Monatshefte für Chemie 125, 743–746 (1994)

Monatshefte für Chemie
Chemical Monthly

Printed in Austria

Selective Aziridination of Olefinic Esters

M. Deshmukh[1,*], **P. Chavan**[2], and **D. Kharade**[2]

[1] Institute for Organic Chemistry, Karl-Franzens University, A-8010 Graz, Austria
[2] Department of Chemistry, Shivaji University, Kolhapur-416004, India

Summary. Oxidation of 3-amino-2-isobutylquinazoline-4-one (**2**) with lead tetraacetate at −20 °C gave N-acetoxyamino-2-isobutylquinazolin-4-one (**3**), which selectively aziridinated olefinic esters to yield substituted 1-(2′-isobutylquinazolin-4′-one-3′-yl)-aziridine-2-carboxylates **5a–q**.

Keywords. Aziridine; Quinazolinone; Olefinic esters.

Selektive Aziridinierung von olefinischen Estern

Zusammenfassung. Oxidation von 3-Amino-2-isobutylchinazolin-4-on (**2**) mit Bleitetraacetat bei −20 °C ergab N-Acetoxyamino-2-isobutylchinazolin-4-on (**3**), welches mit verschiedenen olefinischen Estern selektiv substituierte 1-(2′-Isobutylchinazolin-4′-on-3′-yl)-aziridin-2-carbonsäureester **5a–q** lieferte.

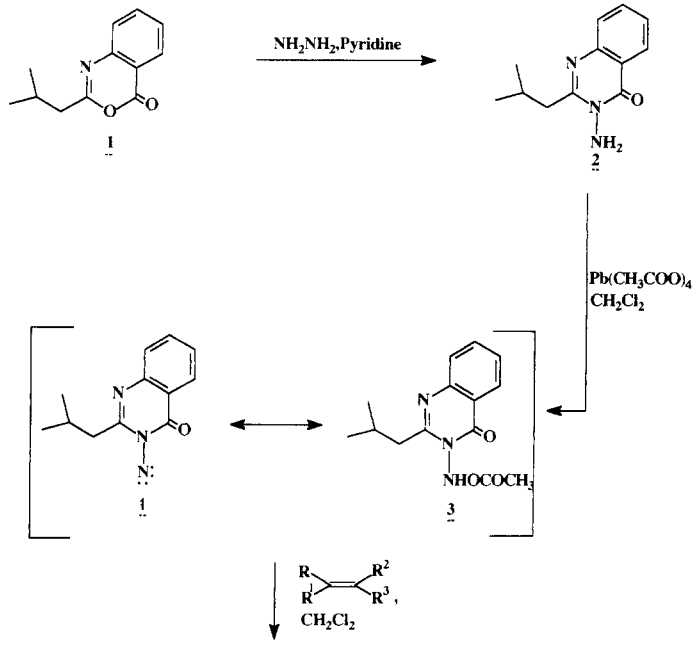
Introduction

Aziridines possess useful biological activities which chemically modify *DNA* [1]. These properties have been investigated for potential antitumor [2] and insect chemosterilant [3] activities. Recently, the immunomodulating [4–6] and immunostimulant tumor suppressant properties [7] of aziridines have been reported. The development of a new method for aziridination of olefins is of great interest. Aziridination of alkenes has been carried out using different reagents [8]. However, the addition of nitrene to alkene cannot be counted as a reliable method for aziridination because of the highly reactive and unselective behaviour of nitrenes which usually leads to a mixture of products. The exception to this behaviour is a family of N-nitrene compounds derived by the oxidation of the corresponding N-amino compounds with lead tetraacetate [9–12]. The oxidation of N-amino-2-isobutyl quinazoline-4-one with lead tetraacetate at low temperature gives N-acetoxyamino-2-isobutyl quinazoline-4-one (**3**) which in turn is used for the selective aziridination of olefinic esters.

