preparation of CD solutions, which were 3.0 mM with respect to hydroxy acid and 2.7 mM with respect to sodium molybdate. Hydrochloric acid and sodium hydroxide solution were added until pH 2.9 – 3.1 was reached. Measurements of the CD spectra were carried out in a 0.5 mm cell using a Cary 60 spectropolarimeter (a Jasco J-40 instrument was used for the measurement on the hexahydro derivative of IV) five days after the solutions had been prepared.

The hexahydro derivative of IV was prepared by hydrogenation (1 atm, 23 °C, 24 h) of the dimethyl ester of IV (3.5 mg) in methanol (3 ml) using 5 % rhodium on alumina as catalyst (16 mg) followed by hydrolysis. The starting material was contaminated by approximately 5 % of an unknown compound, and after hydrogenation one further compound, probably dimethyl (cyclohexylmethyl)tartrate (GLC-MS), contaminated the desired hydrogenation product to the extent of about 5 %. Hydrolysis of the ester and preparation of the molybdate complex were performed as described above.

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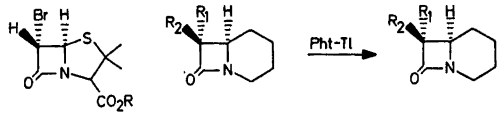
Strained Heterocyclic Compounds. 7. Preparation of α-Phthalimido-β-lactams from α-Halo-β-lactams

BJÖRN ÅKERMARK, INGER LAGERLUND and JOANNA LEWANDOWSKA

Department of Organic Chemistry, Royal Institute of Technology, S-100 44 Stockholm 70, Sweden

For some time we have been trying to develop a general synthesis of penicillins. In particular we are interested in synthesizing penicillin analogues containing a modified nucleus. In one approach carbene insertion has been used to produce halo-β-lactams of the types *1* and *2*.[1]



1

2a R_1=Br, R_2=H
2b R_1=H, R_2=Br
2c R_1=Cl, R_2=H

3a R_1=H, R_2=Pht
3b R_1=Pht, R_2=H
(Pht=Phthalimido)

As expected, these cyclizations yield predominantly the more stable *trans*-halo-β-lactams, *e.g. 1*, *2a*, and *2c*. Nucleophilic displacement of the halogen with an amine function should therefore yield amino-β-lactams with the *cis*-configuration characteristic for the penicillins and cephalosporins. Simple amines were found to destroy the β-lactams *2a* – *2c*, which were used as model compounds. Likewise, the use of metal amides were of no success.[2] Nor was it possible to use sodium azide which has been used for an unfused halo-β-lactam.[3] Therefore, we turned our attention to phthalimide salts. Potassium phthalimide reacted with the halo-β-lactams *2a* and *2c* to give a very low yield of phthalimido-β-lactam *3a*. The major part of the starting material was decomposed. On the other hand mercury(II) and silver(I) phthalimides were completely unreactive towards α-bromo-β-lactams. (In fact, silver phthalimide reacts reluctantly even with dilute HCl.)

In the search for compounds of intermediate reactivity we have now found that thallium(I) phthalimide reacts fairly readily in dimethyl sulfoxide at 150 °C with the bromo-β-lactams *2a* and *2b* to give phthalimido-β-lactams. The *trans*-compound *2a* gave the *cis*-7-phthalimido-8-oxo-1-azabicyclo[4.2.0]octane *3a* (55 % yield, 90 % stereoselectivity as determined by NMR and TLC), while the *cis*-compound *2b* gave *trans*-7-phthalimido-8-oxo-1-azabicyclo[4.2.0]-octane *3b* (24 % yield) with nearly complete stereospecificity. Since the halo-β-lactams isomerize slowly at 150 °C, the 10 % *trans*-phthalimido-β-lactam obtained from *trans*-bromo-β-

lactam probably arises from isomerization rather than from lack of stereospecificity in the displacement reaction. Also the chloro-β-lactam *2c* reacts with thallium phthalimide, but the reaction is sluggish and only low yields of the product *3a* have so far been realized (5 %).

