Synthesis of Mercaptobenzothiazole and Mercaptobenzimidazole Condensed with Inositol Derivatives

João Vitor de Assis,[a] Mara Rubia C. Couri,[a] Ricardo Silva Porto,[b] Wagner B. de Almeida,[c] Leonardo H. R. dos Santos,[a] Renata Diniz,[a] and Mauro V. de Almeida[a]*

[a]Departamento de Química, ICE, Universidade Federal de Juiz de Fora, Campus Universitário, Martelos, 36036-330, Juiz de Fora, MG, Brazil
[b]Instituto de Química e Biotecnologia, IQB, Universidade Federal de Alagoas, Campus A. C. Simões, Tabuleiro do Martins, 57072-970, Maceió, AL, Brazil
[c]Departamento de Química, ICEx, Universidade Federal de Minas Gerais, Campus Universitário, Pampulha, 31270-901, Belo Horizonte, MG, Brazil
*E-mail: mauro.almeida@ufjf.edu.br
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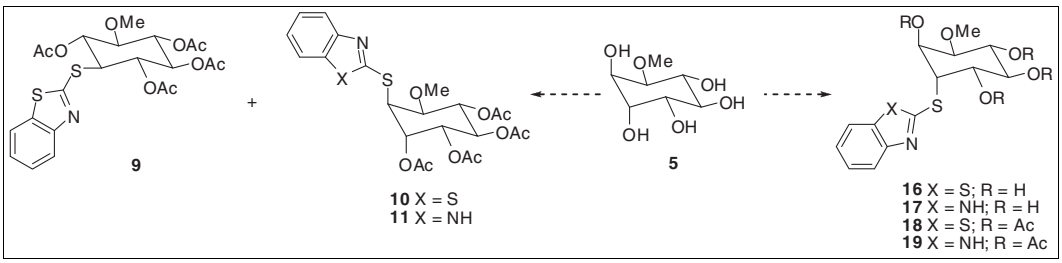
In memory of Dr. S. D. Gero.



This work describes the synthesis of inositol derivatives condensed with 2-mercaptobenzothiazole or 2-mercaptobenzimidazole, potential antimicrobial agents. These compounds were prepared by ring opening of epoxide intermediate (2*S*,3*R*-epoxy-1-*O*-methyl-L-*chiro*-inositol and 2*R*,3*S*-epoxy-1-*O*-methyl-L-*chiro*-inositol), which were obtained from L-quebrachitol (1-*O*-methyl-*chiro*-inositol). Microwave irradiation was used to promote the condensation reaction.

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INTRODUCTION

Numerous heterocyclic compounds have been showing promising activities in the treatment of several diseases [1]. These compounds have gained much attention as important pharmacophores in medicinal chemistry encompassing a diverse range of biological activities including antibacterial [2–4], antioxidant [5,6], anti-HIV [7], anticancer [8], and anti-inflammatory [9]. Thiazole **1** and imidazole **2** (Fig. 1) are found in many natural and synthetic products with a wide range of biological activities that can be well illustrated by the large number of drugs in the market containing this nucleus [10]. Benzothiazole and benzimidazole compounds have attracted the interest of various research groups, especially since it has been reported that the substitution at the 2′ positions of the heterocyclic ring is very important for their pharmacological effects, like antimycobacterial, anticancer, antirheumatic, anti-inflammatory, and anti-glutamate [10,11].

Inositols are present in several substances of biological interest such as pancrastitatin [12] and inositol phosphates, a group of phosphorylated inositols which control and modulate vital physiological processes, such as cell growth and apoptosis. Inositol trisphosphate (IP_3) acts on the IP_3 receptor to release calcium into the cytoplasm [13–15].

Despite significant progress, there are very few reports on the synthesis and bioactivity of heterocyclic compounds condensed with inositol. In this context, the major objective of the present study was the search for novel compounds containing heterocyclic and inositol moieties for biological evaluation.

RESULTS AND DISCUSSION

L-Quebrachitol **5** (1-*O*-methyl-*chiro*-inositol), a natural optically active cyclic polyol isolated from *Hevea brasiliensis* latex, is a useful starting material for the synthesis of chiral compounds (see Scheme 1) [16]. The chiral centers at C-2 and C-3 allows the stereo-specific introduction of an heterocyclic moiety via epoxidation from the methanesulfonate of L-quebrachitol or benzoylated L-quebrachitol followed by regioselective opening of the epoxy ring by nucleophilic heterocycle [17,18].

In this article, we report the preparation of a series of seven compounds based on the coupling of 2-mercaptobenzothiazole

