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Triazolo[4,5-*d*]pyrimidines. V.[1] The Nucleophilic Substitution of 7-Chloro- and 7-(*p*-Tolylsulfonyl)-3-phenyl-*3H*-1,2,3-triazolo[4,5-*d*]pyrimidines

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The substitution reaction of 7-chloro- (**1**) and 7-(*p*-tolylsulfonyl)-3-phenyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidines (**2**) with various nucleophiles (NuH or Nu$^-$) was carried out.

The reaction of **1** with amines (NuH-1 to NuH-11) gave 7-(N-substituted amino)-3-phenyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidines (**3–1** to **3–11**). The reaction with alkoxide ions (Nu$^-$-12 to Nu$^-$-17) resulted in the formation of 7-alkoxy-3-phenyl-3*H*-1,2,3-triazolo-[4,5-*d*]pyrimidines (**3–12** to **3–17**). Moreover, **1** reacted with carbanions which were formed by the reaction of active methylene compounds (NuH-19 to NuH-24) with sodium hydride, resulting in the introduction of a carbon chain into the 7-position of **1** (yielding 7-substituted 3-phenyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidines, **3–19** to **3–24**).

Similarly, the *p*-tolylsulfonyl group of **2** was easily displaced by nucleophiles (NuH-1 to NuH-24) to give the corresponding 7-substituted 3-phenyl-3*H*-1,2,3-triazolo[4,5-*d*]-pyrimidines (**3–1** to **3–24**).

The tautomerism of 7-substituted 3-phenyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidines (**3–19** to **3–24**) formed by the reaction with carbanions is discussed.

Keywords——7-chloro-3-phenyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidine; 7-(*p*-tolylsulfonyl)-3-phenyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidine; nucleophilic substitution; amines; alkoxide ions; carbanions; 7-substituted 3-phenyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidines; tautomerism

It is well known that chloro and *p*-tolylsulfonyl groups located in a π-deficient position of a condensed pyrimidine ring can be replaced by various nucleophiles. For example, 7-chloro-3-methyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidine reacted with nucleophiles to give 7-substituted 3-methyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidines[3] and the reaction of 4-(*p*-tolylsulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine with nucleophiles resulted in the formation of 4-substituted 1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidines.[4]

Anticipating that similar nucleophilic substitution would take place, we reacted 7-chloro-(**1**)[5] and 7-(*p*-tolylsulfonyl)-3-phenyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidines (**2**) with various nucleophiles (NuH or Nu$^-$), and succeeded in obtaining 7-substituted 3-phenyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidines (**3**).

The Reaction of 1 with NuH or Nu$^-$ (General Method A)

The reaction of **1** with amines (NuH-1 to NuH-11) and alkoxide ions (Nu$^-$-12 to Nu$^-$-17) resulted in the formation of 7-(N-substituted amino)- (**3-1** to **3-11**) and 7-alkoxy-3-phenyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidines (**3-12** to **3-17**), respectively, in good yields. In N,N-dimethylformamide (DMF) the cyanide ion (Nu$^-$-18) reacted with **1** at room temperature to give 3-phenyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidine-7-carbonitrile (**3-18**) in 40% yield. In DMF

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[1] Part IV: T. Higashino, T. Katori, S. Yoshida, and E. Hayashi, *Chem. Pharm. Bull.*, **27**, 3176 (1979).
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[3] T. Higashino, T. Katori, and E. Hayashi, *Yakugaku Zasshi*, **99**, 1031 (1979).
[4] E. Hayashi, T. Higashino, and S. Suzuki, *Yakugaku Zasshi*, **98**, 89 (1978).
[5] D.J. Brown and M.N. Paddon-Row, *J. Chem. Soc.* (*C*), **1965**, 1846.

1 reacted with diethyl malonate (NuH-19) in the presence of sodium hydride to give diethyl 3-phenyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidine-7-malonate (**3-19**). Similarly, the reaction with active methylene compounds (NuH-20 to NuH-24) gave 7-substituted 3-phenyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidines (**3-20** to **3-24**) in varous yields (see Table I). In the cases of NuH-20, NuH-21, and NuH-22, ethyl 3-(3-phenyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-7-yloxy)-2-butenoate (**3-20′**), 4-(3-phenyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-7-yloxy)-3-pentene-2-one (**3-21′**) and **3-23**, respectively, were formed as by-products.

