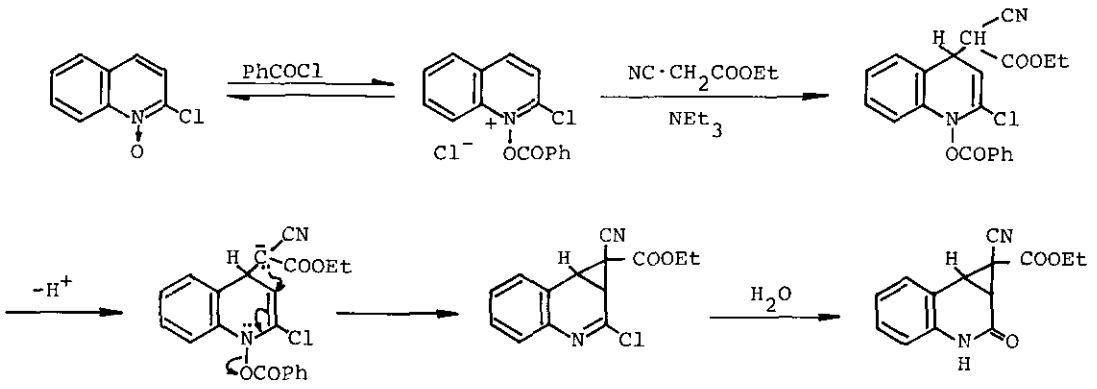
REACTION OF QUINOLINE METHIODIDE WITH BROMO- OR p-TOLUENE-SULFONYLOXY-ACETONITRILE DERIVATIVES. FORMATION OF A NOVEL TRICYCLIC DIAZANONANE SYSTEM

Seitaro Saeki*, Yoshio Kaku, and Masatomo Hamana*
Faculty of Pharmaceutical Sciences, Kyushu University,
Maidashi, Higashi-ku, Fukuoka 812, Japan
Hiroshi Noda
University of Occupational and Enviromental Health, Iseigaoka,
Yahatanishi-ku, Kitakyushu 807, Japan

Abstract —— Quinoline methiodide (1) reacts with ethyl bromocyanoacetate (2a) in the presence of triethylamine to afford ethyl 2-methyl-9-oxo-2,10-diazabenzo[c]tricyclo[4,2,1,$0^{7,11}$]-nonane-8-carboxylate (3a) in 24.1% yield. The products of the same type (3b-d and 3f) are obtained from reactions of 1 with bromocyanoacetamide (2b), α-bromophenylacetonitrile (2c), α-bromo-p-nitrophenylacetonitrile (2d), and O-tosylates of benzaldehyde and p-chlorobenzaldehyde cyanohydrins (2e and 2f).

A previous paper has described that 2-chloroquinoline 1-oxide reacts with ethyl cyanoacetate in the presence of benzoyl chloride and triethylamine to give a cyclopropa[c]quinoline as shown below[1].



In continuation of studies on this reaction we found that the reaction of quinoline methiodide with ethyl bromocyanoacetate in the presence of triethylamine afforded a novel tricyclic diazanonane system.

To a suspension of quinoline methiodide (1: 406 mg) and triethylamine (150 mg, 1 equiv.) in dichloromethane (10 ml) was added ethyl bromocyanoacetate (2a: 280 mg, 1 equiv.), and the resulting clear solution was stirred with ice-cooling for 12 h. The brown reaction mixture was evaporated under reduced pressure, and the residue was directly chromatographed on alumina with dichloromethane and methanol. A fraction eluted with dichloromethane-methanol (48:2) gave 98.2 mg (24.1%) of ethyl 2-methyl-9-oxo-2,10-diazabenzo[c]tricyclo[4,2,1,$0^{7,11}$]nonane-8-carboxylate (3a), colorless needles, mp 220-222° (CH_2Cl_2-n-C_6H_{14}) (Chart 1).

The structure assignment of 3a is based on the satisfactory elemental analysis [$C_{15}H_{16}N_2O_3$], the mass spectrum [m/e: 272 (M^+), 225 (M^+-COOEt)], the IR spectrum [ν_{max}^{Nujol} cm^{-1}: 3140 (NH), 1669 (C=O)], and the PMR and CMR spectra shown in Tables I and II. The stereochemistry of 3a can be unequivocally determined as that formulated in Chart 1 from inspection of model, other ring junctions being impossible owing to steric strain.