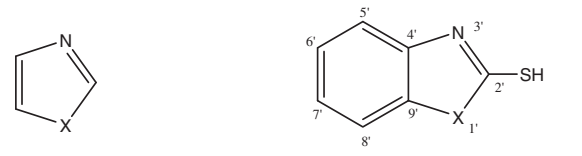
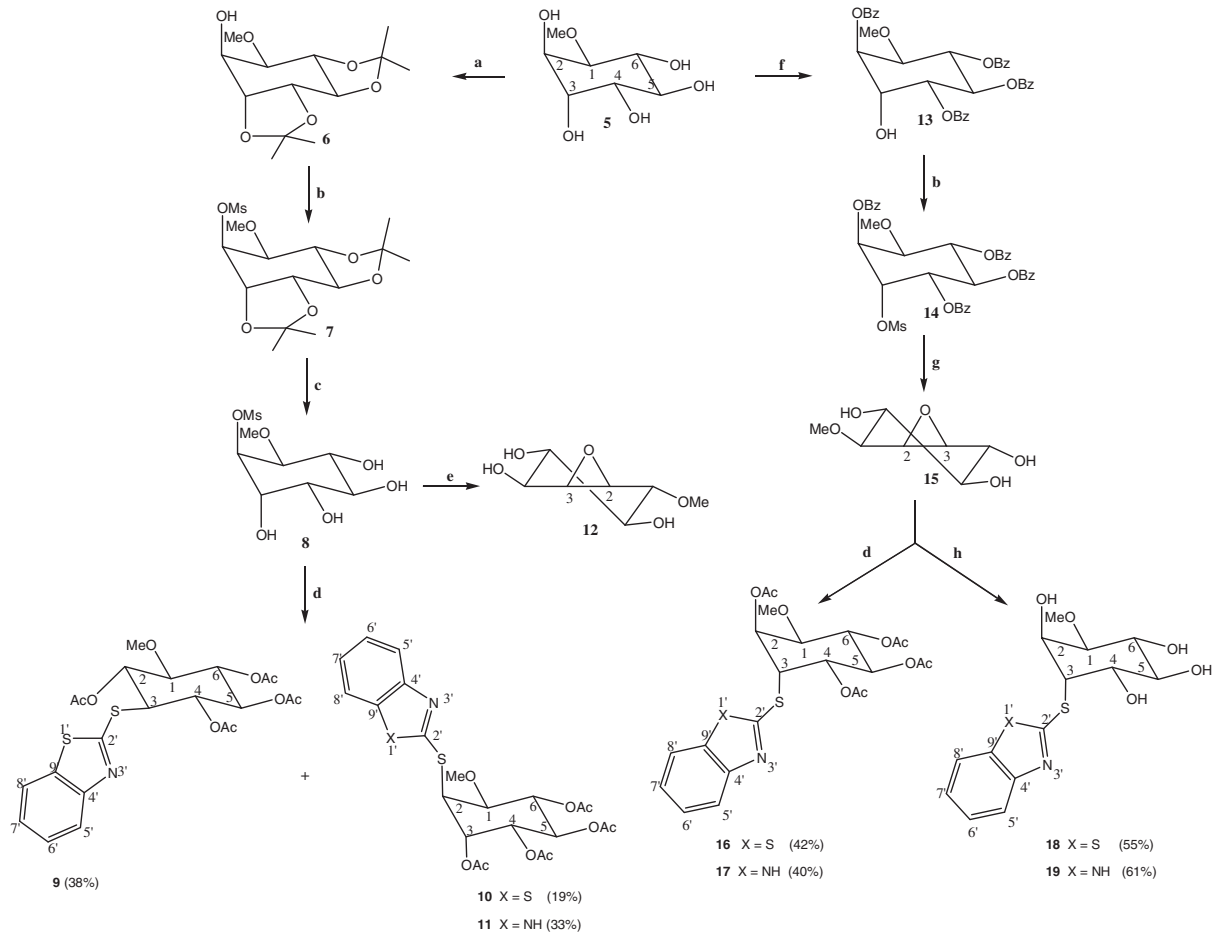


Figure 1. Structure of thiazole **1** and imidazole **2** and derivatives.

3 and 2-mercaptobenzimidazole **4** with inositol derivatives (see Fig. 1). Treatment of **5** with 2,2-dimethoxypropane, in presence of *p*-toluenesulfonic acid, afforded the diacetonide **6** as the major product in 63% yield (Scheme 1) [19,20]. Reaction of alcohol **6** with methanesulfonyl chloride in pyridine gave the mesylated compound **7** in 93% yield. Subsequently, **7** was deprotected by treatment with aqueous trifluoroacetic acid leading to the tetrol **8** [17]. The latter was treated with 2-mercaptobenzothiazole **3** in the presence of sodium hydride in *N,N*-dimethylformamide [10], affording a mixture. In order to facilitate the purification and characterization of the products, the mixture was peracetylated *in situ* by the addition of an excess of acetic anhydride in pyridine at 0°C. As a result, the two diastereoisomers **9** and **10** could be isolated in 38% and 19% yield, respectively. The formation of these compounds should occur by a nucleophilic attack of an intermediate epoxide **12** formed during the reaction. Compound **12** was prepared and isolated by the reaction of compound **8** with sodium hydride in *N, N*-dimethylformamide (Scheme 1). The epoxide ring of **12** was identified from its ^{1}H-NMR spectrum showing signals for H-2 and H-3 at 3.6 and 3.3 ppm, respectively, and in the ^{13}C-NMR spectrum signals for C-2 and C-3 at 54.5 and 58.4 ppm. The reaction of the compound **8** with 2-mercaptobenzimidazole **4** in the same conditions was regioselective, giving only the isomer **11** in 33% yield. This could be explained by the highest nucleophilicity of 2-mercaptobenzimidazole due to the presence of two nitrogen atom which increases the donating capacity of the sulfur [21].

Scheme 1. (a) 2,2-dimethoxypropane, DMF, *p*-TsOH, 85°C, 30 h, 63%; (b) MsCl, py, 0°C–rt, 24 h; (c) 50% aqueous TFA, THF, 60°C, 12 h, 89%; (d) (i) **3** or **4**, NaH, DMF, 140°C, 48 h; (ii) Ac_2O, py, rt, 24 h; (e) NaH, DMF, 110°C, 62%; (f) BzCl, py, 0°C–rt, 48 h, 40%; (g) $MeO^{-}Na^{+}$, MeOH/THF, 70%; (h) **3** or **4**, NaH, DMF, microwave.



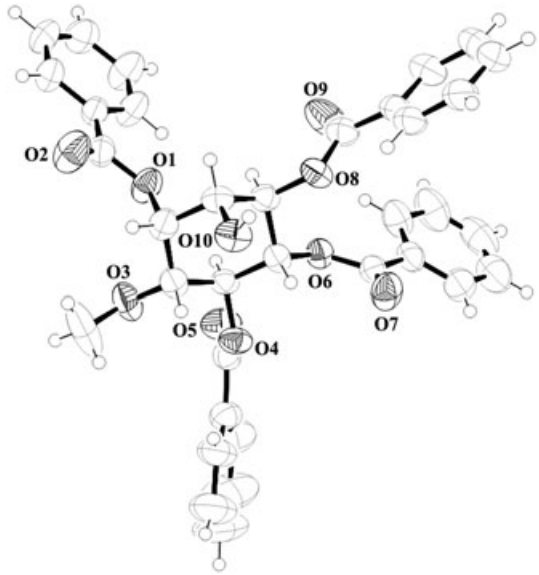


Figure 2. The crystal structure of compound **13**.