Results and Discussion

The reaction of N-acetoxy-2-isobutylquinazoline-4-one (**3**) formed by oxidation of N-amino-2-isobutylquinazoline-4-one (**2**) with lead tetraacetate in dry methylene

chloride at −20 °C with olefinic esters gave **5** in 60–75% yield. The reaction of **3** with olefinic esters has been observed to be stereospecific [9–11]. The above aziridination reaction was found to be 90% stereoselective independent of *cis*- or *trans*-configuration of the olefin. We therefore propose compound **3** to be the reactive species and not the N-nitrene **4**. Tentative assignment of ^{1}H NMR signals of aziridines is based on the likely preferred conformation of the aziridine. Methyl 1-(2′-isobutylquinazole-4′-one-3′-yl)-3-methyl aziridine 2-carboxylate (**5a**) is not observed to be a single compound but a mixture of its invertomers in the proportion 9:1, which can be confirmed by the ^{1}H NMR data. The ester methyl protons are observed as two singlets, one at $\delta = 3.85$ ppm and the other at $\delta = 3.79$ ppm in the ratio 9:1. The signal at 3.85 ppm is assigned to the less sterically hindered major invertomer [12]. The greater selectivity in the aziridination of the olefinic esters can be rationalized assuming steric interactions in the transition state by the 2-isobutyl substituent in **3** which prevents the rotation around the N–N single bond.



5	R	R¹	R²	R³
a	CH_3	CH_3	H	$COOCH_3$
b	CH_3	CH_3	H	$COOC_2H_5$
c	C_6H_5	H	H	$COOCH_3$
d	C_6H_5	H	H	$COOC_2H_5$
e	C_6H_5	H	CH_3	$COOCH_3$
f	C_6H_5	CH_3	H	$COOCH_3$
g	C_6H_5	CH_3	H	$COOC_2H_5$
h	C_6H_5	CH_3	CH_3	$COOCH_3$
i	C_6H_5	C_2H_5	H	$COOCH_3$
j	C_6H_5	C_2H_5	H	$COOC_2H_5$
k	o-$NO_2C_6H_4$	H	CH_3	$COOCH_3$
l	o-$NO_2C_6H_4$	H	CH_3	$COOC_2H_5$
m	p-OH-C_6H_4	H	H	$COOCH_3$
n	p-OH-C_6H_4	H	H	$COOC_2H_5$
o	p-OH-C_6H_4	H	CH_3	$COOCH_3$
p	p-OH-C_6H_4	H	CH_3	$COOC_2H_5$
q	m-OH-C_6H_4	CH_3	H	$COOC_2H_5$

Experimental

Proton magnetic resonance spectra were determined in $CDCl_3$ with *TMS* as an internal standard with a Perkin–Elmer R-32 90 MHz spectrometer. IR spectra were recorded on Shimadzu IR-437 spectrometer. Column chromatography was performed using E. Merck silica gel-G (100–200 μ particle size). Dichloromethane was distilled from calcium hydride prior to use.

2-Isobutyl 3,1,4-benzoxazinone (**1**) was prepared according to the literature [13].

2-Isobutyl-3-aminoquinazole-4-one (**2**)

A mixture of **1** (20.3 g, 0.1 mol) and hydrazine hydrate (5 ml, 0.1 mol) in pyridine (25 ml) was refluxed for 6 h. Pyridine was distilled off under reduced pressure. The syrupy mass was digested with 1*N* HCl (100 ml) for 2 h on a steam bath and the resulting semisolid was treated with distilled water (100 ml). The separated solid was filtered off, dried and recrystallized from ethanol to give **2** (18 g, 83%).

IR (KBr): $\nu(cm^{-1}) = 3300$, 1680; ^1H NMR ($CDCl_3$): $\delta(ppm) = 1.1$ (d, $J = 7.5$ Hz, 6H), 2.1 (d, $J = 7.5$ Hz, CH_2), 3.2 (m, –CH), 4.5 (s, NH), 6.5–7.5 (m, 5H, arom); $C_{12}H_{15}N_3O$ (217.3); calc.: C 66.26, H 6.90, N 19.32; found: C 66.15, H 6.75, N 19.20.

