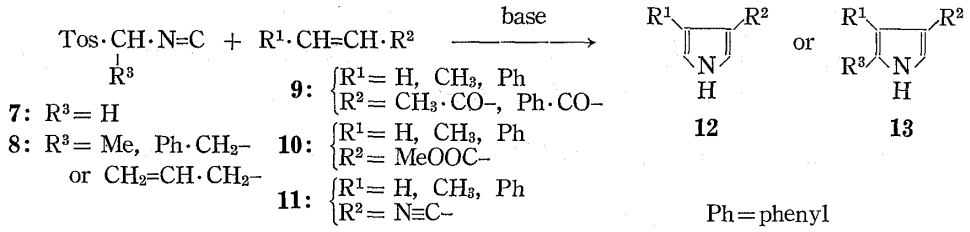


Chart 1

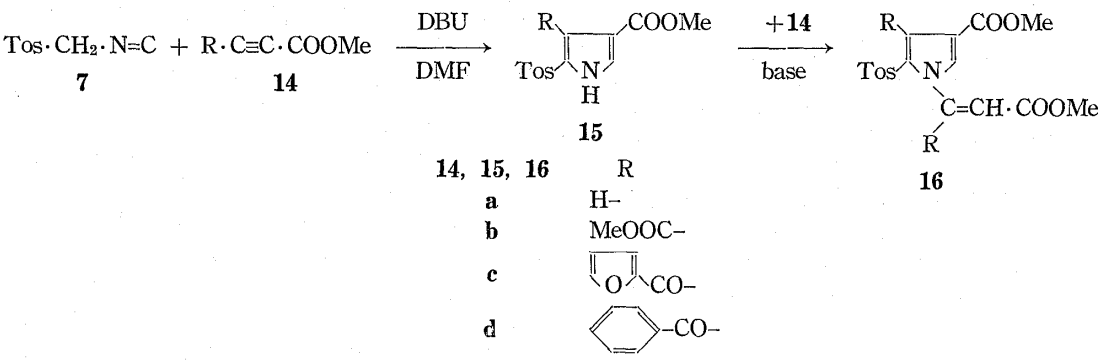


Chart 2

While studying the behavior of the Michael addition reaction,[10] we were prompted to examine the possibility of the reaction of the carbon-carbon triple bond in acetylenic esters (**14**) as Michael acceptors with TosMIC (**7**) for the formation of Pyrroles. In this paper, we report that the reaction of TosMIC (**7**) (1 equiv) with the acetylenic esters (**14a**, **14b**, **14c**, and **14d**)[11] (2 equiv each) at room temperature for 3 hours in the presence of DBU gave four 1:2 adducts (**16a**, **16b**, **16c**, and **16d**, respectively). The structure of each adduct was confirmed by elementary analysis, and measurements of ultraviolet (UV) and infrared (IR) spectra, and mass spectra (MS).

We first speculated that the 1:2 adducts might be 2*H*-azepines of type (**19**), as shown in Chart 3. However, synthetic studies showed that the structure of the final products is actually a methyl 3-(1-pyrrolyl)acrylate structure of type (**16**). On standing at −10° for one hour in the presence of DBU, mixtures of methyl propiolate (**14a**) (1 equiv) and dimethyl acetylenedicarboxylate (DMAD) (**14b**) (1 equiv) with TosMIC (**7**) (1 equiv) gave 4-methoxycarbonyl-2-tosylpyrrole (**15a**) [mp 167—169°, IR: 3220 cm^{-1} (N–H)] and 3,4-dimethoxycarbonyl-2-tosylpyrrole (**15b**) [mp 109—111°, IR: 3250 cm^{-1} (N–H)] in 12% and 7% yields,

10) *a*) T.F. Rutledge, "Acetylenes and Allenes," Reinhold Book Corporation, New York, 1969, p. 241; *b*) E.D. Bergmann, D. Ginsburg, and P. Pappo, "Organic Reactions," Vol. 10, ed. by R. Addams, John Wiley and Sons, Inc., New York, 1959, p. 179.