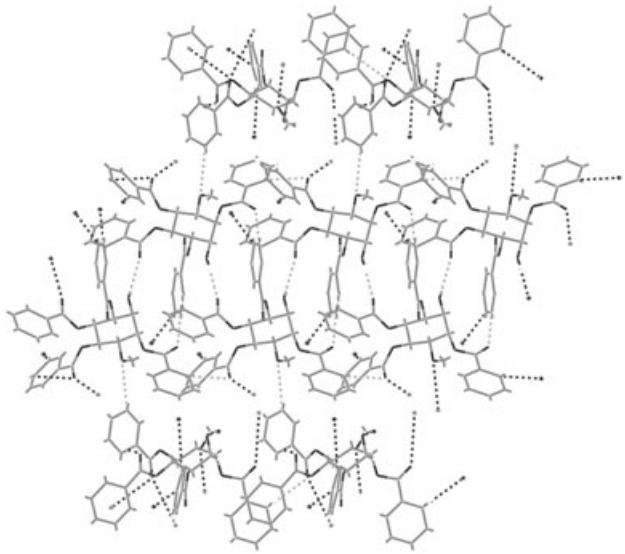


Figure 3. The crystal structure of compound **13**.

In order to obtain the C-3 substituted inositol, compound **5** was first benzoylated, leading to **13** in 40% yield, and then treated with methanesulfonyl chloride furnishing the mesylated compound **14** in 95% yield [16]. Cleavage of the benzoyl groups of **14** with sodium methoxide in methanol and tetrahydrofuran afforded the epoxide **15** in 70% yield. The epoxide ring of **15** was characterized from its ^{1}H- and ^{13}C-NMR spectra showing signals for H-2 and H-3 at 3.4 and 3.3 ppm, respectively, and signals of C-2 and C-3 at 56.7 and 54.3 ppm.

The ring opening of epoxide **15** with 2-mercaptobenzothiazole **3** or 2-mercaptobenzimidazole **4** in the presence of sodium hydride [10] led to the formation of different products. The reactional mixture was peracetylated *in situ* to facilitate the purification and characterization of products. The reactions appeared to be regioselective: as the two C-3 substituted compounds **16** and **17** were obtained in 42 and 40% yields, respectively without the formation of C-2 isomers. When this reaction was conducted using microwave irradiation as the energy source the reactions were cleaner and compounds **18** and **19** could be easily isolated in 55 and 61% yield, respectively, without peracetylation.

The compound **13** was also characterized by single crystal X-ray diffraction (CCDC 798893 contains the crystallographic data for **13**. This data can be obtained free of charge at www.ccdc.cam.ac.uk), and the crystal structure

Table 1

Geometric parameters of hydrogen bonds and π-sacking interaction.

Hydrogen bonds				
D–H···A	D–H (Å)	H·· A (Å)	D···A (Å)	D – H···A (°)
O10–H10A···O7[a]	0.89(3)	1.97(3)	2.846(4)	167(3)
C13–H13···O5[b]	0.930	2.628	3.491(4)	154.59
C18–H18···O3[c]	0.930	2.656	3.435(5)	141.89
C33–H33···O5[d]	0.930	2.633	3.439(5)	145.33
C34–H34···O2[e]	0.930	2.637	3.455(4)	147.13
	π-stacking distances (Å)			
Centroid–centroid	Interplanar	Horizontal shift		
3.98(1)	3.61(1)	1.68(1)		

Symmetry code:
[a]($x - y$, x, ½ + z).
[b](x, y, 1 + z).
[c](y, $-x + y$, –½ + z).
[d](1 – y, 1 + $x - y$, z).
[e](1 – x, 1 – y, –½ + z).

is displayed in Figure 2. The absolute configuration expected was confirmed by diffraction refinement. This compound crystallizes in a hexagonal non-centrosymmetric space group $P6_3$, and the Flack parameters indicate that the absolute is correct [−0.3(1)]. The inositol ring is displayed as a chair conformation and the distances of the extremity carbon atoms to the inositol ring is 0.725(3) and −0.610 (3) Å. The angles between inositol unit and benzene rings are about 81°, except the ring formed by C30 to C35 (Fig. 2) that this angle is 69.1(1)°. The hydroxyl group (O10-H) is involved in medium to weak hydrogen bond to carboxyl group (O7) of the neighbor molecule in which O10···O7 distance is 2.846(4) Å. This interaction gives rise to a unidimensional extended structure parallel to crystallographic axis *c*, as can be seen in Figure 3. The other weak interactions, as non-conventional C–H···O hydrogen bonds and π-stacking interactions, are also responsible for the solid-state stabilization. The C···O distance is 3.543(5) Å and the centroid–centroid distance is 3.98(1) Å. The geometric parameters of these interactions are listed in Table 1.

CONCLUSIONS

The present article reports the synthesis of new compounds derived from 2-mercaptobenzothiazole and 2-mercaptobenzimidazole. These compounds were prepared via the opening of an intermediate epoxide, which was obtained from L-quebrachitol. This reaction could be assisted by microwave irradiation, allowing an easier purification of the desired compounds in higher yields.

