Pergamon

Tetrahedron Letters, Vol. 35, No. 26, pp. 4587-4590, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7 00+0.00

0040-4039(94)00864-7

Novel Benzoyl Migration of the Intermediary 1:1 Adducts of 1,3-Dipolar Cycloaddition of Thiazolo[3,2-*b*][1,2,4]-triazolium *N*-Phenacylides with Dimethyl Acetylenedicarboxylate

Tatsunori Iwamura[a], Takashi Ichikawa[a], Hiroshi Shimizu[a], Tadashi Kataoka[a]*
Toshitsugu Kai[b], Hiroaki Takayanagi[b]
and Osamu Muraoka[c]

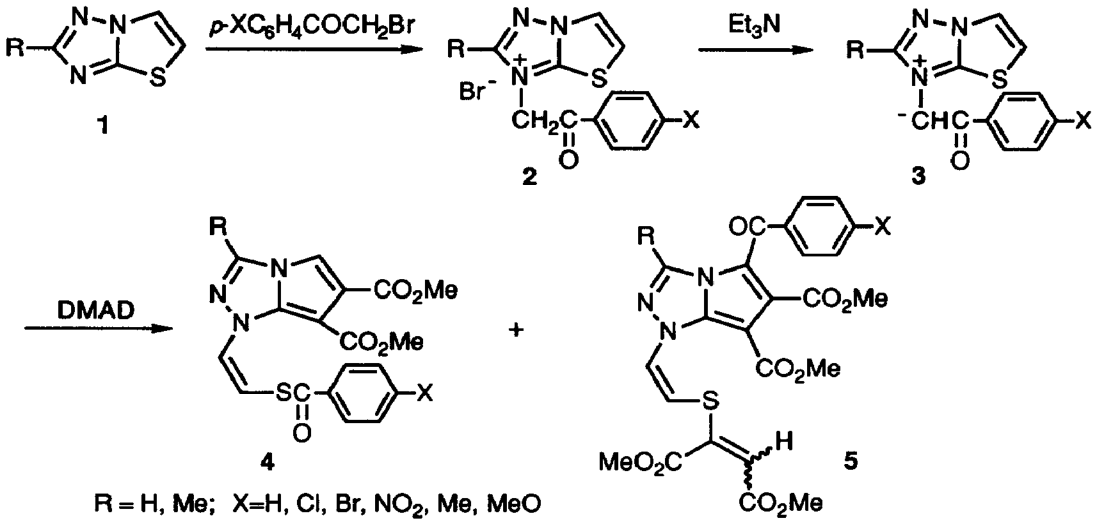
[a]Gifu Pharmaceutical University, 6-1, Mitahora-higashi 5-chome, Gifu 502, Japan
[b]School of Pharmaceutical Sciences, Kitasato University, Shirokane, Minato-ku, Tokyo 108, Japan
[c]Faculty of Pharmacy, Kinki University, 3-4-1, Kowakae, Higashi-Osaka 577, Japan

Abstract: Reaction of thiazolo[3,2-*b*][1,2,4]triazolium *N*-phenacylides **3** with dimethyl acetylenedicarboxylate gave novel compounds, 2-(1*H*-pyrrolo[2,1-*c*]-1,2,4-triazolyl)ethenyl thiobenzoates **4** and 2-[2-(1*H*-pyrrolo[2,1-*c*]-1,2,4-triazolyl)ethenylthio]propenoates **5**. The former products **4** would be formed *via* a new type of intramolecular benzoyl migration of the intermediary 1:1 adducts **6**.

A heterocyclic *N*-methylide is a useful building-block to construct new heterocycles by a one-flask reaction. Previously, we studied the double 1,3-dipolar cycloaddition reactions of fused triazolium *N*-methylides, [1,2,4]triazolo[1,5-*a*]pyridinium[1] and -pyrimidinium *N*-methylides.[2] This paper presents the novel 1,5-benzoyl migration of the 1,3-dipolar cycloadduct of thiazolo[3,2-*b*][1,2,4]triazolium *N*-phenacylides, which possess a heteropentalene type aromatic nucleus, with dimethyl acetylenedicarboxylate (DMAD).