The compound **3-1** was identical with 7-amino-3-phenyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidine prepared by another route[6] (mixed melting point test). The structures of **3-2** to **3-24** and **3-20′** to **3-21′** were suggested by their mass spectra (MS) and confirmed by their infrared (IR) absorption and nuclear magnetic resonance (NMR) spectra, as shown in Tables II and III.

The IR spectrum of **3-18** did not show any absorption band of the cyano group. This is compatible with the reported absence of the absorption band of a cyano group located

TABLE I. The Reaction of **1** with NuH or Nu⁻

NuH	Product			Reaction conditions		
	3	mp (°C)	Yield (%)	Temperature (°C)[h]	Time (min)	Solvent
NuH-1	**3-1**	295[a,g]	64	r.t.	5	DMF
NuH-2	**3-2**	206—207[b]	96	r.t.	10	Benzene
NuH-3	**3-3**	130—131[b]	95	r.t.	30	Benzene
NuH-4	**3-4**	191—192[b]	94	Reflux	5	Benzene
NuH-5	**3-5**	193—194[b]	86	Reflux	30	Benzene
NuH-6	**3-6**	140—142[c]	95	r.t.	20	Benzene
NuH-7	**3-7**	75— 76[b]	82	r.t.	5	Benzene
NuH-8	**3-8**	95— 96[b]	64	r.t.	40	Benzene
NuH-9	**3-9**	204—205[b]	70	r.t.	5	Benzene
NuH-10	**3-10**	160—161[d]	45	r.t.	20	Benzene
NuH-11	**3-11**	239—242[b,g]	55	r.t.	3 hr	Benzene–MeOH
Nu⁻-12	**3-12**	136—137[b]	77	r.t.	30	MeOH
Nu⁻-13	**3-13**	97— 98[c]	74	r.t.	10	EtOH
Nu⁻-14	**3-14**	62— 63[b]	62	r.t.	30	BuOH
Nu⁻-15	**3-15**	124—125[d]	75	Reflux	5	Benzene
Nu⁻-16	**3-16**	125—126[a]	85	Reflux	10	Benzene
Nu⁻-17	**3-17**	117—118[c]	60	85	5	iso-PrOH
Nu⁻-18	**3-18**	166—167[a]	40	r.t.	60	DMF
NuH-19	**3-19**	160—161[d]	46	r.t.	5	DMF
NuH-20	**3-20**	153—155[d]	30	r.t.	10	DMF
	3-20′	110—112[a]	18			
NuH-21	**3-21**	198—200[d]	11	30	30	DMF
	3-21′	146—147[b]	27			
NuH-22	**3-22**	222—226[f]	12	0	20	DMF
	3-23	187—189[f]	3			
NuH-23	**3-23**	187—189[f]	11	0	35	DMF
NuH-24	**3-24**	218—219[f]	53	r.t.	10	DMF
Nu⁻-25	**2**	201—203[e,g]	41	r.t.	12	DMF

a) Colorless scales.
b) Colorless needles.
c) Colorless plates.
d) Slightly yellow needles.
e) White powder.
f) Yellow needles.
g) Decomposition.
h) r.t.=room temperature.