EXPERIMENTAL

General methods. The solvents were pretreated, when necessary, according to the appropriate standard procedures before being used. The compounds were purified by column chromatography on silica gel (70–230 mesh ASTM) with visualization under UV light and by H_2SO_4 charring. All reaction mixtures were stirred magnetically. The melting points were recorded on a MQAPF-Microquimica. NMR spectra were obtained with a Bruker Avancer DRX/300, Bruker Avancer DRX/400, and Bruker AC500 spectrometer using tetramethylsilane as the internal standard. IR spectra were recorded on a BOMEM-FTIR MB-120 spectrometer. Mass spectra were recorded on a KRATOS MS-80 spectrometer. Optical rotations were measured on a Bellingham Stanley ADP410 polarimeter. Microwave assisted reaction was promoted in an adapted domestic microwave apparatus NEWTECH® MO1180 (120 V, 2450 MHz). The crystal was mounted on a Bruker Kappa CCD diffractometer with MoKα(λ = 0.71073 Å) at room temperature (298 K). Data collection, reduction, and cell refinement were performed by COLLECT, EVALCCD, and DIRAX programs [22]. The structures were solved and refined using SHELXL-97 [23]. An empirical isotropic extinction parameter *x* was refined, according to the method described by Larson [24]. A multiscan absorption correction was applied [25]. The structures were drawn by ORTEP-3 for windows [26] and Mercury [27] programs. Crystal data: $C_{35}H_{30}O_{10}$, M_r = 610.59 g mol^{-1}, hexagonal $P6_3$. Unit-cell, a = 24.313(3) Å, b = 24.313(3) Å, c = 9.950(5) Å, V = 5093.7(4) Å^3, Z = 6, $F(000)$ = 1920, d_x = 1.194 g cm^{-3}. The number of measured reflections was 28,707, $-30 \le h \le 30$, $-30 \le k \le 21$, $-11 \le l \le 10$, $2\theta_{max}$ = 55.12° and R_{int} = 0.0293 for 6421 unique reflections. The final refinement presented $R(F)$ = 0.047, $wR(F^2)$ = 0.120 and S = 1.059 for 4201 observed reflections [$F \ge 4\sigma$ (F)].

2-*O*-Methanesulfonyl-1-*O*-methyl-L-*chiro*-inositol (8). To a solution of compound **7** (2.2 g, 6.4 mmol) in tetrahydrofuran (THF) (10 mL) was slowly added 1 mL of an aqueous solution of CF_3CO_2H (1:1). The reaction was stirred for 12 h at 60°C and the solvent was removed under reduced pressure. The residue was purified by column chromatography (ethyl acetate, methanol) furnishing the desired compound **8** (1.54 g, 5.7 mmol, 89%). M.p. 84.2°C. IR (KRS-5): 3403 (O-H.), 2935 (C-$H_{aliphatic}$), 1348 S(=O)$_2$. ^{1}H-NMR (300 MHz, CD_3OD): δ 3.2 (OMs), 3.4 (s, 1H, H6), 3.5 (s, 3H, OMe), 3.6 (m, 3H, H1, H4, H5), 4.2 (s, 1H, H3), 5.1 (s, 1H, H2). ^{13}C-NMR (75 MHz, CD_3OD): δ 38.8 (OMs), 59.1 (OMe), 71.4–74.3 (C3, C4, C5, C6), 79.2 (C1), 80.5 (C2). MS *m/z* calculated for $C_8H_{16}O_8SNa$ [M + Na^+]: 295.0464. Found: 295.0452.

3-Deoxy-3-*S*-(2′-mercaptobenzothiazoyl)-1-*O*-methyl-3,4,5,6-tetra-*O*-acetyl-L-*chiro*-inositol (9) and 2-deoxy-2-*S*-(2′-mercaptobenzothiazoyl)-1-*O*-methyl-2,4,5,6-tetra-*O*-acetyl-L-*scyllo*-inositol (10). To a cold solution of 2-mercaptobenzothiazole **3** (1.5 mmol) in anhydrous *N*, *N*-dimethylformamide (DMF) (5 mL) was added sodium hydride 60% (2.4 mmol). After 10 min under stirring at room temperature a solution of the compound **8** (1.5 mmol) in DMF (5 mL) was added. The reaction mixture was stirred at 140°C for 48 h and acetic anhydride (1 mL) and pyridine (3.0 mL) were added. The reaction mixture was stirred at room temperature for 24 h, water was added (30 mL), and the reaction mixture was extracted with dichloromethane (3× 50 mL). The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure. The residue was purified by column chromatography (hexane, ethyl acetate) furnishing compounds **9** (291.3 g, 0.57 mmol, 38%) and **10** (145.7 g, 0.28 mmol, 19%).

Compound **9**: m.p. 117.4°C; $[\alpha]_D^{20}$ −54.2 (c 0.34, CH_2Cl_2). IR (KRS-5): 3061 (C–$H_{arom.}$), 2942 (C–$H_{aliphatic}$), 1755 (C=O); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 1.9–2.2 (4s, 12H, CH_3COO), 3.4 (s, 3H, OMe), 4.0 (dd, 1H, H1, $J_{1,2}$ = 4.5, $J_{1,6}$ = 9.5 Hz), 5.0 (t, 1H, H2, $J_{2,3}$ = 4.5 Hz), 5.2 (t, 1H, H6, $J_{6,5}$ = 9.5 Hz), 5.4 (t, 1H, H5, $J_{5,4}$ = 9.5 Hz), 5.5 (dd, 1H, H4, $J_{4,3}$ = 4.5 Hz), 5.8 (t, 1H, H3), 7.3 (t, 1H, H6′, $J_{6',7'}$ = $J_{6',5'}$ = 7.5 Hz), 7.4 (t, 1H, H7′, $J_{7',8'}$ = 7.5 Hz), 7.8 (d, 1H, H5′), 7.9 (d, 1H, H8′). ^{13}C-NMR (125 MHz, $CDCl_3$): δ 20.7–21.1 (CH_3COO), 46.9 (C2), 58.6 (OMe), 69.5, 69.6, 70.2 (C3, C4, C5), 71.9 (C6), 121.4, 122.0 (C5′, C8′), 124.9, 126.4 (C6′, C7′). MS *m/z* calculated for $C_{22}H_{25}NO_9S_2Na$ [M + Na^+]: 534.0868. Found: 534.0873.