Treatment of thiazolo[3,2-*b*][1,2,4]triazole **1** with some phenacyl bromides in refluxing acetone gave *N*(1)-phenacylthiazolotriazolium salts **2** in good yields (71.5-97.5%).[3] The thiazolotriazolium *N*-ylides **3** were generated *in situ* from the thiazolotriazolium salts **2** and triethylamine and allowed to react with an equimolar amount of DMAD to give a new type reaction product **4** and an *E*/*Z* mixture of 1:2 adduct **5** (Scheme 1).[3] The products and their yields are summarized in Table 1. As a *para*-substituent on the phenacyl aromatic ring was more electronegative, the more product **4** was obtained. The structures of the adducts **4** and **5** were estimated on the basis of NMR and mass spectral data[4] and those of **4c** and **5c** (*E*-isomer) were confirmed by X-ray analysis.[5] The crystal structures of **4c** and **5c** are depicted in Fig. 1.

The product **4c** possesses a thiobenzoate moiety which would be formed by the benzoyl migration of an intermediary 1:1 cycloadduct. To our knowledge, this is the first example of the benzoyl migration in the 1,3-dipolar cycloadditions of *N*-phenacylides. Potts *et al.*[6] reported that the reaction of 4-methylthiazolium *N*-phenacylides with electron-deficient acetylenes gave 1-aryl-1-hydroxy-1*H*-pyrrolo[2,1-*c*][1,4]thiazines formed



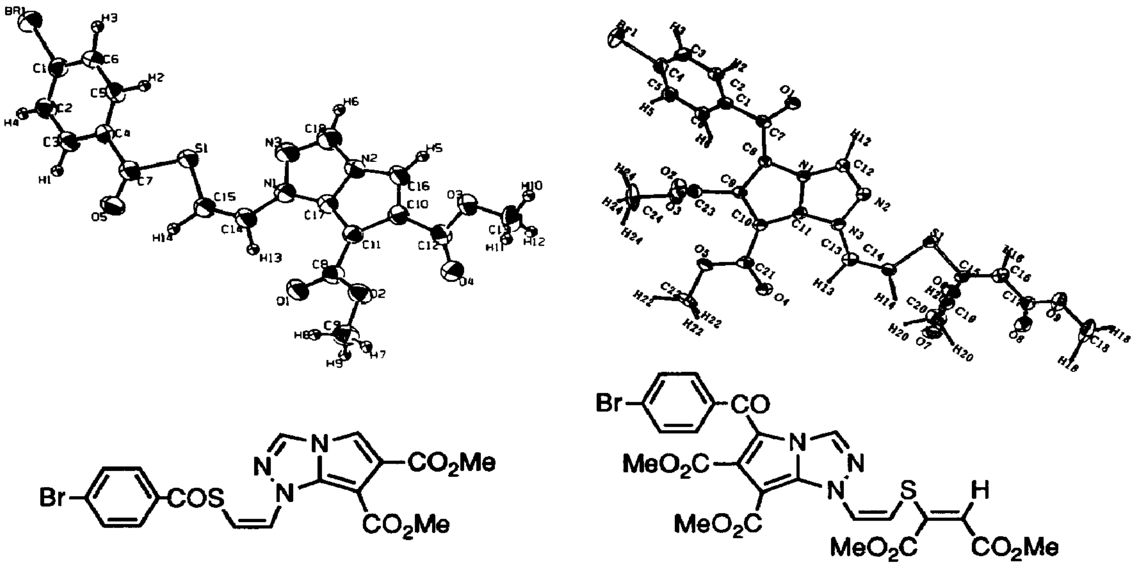
Scheme 1

Table 1. Reactions of Thiazolotriazolium Salts **2** with DMAD.[a]

Com- pound	R	X	Eqiv. of Et3N	 DMAD	Solv.	Temp. (°C)	Products (%) 4	 5	 (*E*:*Z*)[b]
a	H	H	1	1	MeCN	60	1.0	44.5	(3:1)
b	H	Cl	1	1	MeCN	60	10.5	40.5	(3:1)
c	H	Br	1	1	MeCN	60	17.0	36.5	(7:2)
d	H	NO_2	1	1	MeCN	60	44.5	14.0	(18:5)
d	H	NO_2	1	1	MeCN	r.t.	27.5	10.5	(9:1)
e	H	Me	1	1	MeCN	60	—	31.0	(3:1)
f	H	MeO	1	1	MeCN	60	—	31.5	(12:5)
g	Me	Cl	1	1	MeCN	60	32.5	33.0	(5:2)
h	Me	Br	1	1	MeCN	60	32.0	21.0	(4:1)
i	Me	NO_2	1	1	MeCN	60	56.5	18.5	(5:2)
i	Me	NO_2	1	2	MeCN	60	66.0	17.5	(22:9)
i	Me	NO_2	2	1	MeCN	60	62.0	15.0	(14:5)
i	Me	NO_2	2	2	MeCN	60	67.0	10.5	(29:17)
i	Me	NO_2	2	2	CH_2Cl_2	40	82.5	15.0	(17:12)
i	Me	NO_2	1	1	DMF	60	38.5	10.0	(43:9)