11) In the reactions of 7 with phenylacetylene, methyl phenylpropiolate, methyl 3-(2-furyl)propiolate, and methyl 3-(5-bromo-2-furyl)propiolate, the expected compounds of type (16) or type (15) were not isolated; the acetylenic β-carbon may not be reactive to the TosMIC anion (**17**) under the present conditions.

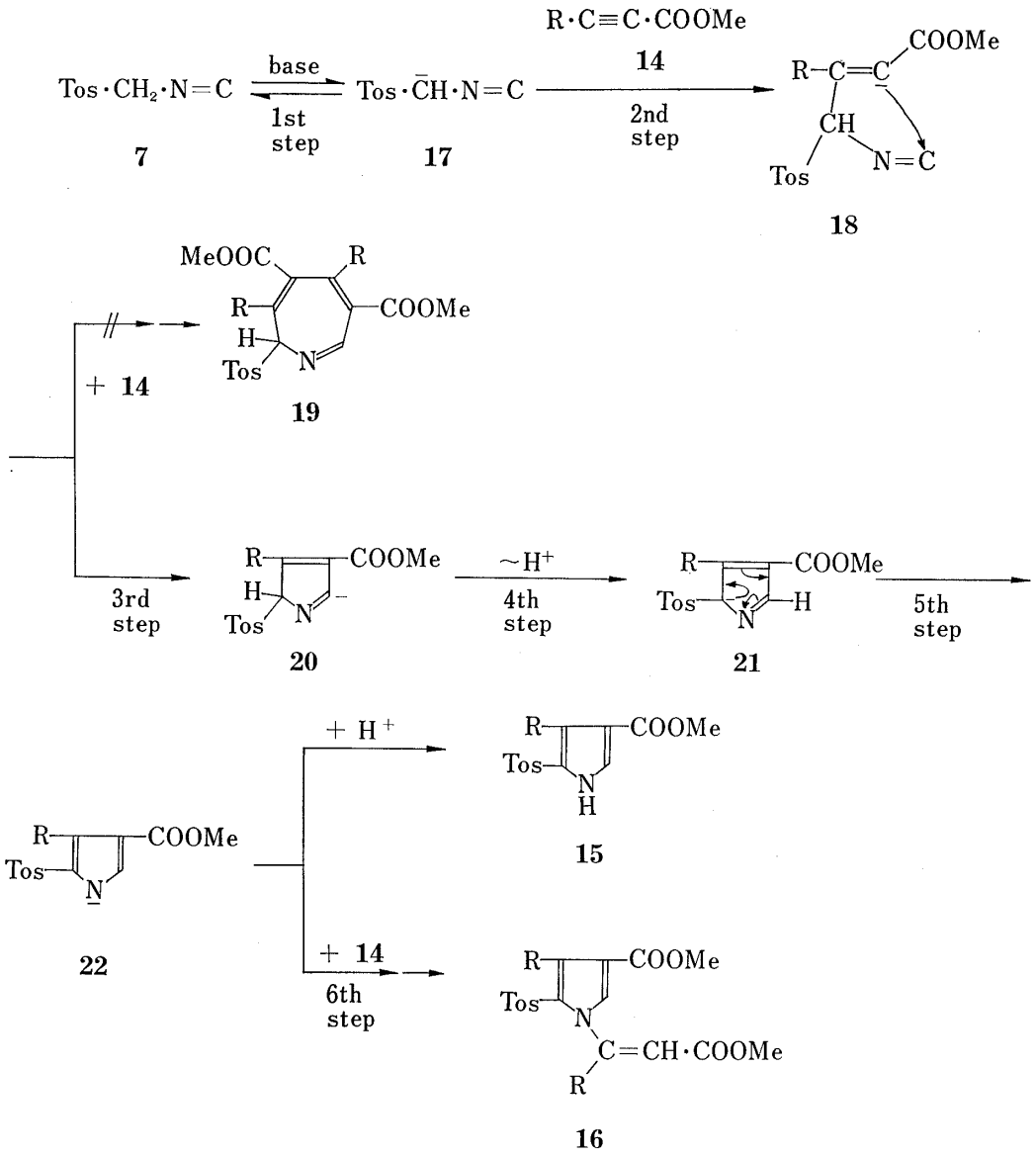


Chart 3

respectively, after chromatography. The corresponding 1: 2 adducts **16a** (mp 222—224°, 3%) and **16b** (mp 201—202°, 10%) were also obtained. The above experimental results suggest that the intramolecular cycloaddition of the carbanionic intermediate (**18**) to form the pyrrole ring (**20**) is much more favorable than the formation of the azepine ring (**19**). To confirm this, the addition of one more equivalent of methyl propiolate (**14a**) to the isolated pyrrole (**15a**) was examined under mild conditions; the expected methyl 3-(4-methoxycarbonyl-2-tosyl-1-pyrrolyl)acrylate (**16a**)[12] was obtained in 82% yield. Similarly, the Michael addition of DMAD (**14b**) to **15b** led to the corresponding acrylate (**16b**).

Judging from the experimental results, intramolecular cyclization of the carbanionic intermediate (**18**) to form the pyrrole ring (**20**) occurs without participation of the acetylenic ester (**14**) in the 3rd step, followed by a proton shift to form the pyrrole anion (**22**), which

12) Although the relative configurations of the substituents in compounds **16a**—**d** have not been established, **16a** may take the *E* configuration, and **16b**, **16c**, and **16d** may take the *Z* configuration. [*a*) R.M. Acheson and J.M. Vernon, *J. Chem. Soc.*, **1962**, 1148; *b*) *Idem, ibid.*, **1963**, 1008; *c*) R.M. Acheson, M.W. Foxton, P.J. Abbot, and K.R. Mills, *J. Chem. Soc.*, (*C*), **1967**, 882; *d*) F. Badea, "Reaction Mechanisms in Organic Chemistry," Abacus Press, Kent, England, 1977, p. 530].

then reacts with **14** in the 6th step to yield methyl 3-(1-pyrrolyl)acrylate (**16**), as shown in Chart 3.

Experimental[13]

