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NEW STEREOSPECIFIC[1] RING CLOSURE REACTION OF 1,2-DIAXIAL AZIDO ALCOHOLS

Csaba Simon[a] and Sándor Makleit[b]

[a]ALKALOIDA Chemical Factory, H-4440 Tiszavasvári, Hungary
[b]Department of Organic Chemistry, Lajos Kossuth University, H-4010 Debrecen, Hungary

Abstract ——— 7β-Azidoneopine possessing 1,2-trans-pseudodiaxial azido and hydroxyl groups gave thiazolidinethione derivative in the presence of triphenylphosphine (TPP) and CS$_2$ which is a new stereospecific ring closure reaction. This procedure can be used on a carbohydrate model as well. The reaction mechanism is also discussed.

Our previous paper[2] described how the 8-deoxy-8β-azido-14-hydroxypseudocodeine (1) gave oxazolidinethione (2) connected to carbon atoms 8 and 14 of the ring C of the morphine skeleton on treatment with triphenylphosphine (TPP) and CS$_2$. The by-product of these reactions is triphenylphosphine sulfide. In compound 1 the 1,2-azido alcohol has a pseudoequatorial-pseudoaxial arrangement.
In our present paper we describe a similar result (4) obtained with the 7α-azidoisoneopine (3) possessing 1,2-cis-pseudoequatorial azido alcohol unit prepared in the following way. 14-Bromocodeine (5) gave 6-O-p-nitrobenzoyl-14-bromoisocodeine (6) on Mitsunobu reaction[3] which yielded 6-O-p-nitrobenzoyl-7α-azidoneopine (7) as a major product (56%) as well as 6-O-p-nitrobenzoyl-9α-azidoindolinoisocodeine (8) (16.2%), respectively, on treatment with azide ion in a possible S$_N$1' reaction. Alkaline hydrolysis of 7 gave compounds 3.
7α-Bromoneopine (9)[5] obtained from 14-bromocodeine (5)[4] yielded the new 7β-azidoneopine (10a) on treatment with azide ion in which the 1,2-azido alcohol

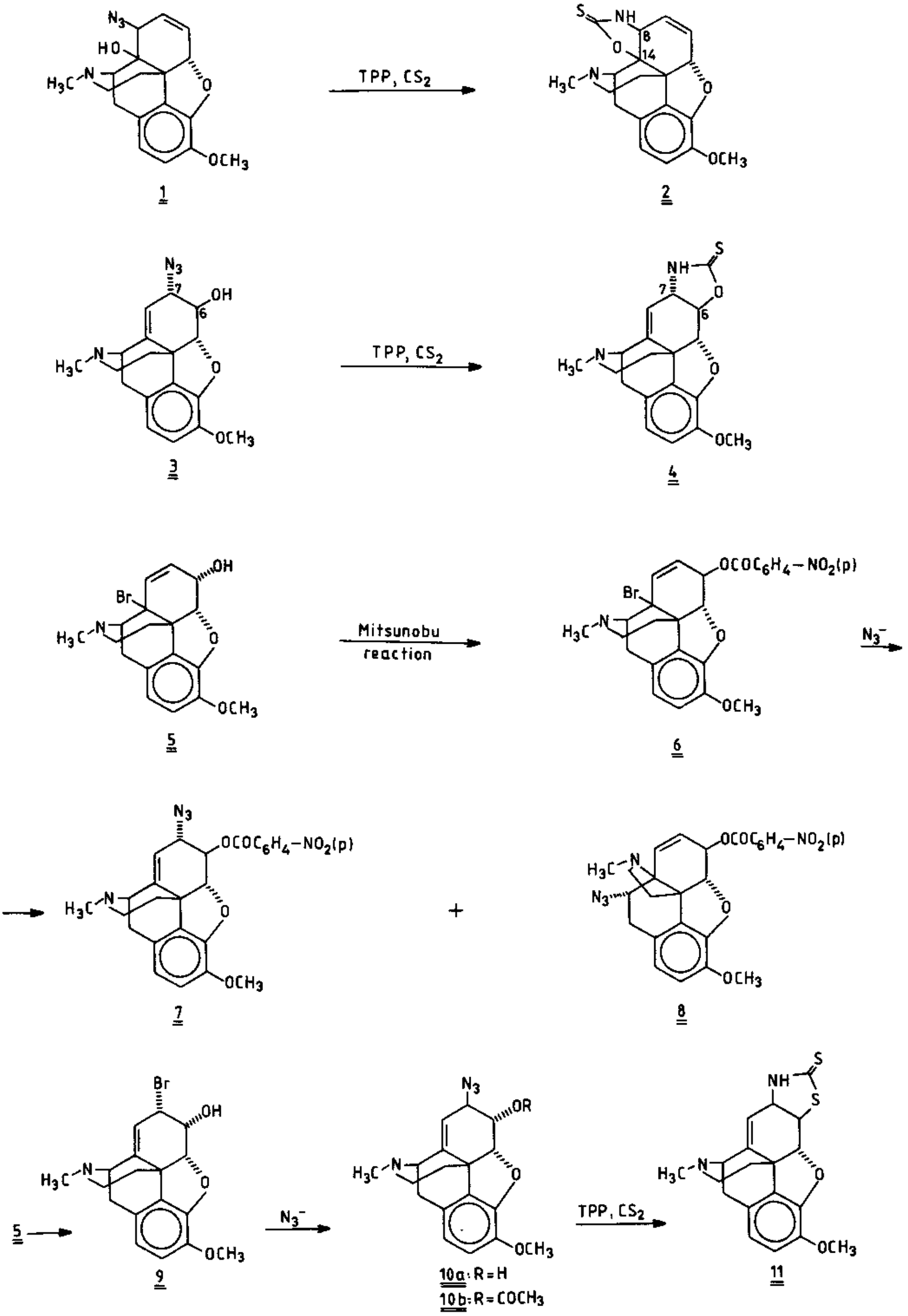
TPP, CS2
TPP, CS2
Mitsunobu reaction
N3⁻
N3⁻
TPP, CS2
+
1
2
3
4
5
6
7
8
9
10a: R = H
10b: R = COCH3
11
N3
HO
H3C
N
OCH3
S
NH
O
8
14
7
6
OH
Br
OCOC6H4–NO2(p)
OR