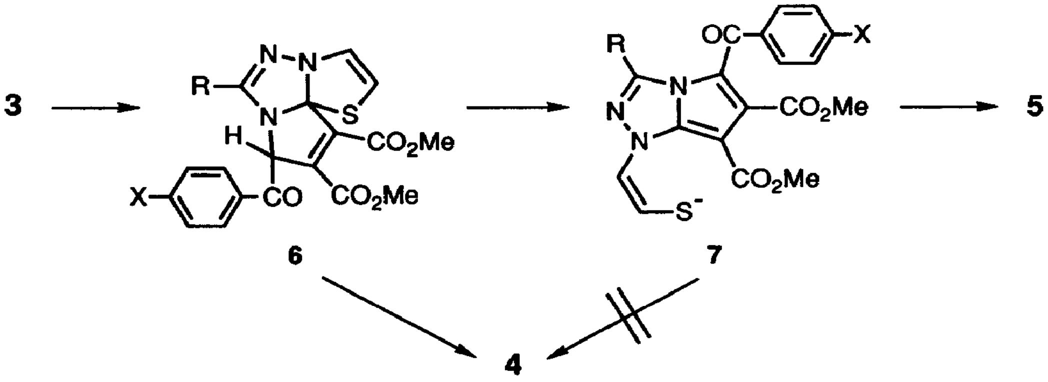
[a] Reactions were carried out in the presence of Et_3N under N_2 for 5 h.

[b] The *E/Z* ratio was determined by ^1H-NMR spectroscopy.



4c **5c**

Fig. 1. X-ray crystal structures of **4c** and **5c** (*E*-isomer).



Scheme 2

by rearrangement of the cycloadducts *via* the nucleophilic attack of a thiolate ion against the benzoyl group. Similar 1,4-thiazine hemiacetal formation has been found in the reaction of the 1:1 adduct of the benzothiazolium *N*-phenacylide and 1,2-dicyanoethenes in the presence of triethylamine.[7] These adducts, hemiacetals, have not undergone the benzoyl migration from the pyrrole ring to the thiolate ion. Chen *et al.*[8] isolated other type products, pyrrolo[2,1-*b*]benzothiazoles, from the reaction of benzothiazolium *N*-phenacylides and acetylenic dipolarophiles. The 1:2 adduct **5c** has a side chain similar to that of a product obtained from the reaction of dihydroimidazo[2,1-*b*]thiazolium ylides and DMAD.[9]

The tricyclic 1:1 adduct **6** would be the common intermediate for formation of **4** and **5**. According to the discussion in the literature,[6,7,9] the tricyclic intermediate **6** would ring-open and form an ethenylthiolate ion

7. The ethenylthiolate ion 7 would attack on the carbonyl group. However, intramolecular attack of the ethenylthiolate ion of 7 on the carbonyl group is improbable stereochemically because the pyrrolotriazole ring of 7 is planar and these two groups are too far to interact. We conducted the crossover experiments of *N*-(*p*-bromophenacyl)triazolium salt **2c** and 2-methyl-*N*-(*p*-chlorophenacyl) derivative **2f** with DMAD in the presence of triethylamine in order to determine whether the intermediary 1:1 adduct **6** directly changes to the thiobenzoate **4** by the intramolecular concerted mechanism or the ethenylthiolate ion 7 intermolecularly attacks on the carbonyl group of another molecule of 7. No crossover products **4b**, **4g** were detected by the NMR and mass spectroscopy and the product was a mixture of **4c** and **4f** with a ratio of 5/18. The PM3 calculation[10] indicates that the sulfur atom of the adduct **6** (R=X=H) has the largest coefficient (0.6819) in HOMO (-8.9982 eV) and the benzoyl carbonyl carbon atom has a large coefficient (0.2800) in second LUMO (-0.5602 eV). From these results, the benzoyl migration would be brought about by the nucleophilic attack of the sulfur atom on the carbonyl group in the intermediary 1:1 adduct **6**.

