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Preliminary communication

Synthesis of (–)-*cis*-rose oxide from D-glucose

TOMOYA OGAWA[#], NOBUO TAKASAKA[*], and MASANAO MATSUI
The Institute of Physical and Chemical Research, Wako-shi, Saitama, 351 (Japan)
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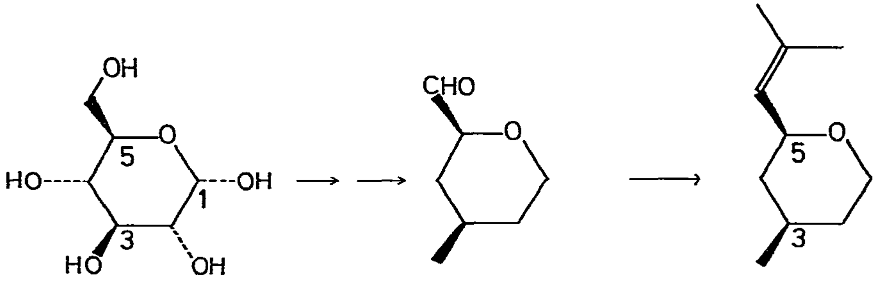
Since its isolation from Bulgarian rose[1] in 1959, and from geranium Bourbon[2] in 1961, several syntheses of rose oxide (1) as a racemate[3], or as an optically active form[4], have been achieved. As all of these approaches gave a mixture of *cis*- and *trans*-rose oxide, without any attempt being made to control the stereochemistry at C-5, we have studied a stereocontrolled synthesis of (–)-*cis*-rose oxide starting from D-glucose, and now report the first example of chemical transformation of a carbohydrate into an optically active perfume (see Scheme 1).



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Scheme 1

1,6:2,3-Dianhydro-4-deoxy-β-D-allose (3), readily available[5] from D-glucose (2), was chosen as the substrate for the regiospecific introduction[6] of a methyl group at C-3. Trans opening of the epoxide ring of 3 by the nucleophilic attack of lithium dimethylcuprate[7] gave, in 67% yield[**], the expected alcohol 4, $[\alpha]_D$ –44.8°. Regiospecific introduction of the methyl group at C-3 was confirmed by ^{1}H-n.m.r. data: two singlets for H-1 and

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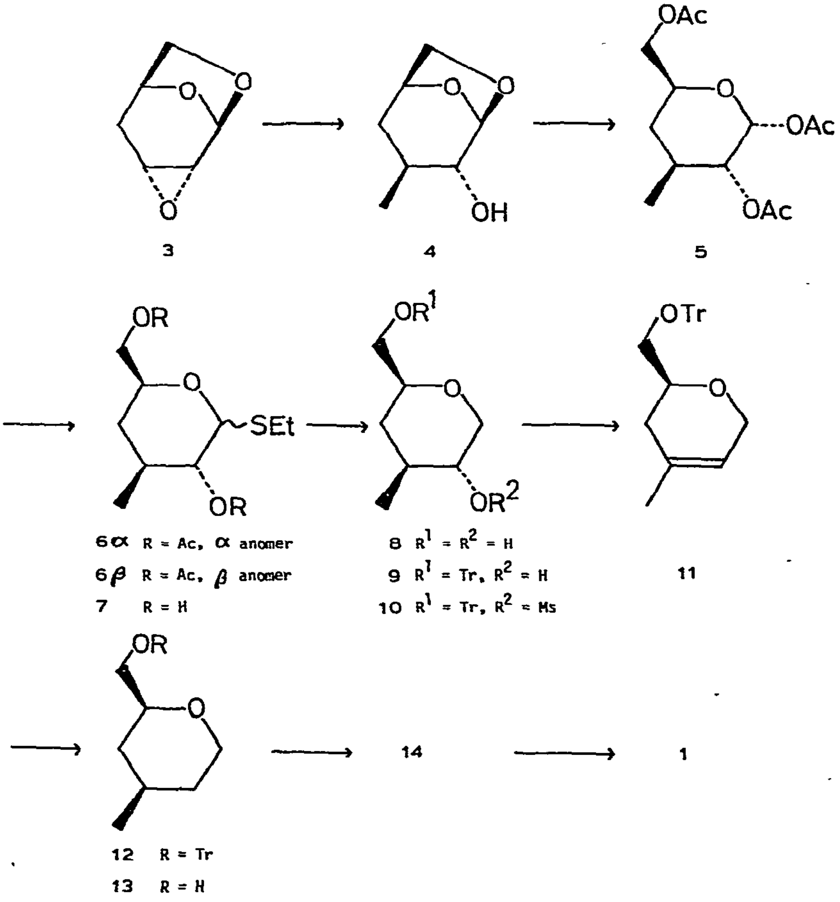
[#] To whom enquiries should be addressed.

