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

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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_N1' 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

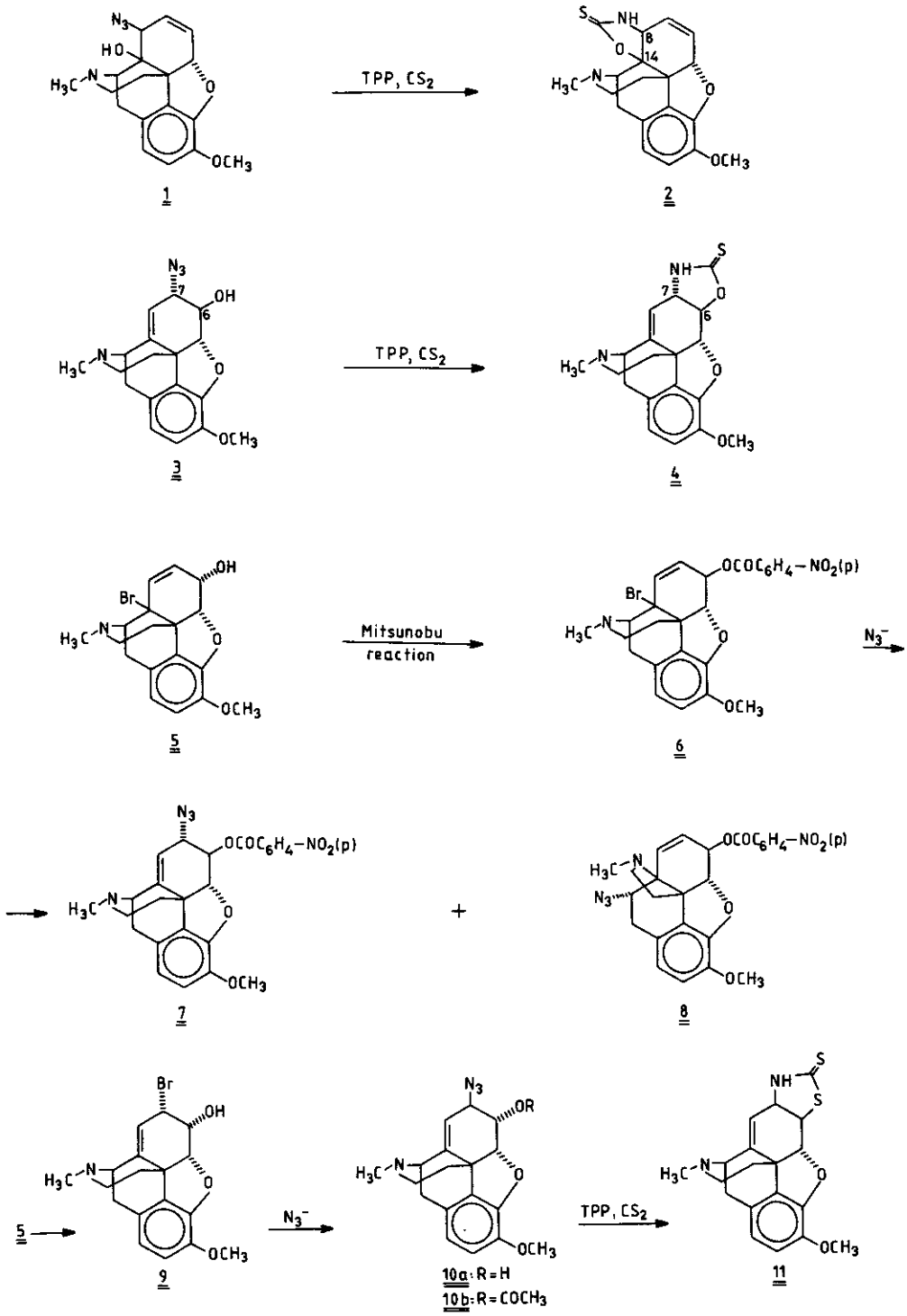
TPP, CS2
TPP, CS2
Mitsunobu reaction
N3−
TPP, CS2
10a: R = H
10b: R = COCH3

Figure 1

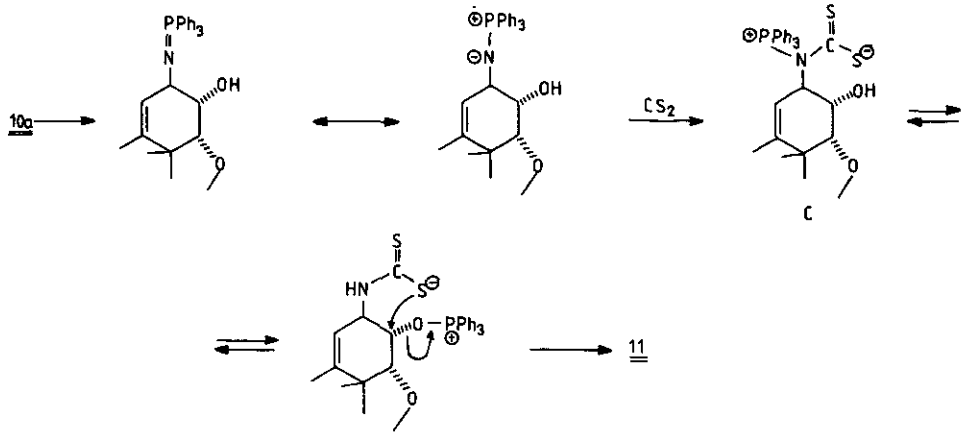

Figure 2

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^+ ; ir ν 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

1. For definition of stereospecificity see A. Ault, J. Chem. Educ., 1977, 54, 614.
2. R. Bognár, T. Mile, S. Makleit, and S. Berényi, Acta Chim. Budapest, 1973, 75, 297.
3. O. Mitsunobu, Synthesis, 1981, 1.
4. H. Conroy, J. Am. Chem. Soc., 1955, 77, 5960.
5. K. Abe, Y. Nakamura, M. Onda, and S. Okuda, Tetrahedron, 1971, 27, 4495.
6. We are grateful to Dr. János Kuszman for the discussion concerning the reaction mechanism.
7. M. Itzstein and I.D. Jenkins, Aust. J. Chem., 1983, 36, 557.
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