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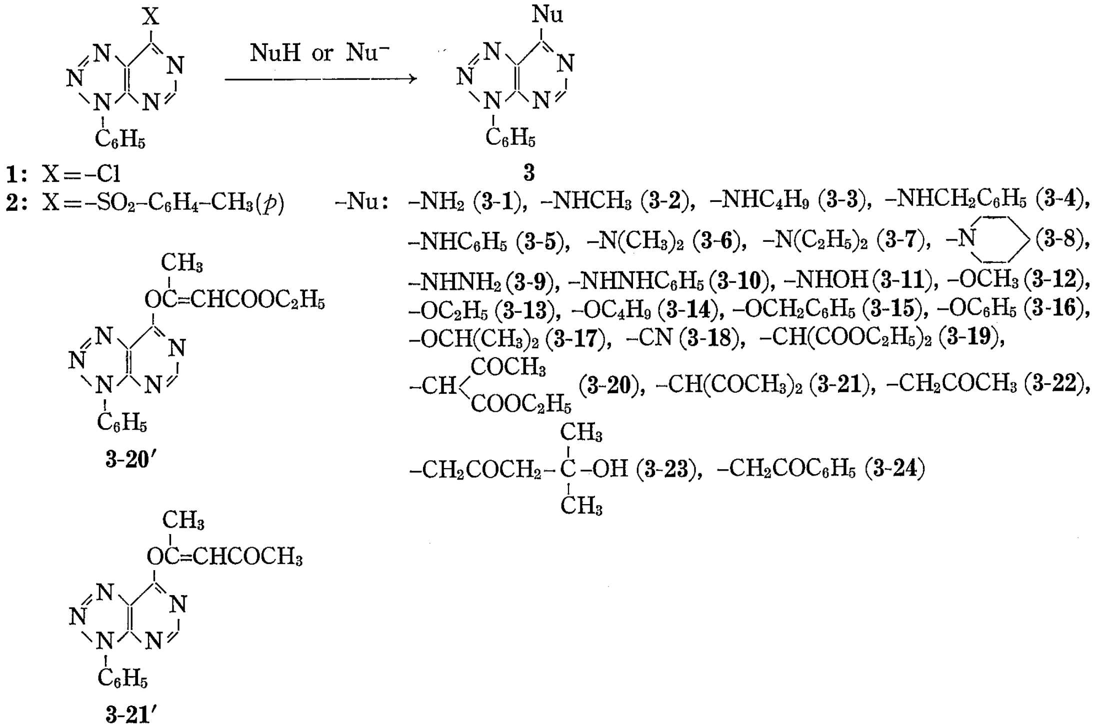
6) H. Bredereck and W. Baumann, *Ann. Chem.*, **701**, 157 (1967).



1: X=-Cl

2: $X=-SO_2-C_6H_4-CH_3(p)$

3

-Nu: $-NH_2$ (**3-1**), $-NHCH_3$ (**3-2**), $-NHC_4H_9$ (**3-3**), $-NHCH_2C_6H_5$ (**3-4**), $-NHC_6H_5$ (**3-5**), $-N(CH_3)_2$ (**3-6**), $-N(C_2H_5)_2$ (**3-7**), $-N\bigcirc$ (**3-8**), $-NHNH_2$ (**3-9**), $-NHNHC_6H_5$ (**3-10**), $-NHOH$ (**3-11**), $-OCH_3$ (**3-12**), $-OC_2H_5$ (**3-13**), $-OC_4H_9$ (**3-14**), $-OCH_2C_6H_5$ (**3-15**), $-OC_6H_5$ (**3-16**), $-OCH(CH_3)_2$ (**3-17**), $-CN$ (**3-18**), $-CH(COOC_2H_5)_2$ (**3-19**), $-CH\begin{smallmatrix}COCH_3\\COOC_2H_5\end{smallmatrix}$ (**3-20**), $-CH(COCH_3)_2$ (**3-21**), $-CH_2COCH_3$ (**3-22**), $-CH_2COCH_2-\overset{CH_3}{\underset{CH_3}{C}}-OH$ (**3-23**), $-CH_2COC_6H_5$ (**3-24**)