General procedure for the preparation of the aziridines **5a–q**

Lead tetraacetate (227 mg, 100 mmol) was added to a suspension of **2** (217 mg, 100 mmol) in dry dichloromethane (5 ml) at −20°C. The reaction mixture was stirred for 15 min. 100 mmol of the olefinic ester was added with stirring and the reaction mixture was allowed to warm up to 25 °C. The insoluble material was filtered off and the filtrate was washed successively with saturated sodium hydrogen carbonate solution (5 ml) and water (2 × 5 ml). The solution was dried and the solvent was removed under reduced pressure. The residue was purified by column chromatography using ethyl acetate – hexane (30:70) as eluent to furnish **5**. For yields and melting points, see Table **1**.

Table 1. Yields and melting points of aziridines **5a–q**. All compounds gave satisfying elemental analyses

Compound	Yield (%)	M.p. (°C)	Molecular formula	Molecular weight
5a	69	134	$C_{18}H_{23}N_3O_3$	329.4
5b	65	120	$C_{19}H_{25}N_3O_3$	343.4
5c	62	145	$C_{22}H_{23}N_3O_3$	377.4
5d	68	111	$C_{23}H_{23}N_3O_3$	391.5
5e	65	102	$C_{23}H_{25}N_3O_3$	391.5
5f	71	75	$C_{23}H_{25}N_3O_3$	391.5
5g	62	65	$C_{24}H_{27}N_3O_3$	405.5
5h	59	90	$C_{24}H_{27}N_3O_3$	405.5
5i	64	80	$C_{24}H_{27}N_3O_3$	419.5
5j	72	132	$C_{25}H_{29}N_3O_3$	419.5
5k	62	118	$C_{23}H_{24}N_4O_5$	436.5
5l	65	131	$C_{24}H_{25}N_4O_5$	450.5
5m	58	63	$C_{22}H_{23}N_3O_4$	393.4
5n	67	95	$C_{23}H_{25}N_3O_4$	407.5
5o	61	119	$C_{23}H_{25}N_3O_4$	407.5
5p	69	96	$C_{24}H_{27}N_3O_4$	421.5
5q	63	73	$C_{24}H_{27}N_3O_3$	421.5

Acknowledgements

We thank the CSIR, New Delhi, India for financial support, and Prof. Junek and Prof. Mittelbach, Institute of Organic Chemistry, Univ. of Graz, Austria, for useful suggestions.

References

[1] Dermer O. C., Han G. E. (1964) Ethylamine and Other Aziridines. Academic Press, New York, p 394
[2] Akhtar M. H., Begielter A., Johnson D., Lawn J. W., MacLaughlin J., Sim S. K. (1975) Can. J. Chem. **53**: 2891
[3] Hynes J. W., Matrix E., Miltin W., Brokovec A. B., Lindia O. H. (1976) U.S. Agri. Res. Ser. South Reg. (Rep.), 30; cit. (1976) C:A: 85:138594h
[4] Brokovec A. B., Woods C. W. Jr. (1976) J. Entamol. **11**: 53
[5] Ardenno V. M., Reitnauer P. G. (1977) Arz. **27**: 1701
[6] Beicker U. (1967) Forsch. Med. **96**: 661
[7] Mannbeon B. G. Belg. Pat. No. 843803, 1976; cit. (1977) C.A. 87:194233
[8] Hassner A. (1983) Small Ring Heterocycles, Part-I. Wiley, New York
[9] Atkinson R. S. (1984) Azides and Nitrenes, Chapter-V.E.I.G. Scriven, New York
[10] Atkinson R. S., Kelly B. (1987) Chem. Commun. 1362
[11] Atkinson R. S., Kelly B. (1984) Chem. Commun. 624
[12] Hogale (Deshmukh) M. B., Shelar A. R., Chavan P. B. (1992) Indian J. Chem. **31B**: 456; Hogale (Deshmukh) M. B., Chavan, P. B. (1993) Indian J. Chem. **32B**: 581
[13] Wheeler O. C., Octs W. M. (1910) J. Am. Chem. Soc. **33**: 770

Received October 20, 1993. Accepted December 18, 1993