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STEROID DERIVATIVES*

BROMINE ADDITION TO 5,6-UNSATURATED STEROIDS

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RECENTLY, we measured the reaction rate of bromine addition to 5,6-double bond in steroidal molecule and found that the reaction is of second order and influenced by the character of both the 3β- and 17β-substituent.[1-3]

Now, we ascertained that the reaction rate of bromine addition to steroidal compounds substituted at C_3 and C_{17}, is simultaneously and independently influenced by both the substituents in question.

As the reaction with unsubstituted steroidal skeleton, i.e. with androst-5-ene, is too fast, we chose 3β-acetoxy-cholest-5-ene as reference. The reaction rate of a 3β-X, 17β-Y- disubstituted androst-5-ene is thus given by an equation

$$pk_2\ (3\beta\text{-X},17\beta\text{-Y-androst-5-ene}) = pk_2\ (\text{cholesteryl acetate}) \cdot a.b$$

where a is a coefficient representing the change in bromine addition velocity caused by substitution of 3β-acetoxy group in cholesteryl acetate by group X; b is a coefficient which represents a change in reaction rate

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* Part XVI. For Part XV see Tetrahedron Letters 860 (1962), preceding paper.

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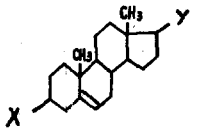
1 V. Schwarz, S. Heřmánek and J. Trojánek, Chem. & Ind. 1212 (1960).

2 V. Schwarz, S. Heřmánek and J. Trojánek, Coll. Czech. Chem. Comm. 26, 1438 (1961).

3 V. Schwarz, S. Heřmánek and J. Trojánek, Coll. Czech. Chem. Comm. In press.

of bromine addition caused by substitution of 17β-side chain in cholesteryl acetate by substituent Y.



$$\underline{a} = \frac{pk_2\ (3\beta\text{-X-cholest-5-ene})}{pk_2\ (\text{cholesteryl acetate})}$$

$$\underline{b} = \frac{pk_2\ (17\beta\text{-Y-}3\beta\text{-acetoxyandrost-5-ene})}{pk_2\ (\text{cholesteryl acetate})}$$

TABLE 1

pk_2 Values of Bromine Addition to 3β-X-cholest-5-enes (Y = C_8H_{17}) and corresponding a Values

X	pk_2	a
OAc	2.55	1
OBz	2.71	1.06
$OCOC_6H_4NO_2$(p)	3.06	1.20
OTs	3.28	1.29
$OCOCCl_3$	3.61	1.42

TABLE 2

pk_2 Values of Bromine Addition to 3β-acetoxy-17β-Y-Androst-5-enes and corresponding b Values

X	pk_2	b
C_8H_{17}	2.55	1
OAc	2.92	1.15
OBz	2.97	1.16
$OCOC_6H_4NO_2$(p)	3.04	1.19
$OCOCCl_3$	3.19	1.25
$COOCH_3$	2.97	1.16
O	3.01	1.18

As an example (cf. Table 3) we present the calculated and measured pk_2 values of some androst-5-ene derivatives.

In Table 1 are summarized pk_2 values of bromine addition to 3β-substituted cholest-5-enes together with the calculated a values. Table 2 shows the pk_2 for bromine addition to 17β-substituted 3β-acetoxy-androst-5-enes and the corresponding b values.

From the data given in Table 3 it may be seen that the deviations of experimentally obtained values do not exceed 10 per cent from the calculated ones and in most cases they are lower.

TABLE 3

Calculated and Measured pk_2 Values of Bromine Addition to 3β-X, 17β-Y- disubstituted Androst-5-enes

X	Y	pk_2 (calculated)	pk_2 (measured)*	Deviation
OBz	$COOCH_3$	3.14	3.03	0.11
OTs	$COOCH_3$	3.82	3.59	0.23
$OCOCCl_3$	$COOCH_3$	4.20	3.91	0.29
OBz	OBz	3.14	3.10	0.04
$OCOC_6H_4NO_2(p)$	$OCOC_6H_4NO_2(p)$	3.64	3.60	0.04
$OCOCCl_3$	$OCOCCl_3$	4.53	4.14	0.39
OBz	O	3.19	3.23	0.04
$OCOCCl_3$	O	4.27	4.06	0.21
$OCOCCl_3$	OBz	4.20	4.10	0.10

* The values represent a mean from three estimations; the maximal deviation in individual experiments exceeding in no case ± 10 per cent.

Further it follows that suitable acylation of hydroxyl groups may, to a predictable extent, exert a remarkable influence on reactivity of steroidal 5,6-double bond. By the above experiments, an unequivocal evidence was given that the previously reported[1-3] effect is inductive in nature, being different from the effects of this type yet observed.

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