3-20′

3-21′

Chart 1

Table II. MS and IR Spectral Data for 3

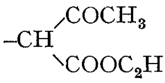
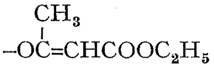
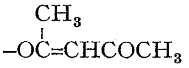
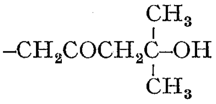
Compd.	Composition	MS: M+ m/e Observed	Error[a]	IR ν_{max}^{KBr} cm^{-1}
3-2	$C_{11}H_{10}N_6$	226.0977	0.9	3250 (=NH)
3-3	$C_{14}H_{16}N_6$	268.1446	0.8	3250 (=NH)
3-4	$C_{17}H_{14}N_6$	302.1300	1.7	3260 (=NH)
3-5	$C_{16}H_{12}N_6$	288.1129	0.3	3250 (=NH)
3-6	$C_{12}H_{12}N_6$	240.1125	0.1	
3-7	$C_{14}H_{16}N_6$	268.1433	−0.4	
3-8	$C_{15}H_{16}N_6$	280.1430	−0.7	
3-9	$C_{10}H_9N_7$	227.0910	−0.8	3240 (=NH, $-NH_2$)
3-10	$C_{16}H_{13}N_7$	303.1225	−0.8	3190, 3340 (=NH)
3-11	$C_{10}H_8N_6O$	228.0783	2.3	3300 (=NH, -OH)
3-12	$C_{11}H_9N_5O$	227.0804	−0.4	
3-13	$C_{12}H_{11}N_5O$	241.0974	0.9	
3-14	$C_{14}H_{15}N_5O$	269.1257	−0.2	
3-15	$C_{17}H_{13}N_5O$	303.1113	−0.8	
3-16	$C_{16}H_{11}N_5O$	289.1002	3.6	
3-17	$C_{13}H_{13}N_5O$	255.1107	−1.4	
3-18	$C_{11}H_6N_6$	222.0662	0.7	
3-19	$C_{17}H_{17}N_5O_4$	355.1285	0.2	1730, 1620 (=C=O)
3-20	$C_{16}H_{15}N_5O_3$	325.1158	−1.8	1730, 1620 (=C=O)
3-20′	$C_{16}H_{15}N_5O_3$	325.1161	−1.5	1720 (=C=O)
3-21	$C_{15}H_{13}N_5O_2$	295.1080	−2.8	1700, 1630 (=C=O)
3-21′	$C_{15}H_{13}N_5O_2$	295.1100	−0.8	1700 (=C=O)
3-22	$C_{13}H_{11}N_5O$	253.0983	1.9	1660 (=C=O)
3-23	$C_{16}H_{17}N_5O_2$	311.1395	1.0	1660 (=C=O), 3400 (-OH)
3-24	$C_{18}H_{13}N_5O$	315.1119	−0.3	1650 (=C=O)
2	$C_{17}H_{13}N_5O_2S$	351.0836	4.5	1150, 1335, 1345 (=SO_2)

a) Difference from the theoretical value in millimass units.

at a π-deficient position in condensed pyrimidine ring systems, such as 4-quinazolinecarbonitrile,[7] 1-substituted 1*H*-pyrazolo[3,4-*d*]pyrimidine-4-carbonitrile,[8] 4-pyrido[2,3-*d*]pyrimidinecarbonitrile,[9] and 3-methyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidine-7-carbonitrile.[3]

The compounds **3-19** to **3-24** will be present either as an enol form or as a mixture of keto and enol forms, as shown in Chart 2. The low frequency shifts of the carbonyl absorp-