[*] Research Fellow from Naoetsu Research Laboratory of Shin-etsu Chemical Industry Co., Nakakubiki, Niigata, Japan.

[**] All compounds for which an $[\alpha]_D$ value is given afforded satisfactory i.r., ^{1}H-n.m.r., and m.s. data. Values of $[\alpha]_D$ in $CHCl_3$ were measured. ^{1}H-N.m.r. spectra were recorded for solutions in $CDCl_3$ (tetramethylsilane as the internal reference standard).

H-2 at δ 6.38 and 3.32, and a three-proton doublet at δ 1.19, *J* 7 Hz, for C-3-CH_3. Opening of the 1,6-anhydro ring was effected with BF_3—Et_2O in acetic anhydride, to give, in 90% yield, the α-triacetate **5**, $[\alpha]_D$ +85.7°. Transformation of **5** into an anomeric mixture of thioglycosides **6α**, $[\alpha]_D$ +115.7°, and **6β**, $[\alpha]_D$ +10.8°, in the ratio of 1 : 1 was performed quantitatively by the stannyl method[8]. Saponification with methanolic sodium methoxide, and subsequent treatment with Raney nickel[9] W-4 in ethanol in the presence of an excess of sodium borohydride*, gave diol **8**, $[\alpha]_D$ +33.0°. The trityl ether (**9**), $[\alpha]_D$ −9.5°, of **8** was obtained in the usual way, and transformed into mesylate **10**, $[\alpha]_D$ +1.1°, m.p. 84–85°. The overall yield of **10** from Černý epoxide **3** was 32%. Reaction of **10** with sodium iodide in hexamethylphosphoric triamide at 100° gave, in 75% yield, elimination product **11**, $[\alpha]_D$ −70.0°; ^1H n.m.r. data: a three-proton singlet at δ 1.68 for olefinic methyl, and a one-



SCHEME 2

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*Without added sodium borohydride, the reaction gave only an anomeric mixture of ethyl glycosides in the ratio of ~1 : 1.

proton, broad singlet at δ 5.39 for olefinic H-2. Palladium–charcoal-catalyzed hydrogenation of **11** occurred mainly from the α side of the molecule, to give **12**, $[\alpha]_D$ −21.0°, in 60% yield after chromatography on silica gel. Treatment of **12** with Amberlist 15 in methanol afforded *cis*-alcohol **13**, $[\alpha]_D$ +8.6°, which was oxidized by the Corey–Suggs reagent[10] to the aldehyde **14**; ^{1}H-n.m.r. data: a one-proton singlet at δ 9.65 for aldehyde. Wittig reaction of **14** with isopropylidenetriphenylphosphorane[11] gave (−)-*cis*-rose oxide, $[\alpha]_D$ −58.1° (lit.[12] $[\alpha]_D$ −41.5°). G.l.c.** showed the absence of *trans* isomer in the synthetic sample. The ^{1}H-n.m.r. spectra of the synthetic and of an authentic sample prepared according to Shono's method[4] were in good agreement (if the presence of ~10% of the *trans* isomer in the authentic sample was taken into account).

In conclusion, we have performed a stereocontrolled synthesis of (−)-*cis*-rose oxide starting from D-glucose, and confirmed the absolute stereochemistry at C-5, which had been assigned through ^{1}H-n.m.r. study[13].

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**Gas–liquid chromatography was performed by using a glass capillary column (50 m × 0.28 mm) coated with poly(ethylene glycol) 20M, at 90°.