

1,3-DIPOLAR CYCLOADDITION REACTION OF CHROMONES AND COUMARIN
WITH PYRIDINIUM YLIDES

Ichiro Yokoe*, Shunsuke Matsumoto, Yoshiaki Shirataki, and Manki Komatsu
Faculty of Pharmaceutical Sciences, Josai University, Keyakidai,
Sakado, Saitama 350-02, Japan

Abstract — 1,3-Dipolar cycloaddition reaction of N-iminopyridinium ylide (2) with chromones (1) gave pyrazolo[1,5-a]pyridines (3) in moderate yields. Similarly coumarin (4) reacted with 2 to give 6H-[1]-benzopyrano[4',3':3,4]pyrazolo[1,5-a]pyridin-6-one (5). Furthermore chromone (1) was cyclized with pyridinium phenacylide (6) to afford 1-(2'-hydroxybenzoyl)-3-benzoylindolizine (7).

1,3-Dipolar cycloaddition reaction of N-ylides has been used to synthesize many heterocyclic systems¹. In the case of intermolecular cycloaddition of N-ylides, many substituted alkenes and alkynes were used as dipolarophiles².

As part of our studies on the new reactivities of chromone ring³, we were interested in the preparation of the pyrazolopyridines fused with oxygen-containing heterocycles by the cycloaddition of pyridinium N-ylides with chromones and coumarin.

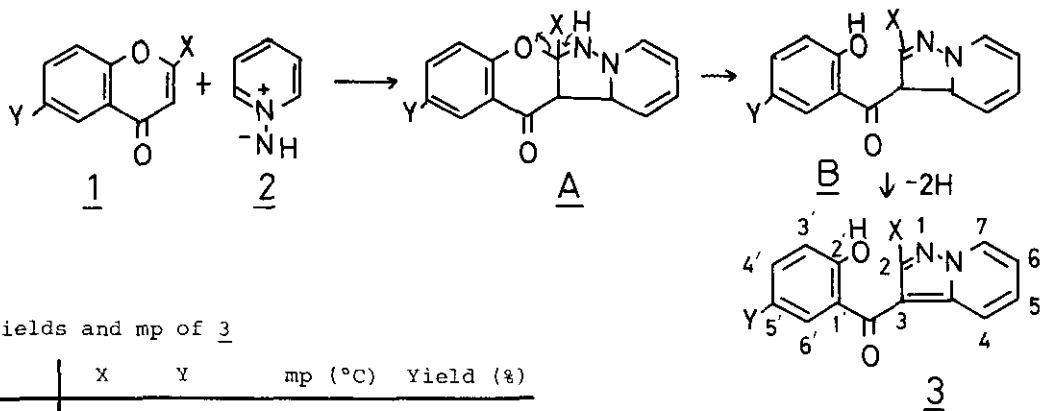
In this communication we report some results obtained with the reaction of N-imino-pyridinium ylide with chromones.

To a solution of chromone (1) and N-aminopyridinium iodide in DMF was added excess K_2CO_3 with stirring under ice cooling. The whole mixture was stirred at room temperature for 4 days. After evaporation of the solvent, the residue was purified by column chromatography on silica gel to give 3-[2'-hydroxybenzoyl]pyrazolo[1,5-a]pyridine (3a) in 51.4 % yield as the sole product. [(3a). mp 123°C; ms m/z: 238 (M^+); IR ν_{max}^{KBr} : 3400 (OH), 1630 (C=O) cm^{-1} ; UV λ_{max}^{MeOH} nm (log ϵ): 262 (3.80), 343 (4.03). $\lambda_{max}^{MeOH+KOH}$ nm (log ϵ): 323 (4.09), 360 (3.77); 1H -NMR δ ($CDCl_3$): 6.98 (1H, t, J=7.0 Hz, 5'-H), 7.03-7.10 (2H, m, 3' and 6-H), 7.49 (1H, t, J=8.1 Hz, 4'-H), 7.52 (1H, t, J=8.8 Hz, 5-H), 7.91 (1H, dd, J=2.0 and 7.5 Hz, 6'-H), 8.37 (1H, d, J=8.8 Hz, 4-H),