Table III. NMR Spectral Data for **3**

Compd.	NMR (in $CDCl_3$): ppm[a]			
	N^3–C_6H_5^{m}	C^5–H^s	C^7–R	
3-1[b]	7.5—8.2	8.70	$-NH_2$	—
3-2[d]	7.5—8.4	8.48	$-NHCH_3$	3.13^d (3H, $J=5$ Hz)[c], 9.0^{bs} (1H)
3-3	7.5—8.3	8.55	$-NH(CH_2)_3CH_3$	3.5—4.0^m (2H), 1.2—2.1^m (4H), 0.8—1.1^m (3H), 7.0^{bs} (1H)
3-4[d]	7.2—8.3	8.45	$-NHCH_2C_6H_5$	4.7—5.0^m (2H), 7.2—8.3^m (5H),[e] 6.9^{bs} (1H)
3-5	7.2—8.4	8.65	$-NHC_6H_5$	7.2—8.4^m (6H)[e]
3-6	7.4—8.3	8.45	$-N(CH_3)_2$	3.2—4.0^m (6H)
3-7	7.4—8.3	8.48	$-N(C_2H_5)_2$	3.6—4.6^m (4H), 1.2—1.6^m (6H)
3-8	7.4—8.3	8.40		3.9—4.9^m (4H), 1.6—2.0^m (6H)
3-9[d]	7.3—8.3	8.47	$-NHNH_2$	4.5—5.7^{bs} (3H)
3-10[d]	7.4—8.3	8.50	$-NHNHC_6H_5$	7.4—8.3^m (5H),[e] 4.3—4.9^{bs} (2H)
3-11[d]	7.4—8.3	8.40	$-NHOH$	3.5—5.0^{bs} (1H), 12.1—13.0^{bs} (1H)
3-12	7.4—8.4	8.74	$-OCH_3$	4.30^s (3H)
3-13	7.4—8.4	8.70	$-OCH_2CH_3$	4.83^q (2H), 1.56^t (3H, $J=7$ Hz)
3-14	7.4—8.4	8.73	$-O(CH_2)_3CH_3$	4.72^t (2H), 1.3—2.1^m (4H), 2.01^t (3H, $J=7$ Hz)
3-15	7.2—8.3	8.73	$-OCH_2C_6H_5$	5.75^s (2H), 7.2—8.3^m (5H)[e]
3-16	7.3—8.4	8.69	$-OC_6H_5$	7.3—8.4^m (5H)[e]
3-17	7.4—8.4	8.67	$-OCH(CH_3)_2$	5.79^{sept} (1H), 1.57^d (6H, $J=7$ Hz)
3-18[d]	7.5—8.3	9.58	$-CN$	—
3-19	7.4—8.1	—[e]	$-CH(COOCH_2CH_3)_2$	4.47^q, 4.25^q, 1.35^t, 1.29^t (10H, $J=7$ Hz), 13.0^{bs} (1H)
3-20	7.4—8.3	—[e]	 $-CH\begin{matrix}\nearrow COCH_3\\ \searrow COOC_2H_5\end{matrix}$	4.51^q (2H), 1.39^t (3H, $J=7$ Hz), 2.38^s (3H), 15.5^{bs} (1H)
3-20′	7.4—8.4	8.77	 $-O\overset{CH_3}{C}=CHCOOC_2H_5$	5.97^s (1H), 4.25^q (2H), 1.33^t (3H, $J=7$ Hz), 2.64^s (3H)
3-21[d]	7.4—8.3	—[e]	$-CH(COCH_3)_2$	3.24^s (3H), 2.40^s (3H), 15.0^{bs} (1H)
3-21′	7.4—8.4	8.80	 $-O\overset{CH_3}{C}=CHCOCH_3$	6.38^s (1H), 2.57^s (3H), 2.30^s (3H)
3-22	7.4—8.4	—[e]	$-CH_2COCH_3$	6.31^s (1H), 2.27^s (3H), 15.5^{bs} (1H)
3-23[b]	7.4—8.3	9.00	 $-CH_2COCH_2\overset{CH_3}{\underset{CH_3}{C}}-OH$	3.08^s (2H), 1.58^s (6H)
3-24[d]	7.2—8.2	8.49	$-CH_2COC_6H_5$	6.93^s (1H), 7.2—8.2^m (5H),[e] 15.5^{bs} (1H)
2	7.2—8.3	9.30	$-SO_2C_6H_4CH_3$ (*p*)	7.2—8.3^m (4H),[e] 2.42^s (3H)

a) bs: broad singlet, exchangeable with D_2O, d: doublet, m: multiplet, q: quartet, s: singlet, sept: septet, t: triplet.
b) In CF_3COOD.
c) Changeable into a singlet by addition of D_2O.
d) In $SO(CD_3)_2$.
e) Overlapping with N^3–C_6H_5.

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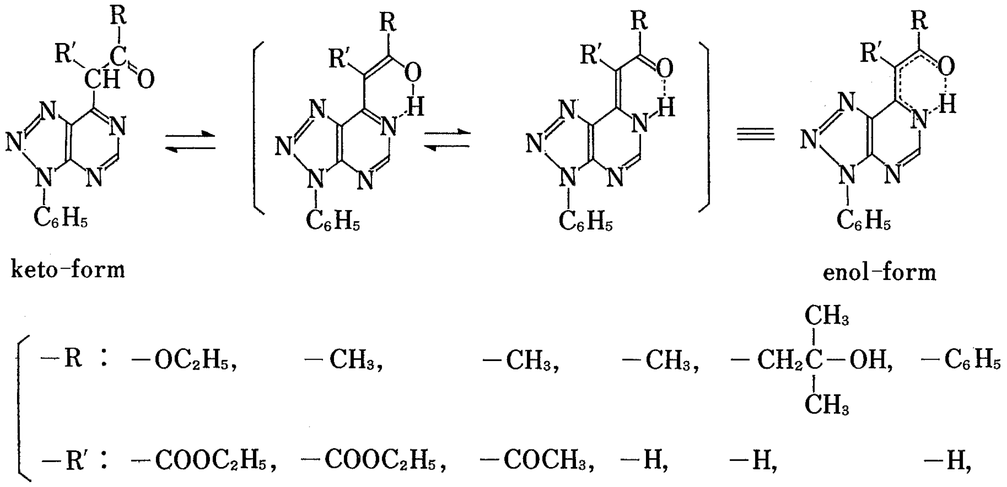
[7] T. Higashino, *Chem. Pharm. Bull.*, **9**, 635 (1961).