REFERENCES AND NOTES

1. Hori, M.; Kataoka, T.; Shimizu, H.; Imai, E.; Yokomoto, M.; Tanaka, K.; Kimura, K.; Hashimoto, Y. *Heterocycles* **1986**, *24*, 2563-2570.
2. Hori, M.; Kataoka, T.; Shimizu, H.; Imai, E.; Tanaka, K.; Kimura, K.; Hashimoto, Y.; Inagaki, S.; Goto, N.; Kido, M. *J. Chem. Soc., Perkin Trans. 1* **1987**, 2531-2537.
3. All new compounds gave satisfactory IR and NMR data and elemental analyses.
4. Spectral data for **4c** and **5c** are shown as representatives. **4c**: IR (KBr) ν_{CO} 1740, 1660 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.86 (3H, s), 3.88 (3H, s), 6.81 (1H, d, *J* = 9 Hz), 7.15 (1H, s), 7.63 (2H, d, *J* = 8 Hz), 7.92 (2H, d, *J* = 8 Hz), 8.22 (1H, s), 8.40 (1H, d, *J* = 9 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 51.56 (q), 52.25 (q), 87.96 (s), 101.31 (d), 105.30(d), 122.69 (d), 125.61 (s), 128.58 (d), 128.88 (d x 2), 128. 92 (s), 132.11 (d x 2), 135.26 (s), 140.54 (s), 163.45 (s), 164.37 (s), 186.92 (s); MS *m/z* 463 (M$^+$). **5c** (*E*-isomer): IR (KBr) ν_{CO} 1730, 1620 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.44, 3.76, 3.83, 3.94 (each 3H, s), 6.09 (1H, d, *J* = 9 Hz), 6.13 (1H, s), 7.51 (2H, d, *J* = 8.5 Hz), 7.61 (2H, d, *J* = 8.5 Hz), 8.32 (1H, d, *J* = 9 Hz), 9.07 (1H, s); ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 51.98 (q), 52.09 (q), 52.51 (q), 53.30 (q), 91.92 (s), 107.08 (d), 113.92 (s), 117.56 (d), 122.26 (d), 125.58 (d), 129.43 (d x 2), 131.46 (d x 2), 131.65 (s), 133.02 (s), 136.75 (s), 140.50 (s), 146.68 (s), 162.30 (s), 163.54 (s), 163.89 (s), 165.42 (s), 183.62 (s); MS *m/z* 605 (M$^+$).
5. Crystal data for **4c**: $C_{18}H_{14}BrN_3O_5S$, triclinic, space group $P1$(#2), a=9.648(2), b=13.894(2), c= 7.466(1) Å, α=95.05(1), β=105.04(1), γ=104.89(1), V=921.1(2) Å^3, Z=2, D_c=1.674 gcm^{-3}, μ(Mo-Kα)=23.51cm^{-1}, R=0.036, R_w=0.039. A Rigaku AFC5R diffractometer was used at 296 K.
   Crystal data for **5c**: $C_{24}H_{20}BrN_3O_9S$, orthorhombic, space group *P*bca, a=19.789(7), b=23.489(4), c= 11.256(1) Å, V=5232.1Å^3, Z=8, D_c=1.488gcm^{-3}, μ(Cu-Kα)=16.832cm^{-1}, R=0.0876, R_w=0.0876. A Rigaku AFC4 diffractometer was used at 296 K. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.
6. Potts, K. T.; Choudhury, D. R.; Westby, T. R. *J. Org. Chem.* **1976**, *41*, 187-191.
7. Tsuge, O.; Shimoharada, H.; Noguchi, M. *Heterocycles* **1981**, *15*, 807-814.
8. Chen, T.-Y.; Liu, J.-H.; Chen, K.-H. *Proc. Natl. Sci. Counc. ROC(A)* **1989**, *13*, 227-233.
9. Kim, D. J.; Yoo, K. H.; Park, S. W. *J. Org. Chem.* **1992**, *57*, 2347-2352.
10. The PM3 calculation was carried out with "PASOCON MOPAC/386" program, which is based on the MOPAC (Ver. 6.0, QCPE No. 455), of Toray System Center. The detail will be published in a full paper.

(*Received in Japan* 19 *March* 1994; *accepted* 22 *April* 1994)