8.40 (1H, s, 2-H), 8.59 (1H, d, J=6.6 Hz, 7-H), 12.04 (1H, s, D₂O exchangeable, chelated OH); ¹³C-NMR δ (CDCl₃): 145.5 (d, C-2), 111.1 (s, C-3), 141.9 (s, C-3a), 129.3 (d, C-4), 120.1 (d, C-5), 115.0 (d, C-6), 128.7 (d, C-7), 120.8 (s, C-1'), 162.0 (s, C-2'), 118.9 (d, C-3'), 135.1 (d, C-4'), 118.4 (d, C-5'), 131.1 (d, C-6'), 191.7 (s, C=O)]. From these spectral data and elemental analysis, 3a was determined as to be 3-(2'-hydroxybenzoyl)pyrazolo[1,5-a]pyridine. The fact that the signals for the C-2 and C-4 protons appear at very low field provides the additional evidence for the assigned structure, because, had the 1,3-dipolar cycloaddition occurred in reverse fashion to give isomeric product, 2-(2'-hydroxybenzoyl)pyrazolopyridine, the signals should occur at much higher field than is observed to be the case⁴.

The structures of other reaction products (3b-3e) were also determined by means of their physical and spectral inspection and by comparison with 3a.

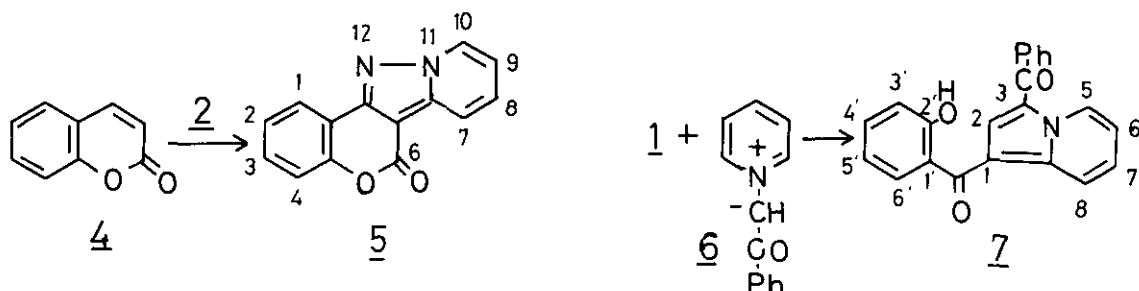
A reasonable mechanism for this cycloaddition reaction involves the initial attack of N-iminopyridinium ylide (2) to C-2 position of chromone ring, followed by an opening of the γ-pyrone ring to give a dihydro intermediate (B). Subsequent elimination of hydrogen furnishes the pyrazolopyridine (3). It has been reported that the cycloaddition reactions of N-aminopyridinium salts occur with spontaneous dehydrogenation of the dihydro intermediate to a completely aromatic product⁵.



Yields and mp of 3

	X	Y	mp (°C)	Yield (%)
a	H	H	123	51.4
b	H	Cl	190	32.9
c	H	CH ₃	143	28.7
d	CH ₃	H	118-119	18.1
e	Ph	H	128-129	19.8

The ylide 2 was found to react with coumarin (4) to give 6H-[1]-benzopyrano[4',3':3,4]pyrazolo[1,5-a]pyridin-6-one (5) in 28.0 % yield.



Other 1,3-dipoles, such as N-pyridinium phenacylide (6), underwent cycloaddition with chromone (1) to give 1-(2'-hydroxybenzoyl)-3-benzoylindolizine (7) in almost quantitative yield. The structures of 5 and 7 were determined by elemental analysis and spectroscopic properties⁶.

In conclusion, the present results indicate that the C-C double bond in pyrone-ring of chromone and coumarin is reactive to 1,3-dipoles.

ACKNOWLEDGEMENT

We would like to express our sincere thanks to Prof. T. Tsuchiya, Hokuriku University for providing the ¹H-NMR spectral data of pyrazolo[1,5-a]pyridines and 3-benzoyl-indolizine.