[8] M. Uchida, T. Higashino, C. Iijima, N. Shimada, and E. Hayashi, *Mass Spectroscopy Japan*, **25**, 169 (1977).

[9] T. Higashino and E. Hayashi, *Chem. Pharm. Bull.*, **18**, 1457 (1970).

tion bands in the IR spectra of these compounds in contrast with normal carbonyl bands are attributable to the conjugate chelation effect (see Table II).[10] This suggests that in the solid state (potassium bromide) the compounds exist in the enol form.

The NMR technique is often a powerful tool to clarify the status of keto-enol equilibria.[11] In the NMR spectra of these compounds, strong deshielding due to internal hydrogen bonding arising from conjugate chelation was seen at 13.0—15.5 ppm as a very broad band which is



$-R:\ -OC_2H_5,\ -CH_3,\ -CH_3,\ -CH_3,\ -CH_2C(CH_3)_2-OH,\ -C_6H_5$

$-R':\ -COOC_2H_5,\ -COOC_2H_5,\ -COCH_3,\ -H,\ -H,\ -H,$

Chart 2

Table IV. The Reaction of **2** with NuH or Nu$^-$

NuH	Product **3**	Product Yield (%)	Reaction conditions Temperature (°C)	Reaction conditions Time (min)	Reaction conditions Solvent
NuH-1	**3-1**	54	r.t.	5	DMF
NuH-2	**3-2**	63	r.t.	5	$CHCl_3$
NuH-3	**3-3**	84	r.t.	30	$CHCl_3$
NuH-4	**3-4**	57	r.t.	20	$CHCl_3$
NuH-5	**3-5**	71	Reflux	60	$CHCl_3$
NuH-6	**3-6**	85	r.t.	30	$CHCl_3$
NuH-7	**3-7**	67	r.t.	5	$CHCl_3$
NuH-8	**3-8**	81	r.t.	30	$CHCl_3$
NuH-9	**3-9**	66	r.t.	30	$CHCl_3$
NuH-10	**3-10**	16	r.t.	180	$CHCl_3$
NuH-11	**3-11**	48	r.t.	180	Benzene–MeOH
Nu$^-$-12	**3-12**	65	r.t.	60	MeOH
Nu$^-$-13	**3-13**	68	r.t.	30	EtOH
Nu$^-$-14	**3-14**	31	85	15	BuOH
Nu$^-$-15	**3-15**	12	Reflux	30	Benzene
Nu$^-$-16	**3-16**	58	Reflux	10	Benzene
Nu$^-$-17	**3-17**	18	r.t.	Overnight	iso-PrOH
NuH-19	**3-19**	32	r.t.	15	DMF
NuH-20	**3-20**	36	r.t.	10	DMF
NuH-21	**3-21**	35	0	30	DMF
NuH-22	**3-22**	6	0	20	DMF
	3-23	2			
NuH-24	**3-24**	48	r.t.	10	DMF

a) r.t.=room temperature.

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[10] L.J. Bellamy, "The Infrared Spectra of Complex Molecules," Methun Co., Ltd., (London), 1958, p. 142.