4-Methoxycarbonyl-2-tosylpyrrole (15a)——A solution of DBU (4.6 g, 0.03 mol) in dimethylformamide (DMF) (5 ml) was added dropwise to a DMF solution (20 ml) of methyl propiolate (**14a**) (2.5 g, 0.03 mol) and TosMIC (**7**) (6 g, 0.03 mol) at −50° during a period of 30 min with stirring. After stirring at −10° for one hour, glacial acetic acid (1.8 g, 0.03 mol) was added. The reaction mixture was poured into ice-water and extracted with two 50 ml portions of ethyl acetate. The extract was washed with water, dried over anhydrous sodium sulfate, and the organic solvent was removed *in vacuo* to give a brown oily material (*ca.* 3 g) which was developed on a silica gel column with (1) benzene/ethyl acetate (4: 1) (100 ml), (2) benzene/ethyl acetate (1: 1) (100 ml), and (3) ethyl acetate (100 ml). Fraction 1; the benzene/ethyl acetate (4: 1) eluate gave TosMIC (**7**) (1.4 g, 23%). Fraction 2; concentration of the benzene/ethyl acetate (1: 1) eluate gave 820 mg (12%) of **15a**, which was recrystallized from benzene/MeOH (4: 1); colorless needles, mp 167—169°. *Anal.* Calcd. for $C_{13}H_{13}NO_4S$: C, 55.91; H, 4.70; N, 5.02. Found: C, 55.73; H, 4.45; N, 5.09. IR ν_{max}^{KBr} cm^{-1}: 3220 (N–H), 1690 (C=O), 1140 and 1320 (SO_2); UV λ_{max}^{EtOH} nm (log ε): 260 (4.26). NMR (DMSO-d_6) δ: 2.38 (3H, s, phenyl-CH_3), 3.74 (3H, s, –$COOCH_3$), 7.13 (1H, d, J=2 Hz, 3-H), 7.40 and 7.86 (each 2H, d, d, each J=8 Hz, phenyl-H), 7.70 (1H, d, J=2 Hz, 5-H), and 12.60 (1H, broad s, N–H). MS (*m/e*): 279 (M^+). Fraction 3; concentration of the ethyl acetate eluate gave 270 mg (3%) of **16a**, which was recrystallized from DMF/MeOH (4: 1); pale yellow needles, mp 222—224°. *Anal.* Calcd. for $C_{17}H_{17}NO_6S$: C, 56.20; H, 4.72; N, 3.86. Found: C, 56.64; H, 4.72; N, 4.00. IR ν_{max}^{KBr} cm^{-1}: 1710 (C=O), 1660 (C=C), 1150 and 1320 (SO_2). UV λ_{max}^{EtOH} nm (log ε): 245 (4.52) and 285 (4.39). NMR (DMSO-d_6) δ: 2.38 (3H, s, phenyl-CH_3), 3.72 and 3.76 (each 3H, s, s, nuclear and side-chain esters-CH_3), 6.74 (1H, d, J=14 Hz, side-chain 2-H), 7.50 (2H, d, J=8 Hz, phenyl 3- and 5-H), 7.82 (2H, d, J=8 Hz, phenyl 2- and 6-H), 7.40 (1H, d, J=2 Hz, nuclear 3-H), 8.28 (1H, d, J=14 Hz, side-chain 3-H), and 8.54 (1H, d, J=2 Hz, nuclear 5-H). MS (*m/e*): 363 (M^+).

3,4-Dimethoxycarbonyl-2-tosylpyrrole (15b)——Compound **15b** was prepared by the method used for the preparation of **15a** from **7** (6 g, 0.03 mol) and DMAD (4.2 g, 0.03 mol) and was recrystallized from benzene; colorless needles, 0.6 g (7%), mp 109—111°. *Anal.* Calcd. for $C_{15}H_{15}NO_6S$: C, 53.41; H, 4.48; N, 4.15. Found: C, 53.35; H, 4.70; N, 3.97. IR ν_{max}^{KBr} cm^{-1}: 3250 (N–H), 1740 and 1690 (C=O), and 1150 and 1320 (SO_2); UV λ_{max}^{EtOH} nm (log ε): 262 (4.21). NMR (DMSO-d_6) δ: 2.38 (3H, s, phenyl-CH_3), 3.70 and 3.84 (each 3H, s, s, esters-CH_3), 7.44 (2H, d, J=8 Hz, phenyl 3- and 5-H), 7.82 (2H, d, J=8 Hz, phenyl 2- and 6-H), 7.68 (1H, s, 2-H), and 12.90 (1H, broad s, N–H). MS (*m/e*): 337 (M^+).

Methyl 3-(4-Methoxycarbonyl-2-tosyl-1-pyrrolyl)acrylate (16a)——Method A: A DMF solution (3 ml) of DBU (380 mg, 2.5 mmol) was added dropwise to a DMF solution (5 ml) of methyl propiolate (**14a**) (420 mg, 5 mmol) and **7** (500 mg, 2.5 mmol) at 0° during a period of 10 min with stirring. After stirring for 3 hr at room temperature, the reaction mixture was poured into ice-water. The crystalline mass obtained was recrystallized from DMF/MeOH (4: 1) to give 400 mg (30%) of **16a**, mp 222—224°, which was identified by mixed melting point determination and from the IR spectrum of the sample obtained from fraction 3 as described in the preparation of **15a**.