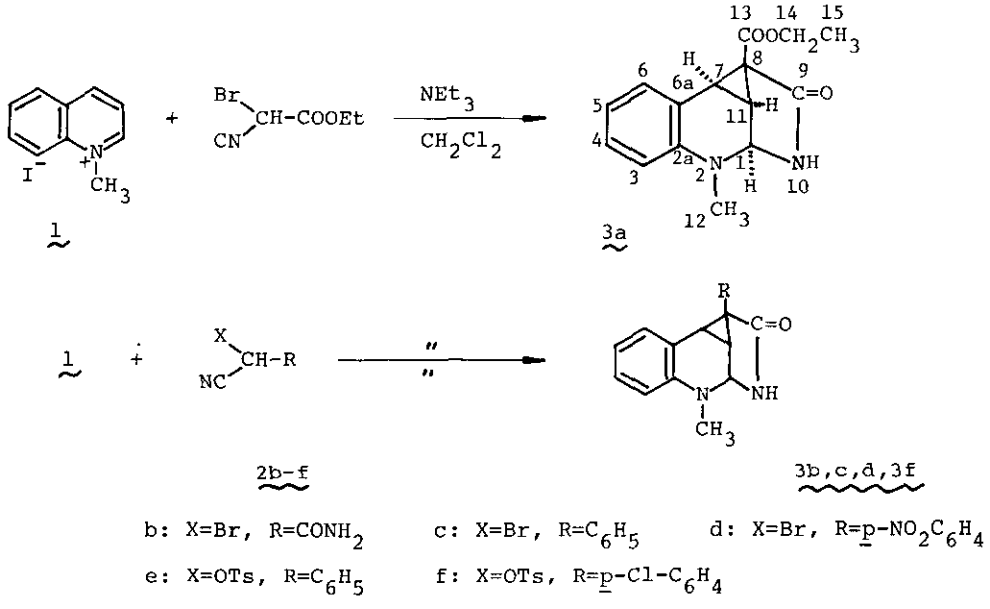
Table I. PMR Chemical Shifts of 3a (δ) ($CDCl_3$)

C_{15}-H	C_{12}-H	C_{11}-H	C_7-H
1.34 (3H, t) J=7.6 Hz	2.80 (3H, s)	2.96 (1H, dd) $J_{1,11}$=8.0, $J_{7,11}$=8.0 Hz	3.19 (1H, d) J=8.0 Hz
C_{14}-H	C_1-H	N_{10}-H	aromatic-H
4.26 (2H, q) J=7.6 Hz	5.0 (1H, d) J=8.0 Hz	5.92 (1H, s)	6.58-7.36 (4H, m)

Table II. CMR Chemical Shifts (multiplicity) of 3a (δ) ($CDCl_3$)

C_1	C_{2a}	C_3,C_4,C_5,C_6	C_{6a}
69.04 (d)	143.19 (s)	113.60 (d), 119.89 (d) 129.16 (d), 131.33 (d)	118.36 (s)
C_7	C_8	C_9	C_{11}
26.42 (d) or 29.53 (d)	35.40 (s)	168.26 (s)	26.42 (d) or 29.53 (d)
C_{12}	C_{13}	C_{14}	C_{15}
38.16 (q)	171.49 (s)	61.76 (t)	14.2 (q)

Reactions of 1 with bromocyanoacetamide (2b), α-bromophenylacetonitrile[2] (2c) and α-bromo-p-nitrophenylacetonitrile[3] (2d), similarly proceeded under the same conditions to produce the corresponding products [3b: colorless prisms, mp 241-242°, 3c: colorless needles, mp 214-216° (dec.), and 3d: yellow needles, mp 263-264° (dec.)] in 36.4, 15.2 and 16.2% yields, respectively; however curiously, no definite product was obtained from the reaction with bromomalononitrile. Further, O-tosylates of benzaldehyde[4] and p-chlorobenzaldehyde cyanohydrins (2e and 2f) were found to undergo the same type of reaction with 1, giving 3c and 8-p-chlorophenyl analogue [3f: colorless rhombs, mp 264-266° (dec.)] in 6.7 and 24.5% yields, respectively. The identity of these products was established by elemental analyses, the IR, PMR, CMR and mass spectrometry in the same way with the case of 3a.