[11] S.J. Rhoads, *J. Org. Chem.*, **31**, 171 (1966).

equivalent to just one hydrogen in the integration and is easily removed by deuterium oxide exchange. The spectra of **3-22** and **3-24** showed one olefinic hydrogen as a sharp singlet at 6.31 and 6.39 ppm. Usually the hydrogens at the 5-position of 3-phenyl-3*H*-1,2,3-triazolo-[4,5-*d*]pyrimidine[12] and its 4-alkyl derivatives[1] resonate at low magnetic field (9.0—9.3 ppm). However, in each of these compounds the hydrogen of the 5-position appeared at higher magnetic field than expected, as shown in Table III. From the NMR data it is thus concluded that in solution (deuteriochloroform) these compounds exist in the enol form with internal hydrogen bonding in a conjugate chelation system.

The Reaction of 2 with NuH or Nu$^-$ (General Method B)

7-(*p*-Tolylsulfonyl)-3-phenyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidine (**2**) was obtained by the nucleophilic substitution of **1** with sodium *p*-toluenesulfinate (Nu$^-$-25) in DMF. The structure was suggested by the MS spectrum and confirmed by the IR and NMR spectra, as shown in Tables II and III.

The *p*-tolylsulfonyl group in **2** acted as a leaving group and was easily displaced by various nucleophiles. Thus, the reactions with amines (NuH-1 to NuH-11) and alkoxide ions (Nu$^-$-12 to Nu$^-$-17) gave 7-(N-substituted amino)- (**3-1** to **3-11**) and 7-alkoxy-3-phenyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidines (**3-12** to **3-17**). Smilarly, **2** reacted with active methylene compounds (NuH-19 to NuH-24) in DMF in the presence of sodium hydride to give 7-substituted 3-phenyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidines (**3-19** to **3-24**). The results are shown in Table IV.

Thus, nucleophilic substitution of **1** and **2** with a carbanion provides a facile method for the introduction of a carbon chain into the 7-position of the 3*H*-1,2,3-triazolo[4,5-*d*]-pyrimidine ring system.

Experimental[13]

IR spectra were recorded on a Jasco IRA-1 grating infrared spectrophotometer. NMR spectra were measured at 60 Mc and at 23° on a Hitachi R-24 high resolution NMR spectrometer using tetramethylsilane as an internal standard. MS was carried out on a JEOL JMS-01SG-2 mass spectrometer combined with a JEC-6 spectrum computer. Samples were vaporized in a direct inlet system.

General Method A——7-(N-Substituted Amino)-3-phenyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidines (**3–1** to **3–11**): A mixture of 501 mg (2.2 mmol) of **1** and 2.2 to 6.0 mmol of amine (NuH-1 to NuH-11) in 10.0 ml of benzene was stirred under the conditions described in Table I. Benzene was removed under reduced pressure, and the separated crystals were collected, washed with H_2O and recrystallized from MeOH or benzene. The yields and melting points of **3–1** to **3–11** are shown in Table I.

7-Alkoxy-3-phenyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidines (**3–12** to **3–17**): A mixture of 463 mg (2.0 mmol) of **1** and a solution of sodium alkoxide (Nu$^-$-12 to Nu$^-$-17), prepared from 43 mg of Na and 20.0 ml of alcohol (MeOH, EtOH, BuOH, BzOH, PhOH, or iso-PrOH), was stirred under the conditions described in Table I. The solvent was removed under reduced pressure, and the residue was poured into 15.0 ml of H_2O. The separated crystals were collected and recrystallized from MeOH or petr. ether. The yields and melting points of **3–12** to **3–17** are shown in Table I.

In the case of Nu$^-$-15 and Nu$^-$-16, sodium alkoxides were prepared from 43 mg of Na and 0.5 ml of the alcohol in 10.0 ml of benzene.

3-Phenyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidine-7-carbonitrile (**3–18**): A mixture of 1000 mg (4.3 mmol) of **1** and 564 mg (8.6 mmol) of KCN in 10.0 ml of DMF was stirred for 1 hr, and the reaction mixture was poured into 20.0 ml of H_2O. The separated crystals were collected, washed with H_2O and extracted with benzene. The benzene extract was dried over Na_2SO_4 and chromatographed on a column of silica gel using benzene as an eluent. The first fraction gave **3–18**. The yield and melting point are shown in Table I.