Compound **10**: m.p. 196.1°C. $[\alpha]_D^{20}$ −53.6 (c 0.69, CH_2Cl_2). IR (KRS-5): 3065 (C–$H_{arom.}$), 2946–2926 (C–$H_{aliphatic}$), 1756 (C=O). ^{1}H-NMR (500 MHz, $CDCl_3$): δ 1.9–2.1 (4s, 12H, CZH_3COO), 3.5 (s, 3H, OMe), 3.6 (t, 1H, H1, $J_{1,2}$ = $J_{1,6}$ = 9.5 Hz), 4.2 (t, 1H, H3, $J_{3,2}$ = $J_{3,4}$ = 11.0 Hz), 5.2 (m, 2H, H5, H6), 5.5 (m, 2H, H2, H4) 7.3 (t, 1H, H6′, $J_{6',7'}$ = $J_{6',5'}$ = 7.5 Hz), 7.5 (t, 1H, H7′, $J_{7',8'}$ = 7.5 Hz), 7.7 (d, 1H, H5′), 8.0 (d, 1H, H8′). ^{13}C-NMR (125 MHz, $CDCl_3$): δ 20.6–20.9 (CH_3COO), 51.1 (C3), 60.4 (OMe), 70.0, 70.1 (C2, C4), 71.5, 72.6 (C5, C6), 81.6 (C1) 121.2, 122.4 (C5′, C8′), 125.0, 126.5 (C6′, C7′),

135.4 (C9′), 153.0 (C4′), 163.5 (C2′), 169.6–170.2 (C=O). MS *m/z* calculated for $C_{22}H_{25}NO_9S_2Na$ [M + Na^+]: 534.0868. Found: 534.0876.

2-Deoxy-2-*S*-(2′-mercaptobenzimidazoyl)-1-*O*-methyl-3,4,5,6-tetra-*O*-acetyl-L-*chiro*-inositol (11). Following the same experimental conditions used for the preparation of compounds **9** and **10** using mercaptobenzimidazole **4** instead of reagent **3**, the compound **11** was isolated in 33% yield from **8** (244.5 mg, 0.47 mmol). $[\alpha]_D^{20}$ −54.2 (*c* 0.24, CH_2Cl_2). IR (KRS-5): 3024 (C–$H_{arom.}$), 2961–2931 (C–$H_{aliphatic}$), 1754 (C=O). ^{1}H-NMR (500 MHz, $CDCl_3$): δ 2.0–2.1 (4s, 12H, CH_3COO), 3.4 (s, 3H, OMe), 4.0 (s, 1H, H1), 4.9 (s, 1H, H2), 5.3 (t, 1H, H6, $J_{6,1} = J_{6,5} = 9.5$ Hz), 5.4 (t, 1H, H5, $J_{5,4} = 9.5$ Hz), 5.5 (d, 1H, H4, $J_{4,3} = 9.5$ Hz), 5.6 (s, 1H, H3), 7.3 (s, 2H, H6′, H7′), 7.6 (s, 2H, H5′, H8′). ^{13}C-NMR (125 MHz, $CDCl_3$): δ 20.9–21.1 (CH_3COO), 47.7 (C2), 58.5 (OMe), 69.4, 69.7, 69.9 (C3, C4, C5), 71.8 (C6), 116.0 (C5′, C8′), 123.9 (C6′, C7′), 145.7 (C4′, C9′), 169.5–170.5 (C=O). MS *m/z* calculated for $C_{22}H_{26}N_2O_9SNa$ [M + Na^+]: 517.1257. Found: 517.1257.

2*R*,3*S*-Epoxy-1-*O*-methyl-L-*chiro*-inositol (12). To a solution of sulfonate **8** (0.22 g, 0.82 mmol) in 5 mL of anhydrous DMF was added sodium hydride 60% (0.032 g, 1.32 mmol) and the mixture was stirred at 110°C for 48 h. The mixture was then concentrated under reduced pressure and the residue was purified by column chromatography (ethyl acetate, methanol) to afford **12** (0.09 g, 62%) as an oil. $[\alpha]_D^{20}$ −70.8 (*c* 0.22, CH_3OH): IR (KRS-5): 3390 (O–H), 2927 (C–$H_{aliphatic}$), 918 (C–O–C_{epox}). ^{1}H-NMR (300 MHz, CD_3OD): δ 4.3 (d, 1H, H4, $J_{4,5} = 9.0$ Hz), 4.0 (t, 1H, H5), 3.9 (d, 1H, H1, $J_{1,6} = 9.0$ Hz), 3.8 (t, 1H, H6, $J_{6,1} = J_{6,5} = 9.0$ Hz), 3.6 (s, 1H, H2), 3.5 (s, 3H, OMe), 3.3 (s, 1H, H3). ^{13}C-NMR (75 MHz, CD_3OD): δ 54.5 (C2 or C3), 58.4 (C2 or C3), 58.8 (OMe), 72.4, 73.0, 76.2 (C4/C5/C6), 82.5 (C1). MS *m/z* calculated for $C_7H_{12}O_5Na$ [M + Na^+]: 199.0. Found: 199.0.

2*S*,3*R*-Epoxy-1-*O*-methyl-L-*chiro*-inositol (15). A solution of **14** (3.2 g, 4.7 mmol) in 30 mL of anhydrous MeOH and 5 mL of anhydrous THF was treated with a solution of sodium methoxide (0.94 g of sodium in 10 mL of anhydrous methanol). The mixture was stirred at room temperature for 24 h and the solvent was removed under reduced pressure. The residue was purified by column chromatography (ethyl acetate, methanol) to afford **15** (0.57 g, 3.2 mmol, 70%) as an oil. $[\alpha]_D^{20}$ −41.4 (*c* 0.29, CH_3OH): IR (KRS-5): 3398 (O–H), 2934 (C–$H_{aliphatic}$), 919 (C-O-C_{epox}). ^{1}H-NMR (300 MHz, C_5D_5N): δ 4.2 (d, 1H, $J_{4,5} = 7.6$ Hz, H4), 3.9 (m, 2H, H5/H6), 3.7 (d, 1H, H1, $J_{1,6} = 7.6$ Hz), 3.5 (s, 3H, OMe), 3.4 (s, 1H, H2), 3.3 (s, 1H, H3). ^{13}C–NMR (75 MHz, C_5D_5N): - 56.7 (C2 or C3), 54.3 (C2 or C3), 57.4 (OMe), 69.9, 71.4, 76.3 (C4, C5, C6), 81.4 (C1).