REFERENCES AND NOTES

- (a). Y. Tamura, and M. Ikeda, "Advances in Heterocyclic Chemistry", Vol. 29., ed. by A. R. Katritzky and A. J. Boulton, Academic Press, London, 1981, p. 71; (b). T. Tsuchiya, H. Sashida, and A. Konoshita, *Chem. Pharm. Bull.*, 1983, 31, 4568; (c). C. G. Stuckwisch, *Synthesis*, 1973, 469; (d). W. J. McKillip, E. A. Sedor, M. B. Culbertson, and S. Wawzonek, *Chem. Rev.*, 1973, 73, 255.
- R. Huisgen, *Angew. Chem.*, 1963, 75, 604, 742; V. Boekelheide, K. Fahrenholtz *J. Am. Chem. Soc.*, 1961, 83, 458.
- I. Yokoe, K. Nakamura, K. Higuchi, Y. Shirataki, M. Komatsu, and H. Miyamae, *Heterocycles*, 1985, 23, 291.
- T. Sasaki, K. Kanematsu, and Y. Yukimoto, *J. Chem. Soc. [C]*, 1970, 481; T. Sasaki, K. Kanematsu, A. Kakehi, *J. Org. Chem.*, 1971, 36, 2978; K. T. Potts, H. P. Youzwak,

and S. J. Zurawal, Jr., *J. Org. Chem.*, 1980, 45, 90.

5. T. Sasaki, K. Kanematsu, and A. Kakehi, *Tetrahedron Letters*, 1972, 5245; V. Boekelheide, and N. A. Fedoruk, *J. Org. Chem.*, 1968, 33, 2062.

6. Compound 5. mp 262°C, MS m/z 236 ($M^+ = C_{14}H_8N_2O_2$), 208, 179, 153, 118, 103. IR ν_{\max}^{KBr} 1750 cm^{-1} . 1H -NMR δ ($CDCl_3$): 7.22 (1H, td, J=6.9 and 1.6 Hz, 9-H), 7.38 (1H, td, J=7.4 and 1.2 Hz, 2-H), 7.46 (1H, dd, J=7.4 and 0.8 Hz, 4-H), 7.53-7.67 (2H, m, 3 and 8-H), 8.21 (1H, dd, J=7.4 and 1.2 Hz, 1-H), 8.30 (1H, dt, J=8.6 and 1.0 Hz, 7-H), 8.75 (1H, dt, J=6.9 and 1.0 Hz, 10-H). ^{13}C -NMR δ ($CDCl_3$): 97.41 (s), 114.54 (s), 115.87 (d), 117.77 (d), 118.98 (d), 123.45 (d), 124.34 (d), 128.66 (d), 129.70 (d), 131.28 (d), 140.98 (s), 152.04 (s), 154.06 (s), 157.91 (s).

Compound 7. mp 149-151°C, MS m/z 341 ($M^+ = C_{22}H_{15}NO_3$), 264, 248, 236, 221, 193, 180, 144, 121. IR ν_{\max}^{KBr} 3400 (OH), 1630, 1620 (C=O) cm^{-1} . 1H -NMR δ ($CDCl_3$): 6.88 (1H, t, J=8.0 Hz, 5'-H), 7.06 (1H, d, J=7.7 Hz, 3'-H), 7.21 (1H, t, J=7.3 Hz, 6-H), 7.42-7.62 (5H, m, 7, 4', 3'', 4'', 5''-H), 7.72 (1H, s, 2-H), 7.77 (1H, dd, J=8.0 and 1.6 Hz, 6'-H), 7.83 (2H, dd, J=7.3 and 1.6 Hz, 2'', 6''-H), 8.50 (1H, d, J=8.8 Hz, 8-H), 10.03 (1H, d, J=7.3 Hz, 5-H), 11.97 (1H, s, 2'-OH, D_2O exchangeable). ^{13}C -NMR δ ($CDCl_3$): 112.68 (s), 116.02 (d), 117.98 (d), 118.38 (d), 119.76 (d), 120.42 (s), 122.35 (s), 128.08 (d), 128.49 (d), 128.60 (d), 128.83 (d), 129.55 (d), 131.16 (d), 131.37 (d), 134.62 (d), 139.20 (s), 140.41 (s), 161.80 (s), 185.13 (s), 192.56 (s).

Received, 8th March, 1985