7-Substituted 3-Phenyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidines (**3–19** to **3–24**): A solution of 600 mg (2.6 mmol) of **1** in 6.0 ml of DMF was added to a solution of 2.6 to 16.6 mmol of active methylene compound (NuH-19 to NuH-24) and 125 to 400 mg of 50% NaH (in oil) in 10.0 ml of DMF, and the mixture was stirred under the conditicns described in Table I. The reaction mixture was poured into 20.0 ml of H_2O and

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12) T. Higashino, T. Katori, and E. Hayashi, *Chem. Pharm. Bull.* **27**, 2431 (1979).
13) Melting points are uncorrected.

neutralized with dilute AcOH. The separated crystals were collected and recrystallized from MeOH or benzene–petr. ether. The yields and melting points of **3–19** to **3–24** are shown in Table I.

In the case of NuH-20, the mother liquor was concentrated to dryness, and the residue was extracted with benzene. The benzene extract was dried over Na_2SO_4 and chromatographed on a column of silica gel using benzene as an eluent. The first fraction gave **3–20′** in 18% yield.

In the case of NuH-21, the material insoluble in MeOH (recrystallization solvent) was dissolved in benzene and chromatographed on a column of silica gel using benzene as an eluent. The first fraction gave **3–21′** in 27% yield.

In the case of NuH-22, the mother liquor was concentrated to dryness, and the residue was chromatographed on a column of silica gel using $CHCl_3$ as an eluent. The first fraction gave **3–23** in 3% yield.

7-(*p*-Tolylsulfonyl)-3-phenyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidine (**2**): Sodium *p*-toluenesulfinate·$4H_2O$ (Nu^--25) (200 mg, 8.0 mmol) was added to a solution of 2000 mg (8.6 mmol) of **1** in 15.0 ml of DMF, and the mixture was stirred for 12 min at 15°. The reaction mixture was poured into 20.0 ml of H_2O, and the separated crystals were collected and extracted with $CHCl_3$. The $CHCl_3$ extract was dried over Na_2SO_4 and chromatographed on a column of silica gel using $CHCl_3$ as an eluent. The first fraction gave **2**. The yield and melting point are shown in Table I.

General Method B——7-(N-Substituted Amino)-3-phenyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidines (**3–1** to **3–11**): A mixture of 250 mg (0.7 mmol) of **2** and 1.4 to 6.0 mmol of amine (NuH-1 to NuH-11) in 20.0 ml of $CHCl_3$ was stirred under the conditions described in Table IV. $CHCl_3$ was removed under reduced pressure, and the residue was recrystallized from MeOH or benzene. The yields of **3–1** to **3–11** are shown in Table IV.

7-Alkoxy-3-phenyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidines (**3–12** to **3–17**): A mixture of 250 mg (0.7 mmol) of **2** and a solution of sodium alkoxide (Nu^--12 to Nu^--17), prepared from 17 mg of Na and 20.0 ml of alcohol (MeOH, EtOH, BuOH, BzOH, PhOH, or iso-PrOH), was stirred under the conditions described in Table IV. The solvent was removed under reduced pressure, and 20.0 ml of H_2O was added to the residue. The separated crystals were collected and recrystallized from MeOH. The yields of **3–12** to **3–17** are shown in Table IV.

In the case of Nu^--15 and Nu^--16, sodium alkoxide solution was prepared from 18 mg of Na and 0.5 ml of alcohol (BzOH or PhOH) in 6.0 ml of benzene.

7-Substituted 3-Phenyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidines (**3–19** to **3–24**): A solution of 250 mg (0.7 mmol) of **2** in 20.0 ml of DMF was added to a solution of 0.7 to 7.0 mmol of active methylene compound (NuH-19 to NuH-24) and 70 to 170 mg of NaH (in oil) in 8.0 ml of DMF, and the mixture was stirred under the conditions described in Table IV. The reaction mixture was poured into 50.0 ml of H_2O and neutralized with dilute AcOH. The separated crystals were collected and recrystallized from MeOH or benzene-petr. ether. The yields of **3–19** to **3–24** are shown in Table IV.

In the case of NuH-22, the separated crystals were chromatographed on a column of silica gel using $CHCl_3$ as an eluent. The first fraction gave **3–22** and the second afforded **3–23**.

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