1 + 2b-f → 3a (b: X=Br, R=CONH2; c: X=Br, R=C6H5; d: X=Br, R=p-NO2C6H4; e: X=OTs, R=C6H5; f: X=OTs, R=p-Cl-C6H4) → 3b,c,d,3f

Chart 1

The formation of 3 may be rationalized by the course shown in Chart 2. Initially, nucleophilic addition of a carbanion of 2 to 1 gives preferentially a 1,4-dihydroquinoline (4) in the usual way[5]. The next step is the transformation of 4 to a cyclopropa[c]quinoline intermediate (5) by nucleophilic attack of the 3-position at the side chain carbon bearing bromine or tosyloxy group with the concerted elimination of the nucleofugic group. Consecutively, the C-N bond is formed between the immonium carbon and the nitrogen atom of the cyano group in 5 to

produce a tricyclic diazanonane skeleton (6), which is finally converted to product 3 possibly during the work-up though its detailed feature is not clear.

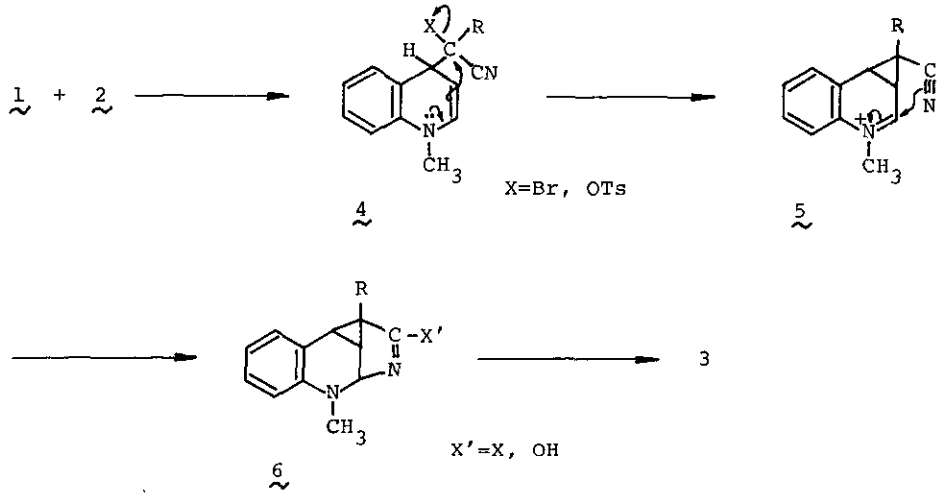


Chart 2.

It is very noticeable that the pattern of cyclopropane formation in the above reactions is completely reverse to that in the first-mentioned reaction; the nucleophilicity of the enamine moiety of 4 operates in the former reaction, but on the contrary in the latter case the electrophilicity of the O-benzoyl ene-hydroxylamine system[6] caused by extrusion of the benzoyloxy group promotes the reaction. Further work on exploring the reactivity of this novel ring system is in progress.

REFERENCES

1. S. Saeki, H. Honda, Y. Kaku, K. Funakoshi, and M. Hamana, Heterocycles, 1977, 7, 801.
2. C. M. Robb and E. M. Schultz, "Organic Syntheses", Coll. Vol. III, ed. by E. C. Horning, John Wiley and Sons, Inc., New York, 1955, p. 347.
3. J. W. Baker and C. K. Ingold, J. Chem. Soc., 1927, 446.
4. D. G. Coe, M. M. Gale, R. P. Linstead, and C. J. Simmons, J. Chem. Soc., 1957, 123.
5. N. Leonard and R. L. Foster, J. Am. Chem. Soc., 1952, 74, 3671.
6. T. Nagayoshi, S. Saeki, and M. Hamana, Heterocycles, 1977, 6, 1666.

Received, 7th April, 1980