Figure 1

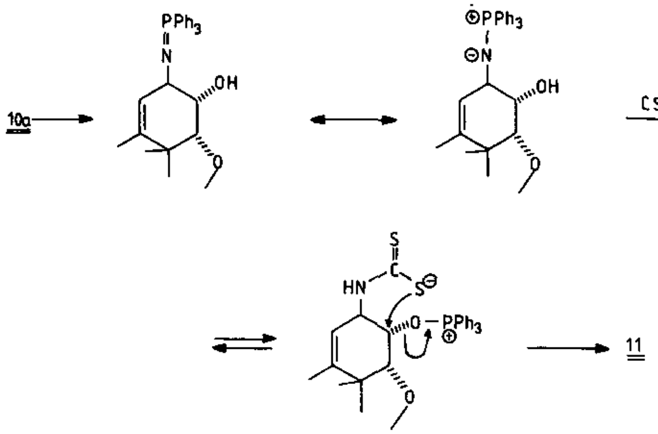

Figure 2

is trans-pseudodiaxial. On treatment with TPP and CS_2 substance (10a) gave thiazolidinethione (11) connected to carbons 6 and 7 of the ring C of the morphine skeleton with triphenylphosphine oxide as by-product (Figure 1). (Spectral data of compound (11) are as follows: ms: m/z 372 M^+ ; irν cm^{-1}: 1500, 1272, 1154 (NH-C=S); ^{1}H-nmr ($CDCl_3$, δ ppm): 2.45(s, 3H, NCH_3), 3.40(m, 2H, $C_{6\alpha}H$, $C_{10}H$), 3.87(s, 3H, OCH_3), 4.6(dd, $J_{6\alpha,7\alpha}$=6Hz, $J_{7\alpha,8}$ =6Hz, 1H, $C_{7\alpha}H$), 4.95(d, $J_{5\beta,6\alpha}$=8.5Hz, 1H, $C_{5\beta}H$), 5.69(d, $J_{7\alpha,8}$=6Hz, 1H, C_8H), 6.67(ABq, $J_{1,2}$=9Hz, 2H, Ar-H). The following mechanism is suggested for this reaction (Figure 2). A possible reason for the difference between the reactions leading to oxazolidinethione (1 ⟶ 2 and 3 ⟶ 4) and thiazolidinethione (10 ⟶ 11) is that in the 1 ⟶ 2 and 3 ⟶ 4 conversions Ph_3PS is eliminated from intermediate (C) and the intramolecular attack of the hydroxyl group in spatial proximity yields oxazolidinethione. While in the case of the 10a ⟶ 11 reaction intermediate (C) is stabilized by heterolysis and the PPh_3 moiety is replaced by the hydrogen of the hydroxyl group of another molecule (intramolecular reaction). As a result of an anionic attack, bond C-O activated in this way forms a thiazolidinethione ring with inversion. 6-O-Acetyl derivative (10b) yields 7β-isothioxyanato derivative on treatment with TPP and CS_2. Alkoxyphosphonium ion as intermediate is supposed in the Mitsunobu reaction[7] as well. Extensibility of the reaction has also been investigated on carbohydrate model possesing a 1,2-trans-diaxial azido alcohol unit (model was methyl 2-deoxy-2-azido-4,6-O-benzylidene-α-D-altroside)[8] and thiazolidinethione connected to carbons 2 and 3 of the carbohydrate was obtained. This reaction is unknown in the carbohydrate chemistry as well.

REFERENCES AND NOTES

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