General procedure to prepare 3-deoxy-3-*S*-(2′-mercaptobenzothiazoyl)-1-*O*-methyl-2,4,5,6-tetra-*O*-acetyl-L-*chiro*-inositol (16) and 3-deoxy-3-*S*-(2′-mercaptobenzimidazoyl)-1-*O*-methyl-2,4,5,6-tetra-*O*-acetyl-L-*chiro*-inositol (17). The same procedure described for the synthesis of the compounds **9** and **10** was carried out using epoxide **15** as starting material. The desired compounds **16** (0.32 g, 42%) and **17** (0.31 g, 40%) were obtained as oils.

Compound **16**: $[\alpha]_D^{20}$ −55.9 (*c* 0.32, CH_2Cl_2). IR (KRS-5): 3063 (C–$H_{arom.}$), 2960–2939 (C–$H_{aliphatic}$), 1754 (C=O). ^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.8–2.2 (4s, 12H, CH_3COO), 3.4 (s, 3H, OMe), 3.6 (dd, 1H, H1, $J_{1,2} = 3.4$, $J_{1,6} = 9.5$ Hz), 5.0 (t, 1H, H3, $J_{3,2} = J_{3,4} = 3.4$ Hz), 5.3 (t, 1H, H6, $J_{6,5} = 9.5$ Hz), 5.4 (t, 1H, H5, $J_{5,4} = 9.5$ Hz), 5.6 (dd, 1H, H4), 5.8 (t, 1H, H2), 7.3 (t, 1H, H6′, $J_{6',7'} = J_{6',5'} = 7.5$ Hz), 7.4 (t, 1H, H7′, $J_{7',8'} = 7.5$ Hz), 7.8 (d, 1H, H5′), 7.9 (d, 1H, H8′). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 20.8–21.2 (CH_3COO), 47.1 (C3), 58.7 (OMe), 68.3, 69.1, 70.1, 71.7 (C2, C4, C5, C6), 78.0 (C1), 121.3, 122.2 (C5′, C8′), 125.1, 126.6 (C6′, C7′), 136.1 (C9′), 152.6 (C4′), 162.5 (C2′). MS *m/z* calculated for $C_{22}H_{25}NO_9S_2Na$ [M + Na^+]: 534.0868. Found: 534.0878.

Compound **17**: $[\alpha]_D^{20}$ −43.8 (*c* 0.16, CH_2Cl_2). IR (KRS-5): 3060 (C–$H_{arom.}$), 2925 (C–$H_{aliphatic}$), 1754 (C=O). ^{1}H-NMR (300 MHz, $CDCl_3$): δ 2.0–2.2 (4s, 12H, CH_3COO), 3.3 (s, 3H, OMe), 3.6 (d, 1H, H1, $J_{1,6} = 9.2$ Hz), 4.8 (s, 1H, H3), 5.3 (t, 1H, H6, $J_{6,5} = 9.2$ Hz), 5.4 (t, 1H, H5, $J_{5,4} = 9.2$ Hz), 5.5 (s, 1H, H4), 5.7 (s, 1H, H2), 7.2 (s, 2H, H6′, H8′), 7.5 (s, 2H, H5′, H8′). ^{13}C-NMR (75 MHz, $CDCl_3$): δ 20.3–20.9 (CH_3COO), 46.3 (C3), 58.6 (OMe), 68.7, 68.9 (C2, C4), 70.3, 71.3 (C5, C6), 114.4 (C5′, C8′), 123.2 (C6′, C7′), 138.4 (C4′, C9′), 146.3 (C2′), 169.7, 169.9, 170.0, 170.1 (C=O). MS *m/z* calculated for $C_{22}H_{26}N_2O_9SNa$ [M + Na^+]: 517.1257. Found: 517.1247.

General procedure to prepare 3-deoxy-3-*S*-(2′-mercaptobenzothiazoyl)-1-*O*-methyl-L-*chiro*-inositol (18) and 3-deoxy-3-*S*-(2′-mercaptobenzimidazoyl)-1-*O*-methyl-L-*chiro*-inositol (19). To a cold solution of 2-mercaptobenzothiazole **3** or 2-mercaptobenzimidazole **4** (1.5 mmol) in anhydrous DMF (5 mL) was added sodium hydride 60% (2.4 mmol). After 10 min under stirring at room temperature a solution of the epoxide **15** (1.5 mmol) in DMF (5 mL) was added. The reaction mixture was refluxed under microwave irradiation (three pulses of 15 min), after this time the mixture was concentrated under reduced pressure and purified by column chromatography (ethyl acetate, methanol) furnishing the desired product **18** (0.28 g, 0.82 mmol, 55%) and **19** (0.30 g, 0.92 mmol, 61%).

Compound **18**: $[\alpha]_D^{20}$−82.6 (*c* 0.23, CH_3OH). IR (KRS-5): 3396 (O–H), 2934 (C–$H_{aliphatic}$). ^{1}H-NMR (300 MHz, C_5D_5N/D_2O): δ 3.4 (s, 3H, OMe), 3.1 (dd, 1H, H1, $J_{1,2} = 3.1$, $J_{1,6} = 9.5$ Hz), 3.3 (t, 1H, H6, $J_{6,5} = 9.5$ Hz), 3.6 (t, 1H, H5, $J_{5,4} = 9.5$ Hz), 4.1 (t, 1H, H3, $J_{3,2} = J_{3,4} = 3.1$ Hz), 4.2 (t, 1H, H4), 4.3 (m, 1H, H2), 6.8 (t, 1H, H6′, $J_{6',7'} = J_{6',5'} = 7.6$ Hz), 6.9 (t, 1H, H7′, $J_{7',8'} = 7.6$ Hz), 7.2 (d, 1H, H5′), 7.3 (d, 1H, H8′). ^{13}C-NMR (75 MHz, C_5D_5N/D_2O): δ 53.4 (C3), 56.6 (OMe), 67.1, 67.8, 71.6, 73.9 (C2, C4, C5, C6), 80.2 (C1), 120.3, 120.7 (C5′, C8′), 124.4, 125.9 (C6′, C7′), 134.0 (C9′), 151.5 (C4′), 165.9 (C2′). MS *m/z* calculated for $C_{14}H_{17}NO_5S_2Na$ [M + Na^+]: 366.0446. Found: 366.0450.