Method B: A DMF solution (1 ml) of DBU (254 mg, 1.7 mmol) was added dropwise to a DMF solution (3 ml) of **15a** (360 mg, 1.7 mmol) and **14a** (140 mg, 1.7 mmol) at 0° with stirring. After stirring for 3 hr at room temperature, the reaction mixture was poured into ice-water. The crystalline mass obtained was recrystallized from DMF/MeOH (4: 1) to give 410 mg (82%) of **16a**. A mixed melting point determination of this compound and the product obtained by method A showed no depression. The IR spectra of the two samples were identical.

Methyl 3-Methoxycarbonyl-3-(3,4-dimethoxycarbonyl-2-tosyl-1-pyrrolyl)acrylate (16b)——Method A: According to method A described above for the preparation of **16a**, the reaction of **7** (1 g, 5 mmol), DMAD (1.45 g, 10 mmol), and DBU (0.8 g, 5 mmol) in 10 ml of DMF afforded 520 mg (21%) of **16b**; colorless needles from MeOH, mp 201—202°. *Anal.* Calcd. for $C_{21}H_{21}NO_{10}S$: C, 52.61; H, 4.41; N, 2.92. Found: C, 52.28; H, 4.29; N, 2.91. IR ν_{max}^{KBr} cm^{-1}: 1720 (C=O), 1150 and 1330 (SO_2). UV λ_{max}^{EtOH} nm (log ε): 225 (4.58) and 260 (4.55). NMR (DMSO-d_6) δ: 2.38 (3H, s, phenyl-CH_3), 3.72, 3.74, 3.76, and 3.88 (each 3H, each s, nuclear and side-chain esters-CH_3), 7.16 (1H, s, 2-H), 7.42 (2H, d, J=8 Hz, phenyl 3- and 5-H), 7.64 (2H, d, J=8 Hz, phenyl 2- and 6-H), and 7.90 (1H, s, 5-H). MS (*m/e*): 448 ($M^+ - OCH_3$). No parent peak was observable.

Method B: According to method B described above for the preparation of **16a**, the reaction of **15b** (273 mg, 1 mmol), DMAD (142 mg, 1 mmol), and DBU (152 mg, 1 mmol) in 10 ml of DMF afforded 352 mg (85%) of **16b**.

13) All melting points are uncorrected. IR and UV spectra were measured on a Hitachi 215 infrared spectrophotometer and a Hitachi 323 recording spectrophotometer, respectively. NMR spectra were obtained on a Nihondenshi C-100H NMR spectrometer (100 MHz; with tetramethylsilane as an internal reference). MS were taken on a Hitachi mass spectrometer, model RMU-6MG.

Methyl 3-Furoyl-3-(3-furoyl-4-methoxycarbonyl-2-tosyl-1-pyrrolyl)acrylate (16c)——Using method A described above for the preparation of **16a**, the reaction of **7** (234 mg, 1.2 mmol), methyl 3-(2-furoyl)propiolate (**14c**)[14] (427 mg, 2.4 mmol), and DBU (182 mg, 1.2 mmol) in 5 ml of DMF afforded 450 mg (68%) of **16c**; colorless needles from DMF/MeOH (4: 1), mp 248—250°. *Anal.* Calcd. for $C_{27}H_{21}NO_{10}S$: C, 58.80; H, 3.84; N, 2.54. Found: C, 58.75; H, 3.65; N, 2.59. IR ν_{max}^{KBr} cm^{-1}: 1740 and 1670 (C=O), 1630 (C=C), 1150 and 1320 (SO_2). UV λ_{max}^{EtOH} nm (log ε): 224 (4.51) and 300 (4.52). NMR (DMSO-d_6) δ: 2.20 (3H, s, phenyl-CH_3), 3.82 and 3.84 (each 3H, each s, nuclear and side-chain esters $-CH_3$), 6.72—8.10 (10H, m, nuclear and side-chain furyl groups 3-, 4-, and 5-H, phenyl 2-, 3-, 5-, and 6-H), 8.02 (1H, s, vinyl-H), and 8.24 (1H, s, pyrrolyl 5-H). MS (*m/e*): 551 (M^+), 520 (M^+-OCH_3).

