C–C Bond-Cleavage of α-Azido-Steroidal Ketoximes

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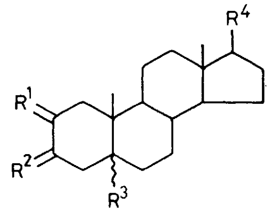
α-Azido-steroidal oximes were cleaved to provide mono- and di-cyano derivatives under standard Beckmann conditions.

Our interest in new synthetic approaches to biologically active steroidal alkaloids led us to investigate C–C bond-cleavage of α-azido steroidal oximes. We recently reported a novel type of C–C bond-cleavage: namely the transformation of a 2α-azido-5α-cholestan-3-one into a 2-nitrilo-2,3-seco-5α-cholestan-3-oic acid.[1] C–C bond-cleavage reactions giving ω-cyano carbonyl

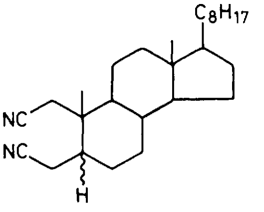
Table 1. Reactions of α-azido steroidal oximes under Beckmann conditions.

Reactant	Reagent	Solvent[a]	Conditions (t/°C ; min)	Product (% yield)[b]
(1)	$POCl_3$	Pyridine	110 ; 20	**(11)** (94)
(1)	TsCl	Pyridine	110 ; 30	**(11)** (85)
(1)	$SOCl_2$	Pyridine	27 ; 60	**(11)** (73)
(1)	$SOCl_2$	Neat	0 ; 15	**(11)** (70)
(1)	PCl_5	Pyridine	110 ; 20	**(11)** (70)
(1)	MsCl	Pyridine	110 ; 30	**(11)** (65)
(1)	PPA	Neat	120 ; 15	**(13)** (36)
(1)	P_2O_5	Benzene	80 ; 20	**(11)** (39) + **(13)** (23)
(2)	Al_2O_3 Column[c]		r.t.	**(11)** (22) + **(6)**[d] (trace)
(3)	$SOCl_2$	Neat	0 ; 15	**(12)** (64)
(4)	$POCl_3$	Pyridine	70 ; 15	**(7)** (20) + **(9)** (45)
(5)	$POCl_3$	Pyridine	70 ; 15	**(8)** (32) + **(10)** (47)

[a] The reactions were carried out in dry solvents, with 6 mol. equiv. of reagent. Ts = p-$MeC_6H_4SO_2$; Ms = $MeSO_2$; PPA = polyphosphoric acid. [b] Isolated yield. [c] Carried out by passing a benzene solution of (**1**) through an alumina column. [d] The structure proposed for (**6**) has not been confirmed.

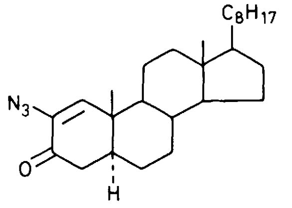


	R^1	R^2	R^3	R^4
(1)	α-N_3,β-H	(E)-NOH	α-H	C_8H_{17}
(2)	α-N_3,β-H	(E)-NOTs	α-H	C_8H_{17}
(3)	β-N_3,α-H	(E)-NOH	β-H	C_8H_{17}
(4)	H_2	β-OAc,α-H	α-H	C(:NOH)CH_2N_3
(5)	H_2	β-OAc,α-H	Δ^5	C(:NOH)CH_2N_3
(6)	NH (or O)	O (or NH)	α-H	C_8H_{17}
(7)	H_2	β-OAc,α-H	α-H	CN
(8)	H_2	β-OAc,α-H	Δ^5	CN
(9)	H_2	β-OAc,α-H	α-H	$NHCOCH_2N_3$
(10)	H_2	β-OAc,α-H	Δ^5	$NHCOCH_2N_3$



(11) 5α-H

(12) 5β-H



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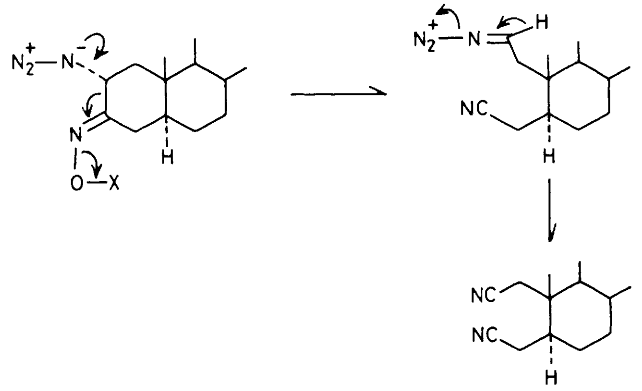

Scheme 1

derivatives have been studied in the Beckmann fragmentation of α-substituted oximes.[2] However, the C–C bond-cleavage of an α-azido oxime giving a dicyano derivative is unknown, and we now report the C–C bond-cleavage of α-azido steroidal oximes under Beckmann conditions.