Compound **19**: $[\alpha]_D^{20}$ −35.4 (*c* 0.45, CH_3OH). IR (KRS-5): 3408 (O–H), 2938 (C–$H_{aliphatic}$). ^{1}H-NMR (300 MHz, D_2O): δ 3.3 (s, 3H, OMe), 3.4 (m, 1H, H1), 3.5 (m, 2H, H5, H6), 3.6 (m, 1H, H3), 4.2 (m, 2H, H2, H4), 7.1 (m, 2H, H6′, H7′) 7.4 (m, 2H, H5′, H8′). ^{13}C-NMR (75 MHz, D_2O): δ 52.0 (C3), 56.6 (OMe), 66.9, 68.2, 71.8, 73.6 (C2, C4, C5, C6), 79.6 (C1), 113.8 (C5′, C8′), 122.6 (C6′, C7′), 138.1 (C4′, C9′), 147.5 (C2′). MS *m/z* calculated for $C_{14}H_{18}N_2O_5SNa$ [M + Na^+]: 349.0834. Found: 349.0844.

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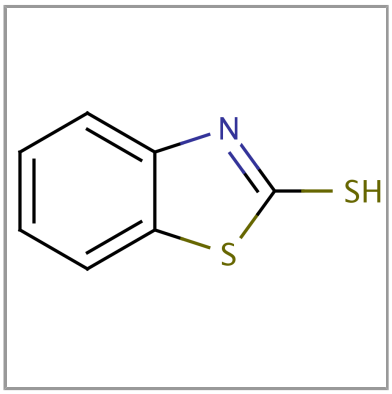

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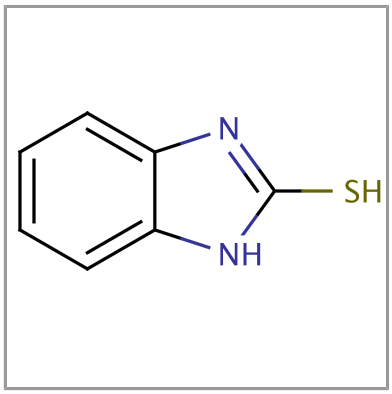

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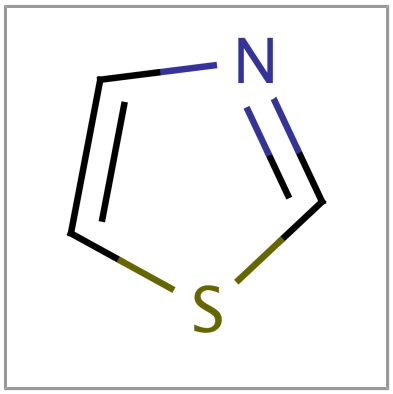

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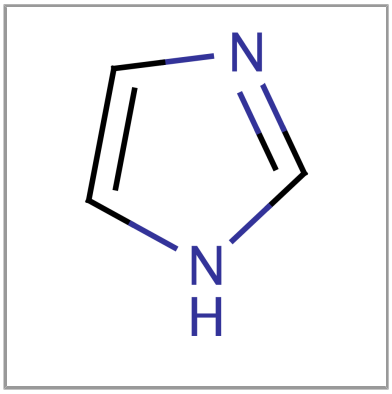

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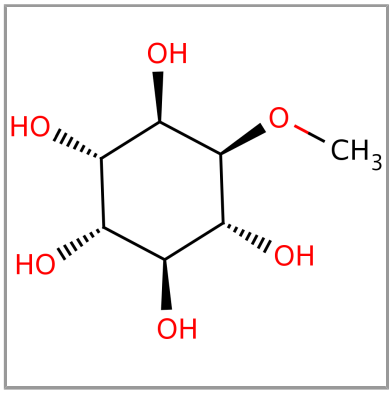

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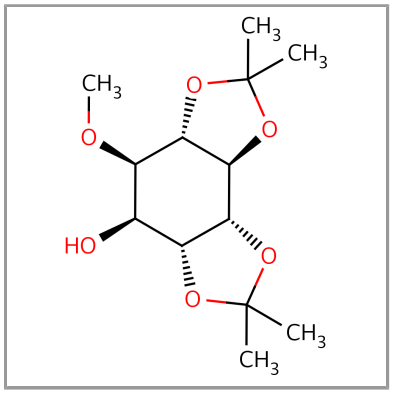

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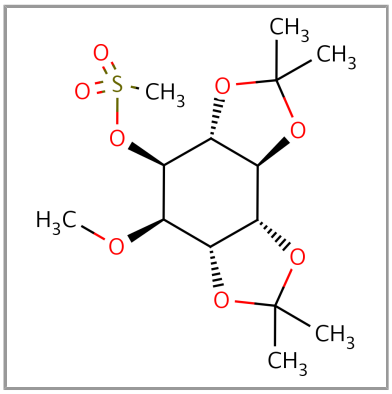

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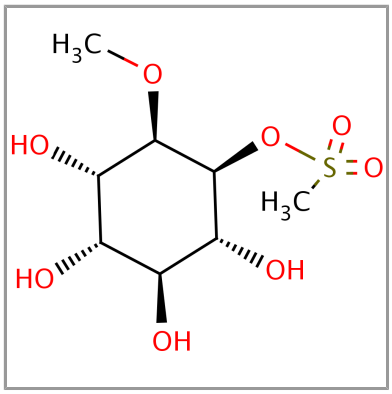