Methyl 3-Benzoyl-3-(3-benzoyl-4-methoxycarbonyl-2-tosyl-1-pyrrolyl)acrylate (16d)——Using method A described above for the preparation of **16a**, the reaction of **7** (584 mg, 3 mmol), methyl 3-benzoylpropiolate (**14d**)[15] (1.13 g, 6 mmol), and DBU (456 mg, 3 mmol) in 10 ml of DMF afforded 441 mg (25%) of **16d**; colorless needles from DMF/MeOH (4: 1), mp 193—194°. *Anal.* Calcd. for $C_{31}H_{25}NO_8S$: C, 65.14; H, 4.41; N, 2.54. Found: C, 65.15; H, 4.27; N, 2.42. IR ν_{max}^{KBr} cm^{-1}: 1735 and 1675 (C=O), 1645 (C=C), 1150 and 1320 (SO_2). UV λ_{max}^{EtOH} nm (log ε): 236 (4.48) and 3.80 (4.39). NMR (DMSO-d_6) δ: 2.16 (3H, s, phenyl-CH_3), 3.74 and 3.80 (each 3H, each s, nuclear and side-chain esters $-CH_3$), 7.08—7.92 (14H, m, nuclear and side-chain phenyl groups), 7.82 (1H, s, vinyl-H), and 8.18 (1H, s, pyrrolyl 5-H). MS (*m/e*): 540 (M^+-OCH_3). No parent peak was observable.

14) H. Saikachi and T. Kitagawa, *Yakugaku Zasshi*, **91**, 454 (1971).
15) A.W. Nineham and R.A. Raphael, *J. Chem. Soc.*, **1949**, 118.

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Triazolo[4,5-*d*]pyrimidines. III.[1] The Transformation of 3-Substituted 3*H*-1,2,3-Triazolo[4,5-*d*]pyrimidines into 3-Substituted 3*H*-1,2,3-Triazolo[4,5-*b*]pyridines

Takeo Higashino,[2a] Tatsuhiko Katori,[2b] and Eisaku Hayashi[2a]

Shizuoka College of Pharmacy[2a] and Central Research Laboratory, S S Pharmaceutical Co., Ltd.[2b]

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Treatment of 3-substituted 3*H*-1,2,3-triazolo[4,5-*d*]pyrimidines (I) with active methylene compounds, such as 1,3-dicarbonyl compounds (A-1 to A-2), aliphatic ketones (A-3 to A-4), and cyclic ketones (A-5 to A-6), in the presence of dilute sulfuric acid gave the 3-substituted 3*H*-1,2,3-triazolo[4,5-*b*]pyridines (IIIm-1 to IIIm-2, IIIm-5 to IIIm-6, and IIIp-1 to IIIp-6).

The mechanism of the transformation is discussed.

Keywords——triazolopyrimidines; triazolopyridines; active methylene compounds; ketones; ring transformation; mechanism

In the previous paper,[1] we reported that 3-substituted 3*H*-1,2,3-triazolo[4,5-*d*]pyrimidines (I) in dilute sulfuric acid easily undergo ring fission to give 1-substituted 5-amino-1*H*-1,2,3-triazole-4-carboxaldehydes (II). It was expected that the presence of active methylene compounds (A) in the reaction system might lead to a type of Friedlaender synthesis between the resulting II and A. In fact, we found that I reacted with A in dilute sulfuric acid and was transformed into 3-substituted 3*H*-1,2,3-triazolo[4,5-*b*]pyridines (III) in moderate yields.

The molar ratio of I to A was set at 1: 2.5. Thus, 3-methyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidine (Im) reacted with 2,4-pentanedione (A-1) in dilute sulfuric acid at room temperature

1) Part II: T. Higashino, T. Katori, and E. Hayashi, *Chem. Pharm. Bull.* (Tokyo), **27**, 2431 (1979).
2) Location: *a) 2-2-1 Oshika, Shizuoka-shi, 422, Japan; b) 1143 Nanpeidai, Narita-shi, 286, Japan.*