In a typical reaction, phosphorus trichloride oxide (0.25 ml) was added to a solution of 2α-azido-5α-cholestan-3-one oxime (**1**) (200 mg) in dry pyridine (5 ml), and the mixture was heated at 110 °C for 20 min. Crystallization of the resulting oil from light petroleum gave (**11**) in 94% yield, m.p. 115—119 °C, which was identified from its i.r. [ν_{max} 2240 cm^{-1} (C≡N)], ^{13}C n.m.r. [δ ($CDCl_3$, Me_4Si) 118.89 and 116.86 p.p.m. (C≡N)], and mass spectrum [m/z 396 (M^+), 356 ($M^+ - CH_2CN$), and 316 ($M^+ - 2CH_2CN$)]. Similarly, the side-chain α-azido oxime (**5**) gave (**8**) (32%) and (**10**) (47%).

Results for other conditions are in Table 1. Thus, the α-azido oximes (**1**)—(**5**) are cleaved to give the cyano derivatives in 20—94% yield after a short reaction time. All new compounds had satisfactory analytical and spectroscopic data.†

We propose the mechanism in Scheme 1 for this interesting cleavage: Beckmann fragmentation is followed by elimination of N_2 from an iminodiazonium ion intermediate.

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References

1 T. T. Takahashi and J. Y. Satoh, *J. Chem. Soc., Perkin Trans. 1*, 1980, 1916.

2 R. K. Hill, *J. Org. Chem.*, 1962, **27**, 29; C. W. Shoppee and S. K. Roy, *J. Chem. Soc.*, 1963, 3774; A. Hassner and W. A. Wentworth, *Chem. Commun.*, 1965, 44; J. K. Paisley and L. Weiler, *Tetrahedron Lett.*, 1972, 261; G. Rosini, A. Medici, and S. Cacchi, *Synthesis*, 1975, 665; D. Miljkovic and J. Petrovic, *J. Org. Chem.*, 1977, **42**, 2101.

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† M.p.s and selected spectroscopic data; (**1**), m.p. 134—136 °C; i.r. (KBr) 3500—3100, 2100, and 1659 cm^{-1}; ^1H n.m.r. (60 MHz, CCl_4, Me_4Si) δ 3.10 (br.d, 1H, 4α-H), 3.94 (dd, 1H, J 6 and 12 Hz, 2β-H), and 9.04 (br.s, 1H, =N–OH); (**2**), m.p. 103—106 °C; (**3**), (oil); (**4**), m.p. 182—184 °C; i.r. (KBr) 3370, 2130, 1710, and 1280 cm^{-1}; ^1H n.m.r. ($CDCl_3$) δ 4.05 (br.s, 2H, 21-H_2), 4.45—4.90 (br.m, 1H, 3α-H), and 8.85—9.05 (br.s, 1H, =N–OH); (**5**), m.p. 177—178 °C; (**6**), m.p. 160—163 °C; i.r. (KBr) 3500—3100 and 1620 cm^{-1}; ^1H n.m.r. (CCl_4) δ 9.49 (s, 1H, =NH); ^{13}C n.m.r. ($CDCl_3$, Me_4Si) δ 167.34 (C=NH) and 187.93 p.p.m. (C=O); (**7**), m.p. 196—199 °C; i.r. (KBr) 2240, 1730, and 1240 cm^{-1}; ^1H n.m.r. ($CDCl_3$) δ 4.55—4.95 (m, 1H, 3α-H); (**8**), m.p. 226—228 °C; (**9**), m.p. 178—179 °C; (**10**), m.p. 214—216 °C; (**12**), (oil) i.r. (NaCl) 2240 cm^{-1}; ^{13}C n.m.r. ($CDCl_3$) δ 117.67 (CN) and 118.84 p.p.m. (CN); (**13**), m.p. 119—122 °C; i.r. (KBr) 2100, 1675, and 1602 cm^{-1}; ^1H n.m.r. ($CDCl_3$) δ 6.40 (s, 1H, 1-H); ^{13}C n.m.r. ($CDCl_3$) δ 133.94, 141.00, and 194.09 p.p.m. (C=O).