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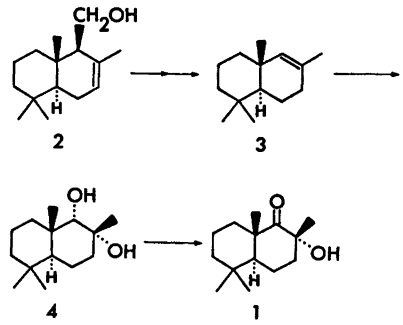
Tobacco Chemistry. 30. The Absolute Configuration of 11-Nor-8-hydroxy-9-drimanone, a Constituent of Greek *Nicotiana tabacum* L.

ARNE J. AASEN and CURT R. ENZELL*

Research Department, Swedish Tobacco Co., Box 17 007, S-104 62 Stockholm 17, Sweden

Schumacher and Vestal [1] have recently reported 11-nor-8-hydroxy-9-drimanone** (*1*) as a new constituent of Turkish tobacco leaves but without elaborating on the chirality of its three asymmetric centres. The gross structure of this ketol indicates a genetic relationship with tobacco terpenoids of the drimane/labdane group or, although less likely, of the carotenoid group.[2] Since all tobacco terpenoids of the labdane/drimane group possess the "normal" stereochemistry at the A/B-ring junction (5α-H, 10β-CH_3) and this would not be expected in the case of carotenoid derived tobacco nor-isoprenoids, elucidation of the absolute configuration of the ketol (*1*), now isolated from Greek tobacco, would indicate the nature of its precursor(s).

** Nomenclature and stereochemistry as defined in Ref. 3.



The absolute configuration of drimenol (*2*) has been determined through correlation with oleanolic and abietic acid,[3] and it was envisaged that a stereospecific conversion of drimenol to 11-nor-8-hydroxy-9-drimanone (*1*) would unravel the chirality of the three asymmetric centres of the latter compound. This was accomplished using as starting material the olefin *3*, which was prepared from drimenol (*2*) as previously described [4] by catalytic hydrogenation followed by oxidation to the corresponding saturated acid and subsequent decarboxylation using lead tetraacetate. Preferential attack by osmium tetroxide from the less hindered α-side of the olefin (*3*) furnished the *cis*-diol (*4*) in good yield. Subsequent mild oxidation employing chromic acid in a two-phase system [5] gave the desired product, 11-nor-8-hydroxy-9-drimanone (*1*), which possesses a cedar-like, woody fragrance.[1] The synthetic and natural materials were found indistinguishable when comparing NMR, IR, MS and retention times on a capillary column (co-injection), and they exhibited rotatory powers of the same sign and magnitude. Since several syntheses of drimenol have been accomplished,[6–10] its conversion, portrayed above, to 11-nor-8-hydroxy-9-drimanone (*1*) formally represents a total synthesis of the latter.

Possessing the same absolute configuration as the previously detected tobacco terpenoids of the drimane/labdane group,[2] it seems highly probable that the ketol (*1*) is derived from representatives of this group, *e.g.* from 8,11-drimandiol [11] by a route similar to the present synthetic one or by direct oxidation of 9,11-didehydronorambreinolide.[1]

Experimental. NMR, IR, UV, and mass spectra were recorded on Varian XL-100, Digilab FTS-14, Beckman DB-2A and LKB 9000 instruments, respectively. Rotations were measured on a Perkin-Elmer 141 instrument.

11-Nor-8-hydroxy-9-drimanone (*1*, 4 mg) was isolated from a volatile, neutral fraction (B 5) of an extract obtained from 295 kg sun-cured Greek *Nicotiana tabacum* L.[12] The separation of this fraction will be described elsewhere.[13] $[\alpha]^{20}$ +39.5° (589 mn), +41° (578), +50.5° (546), +124° (436), +337° (365) (*c* 0.29, $CHCl_3$);