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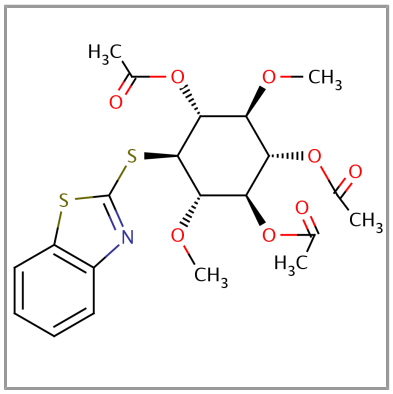

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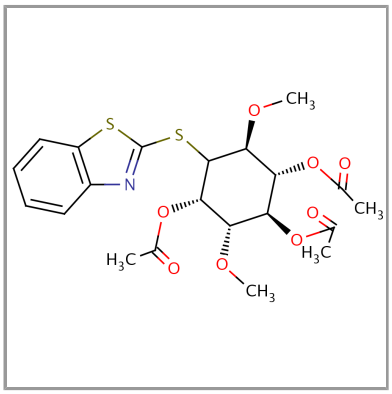

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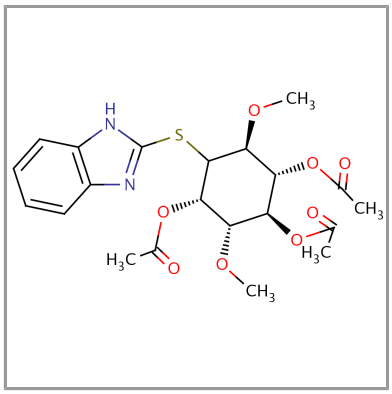

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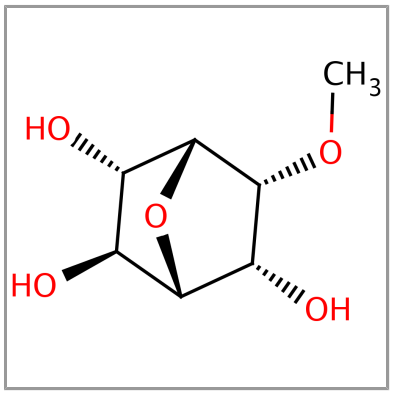

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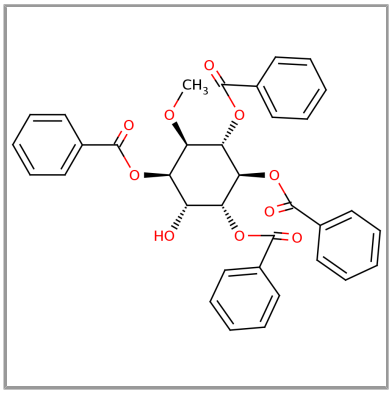

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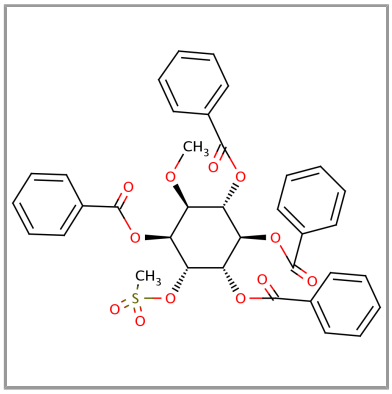

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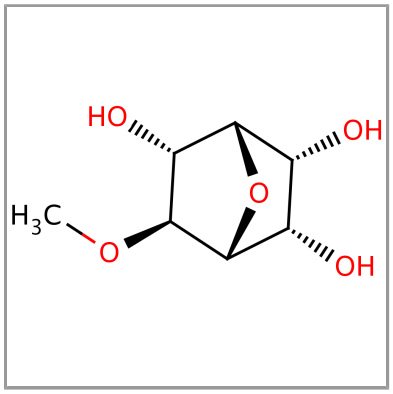

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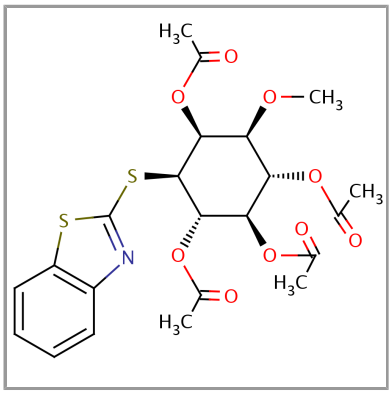

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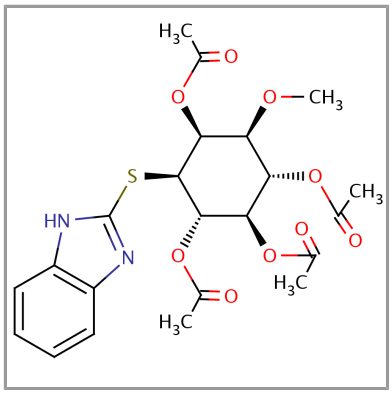

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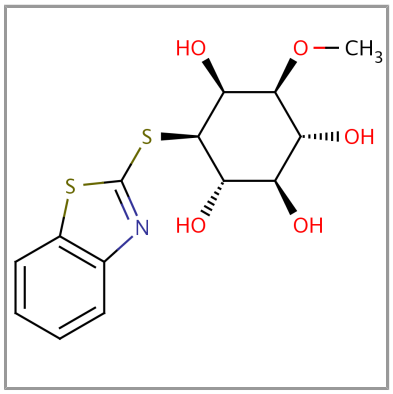

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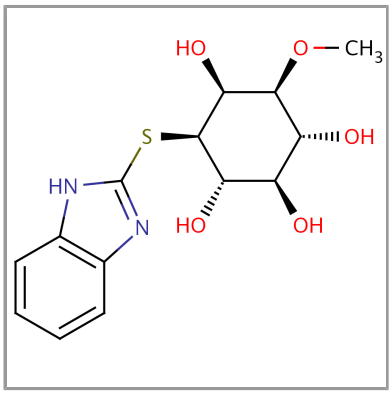

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