Synthesis and Antiviral Evaluation of Bisnoradamantane Sulfites and Related Compounds

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Abstract: The reaction of a series of 1,2-diols with thionyl chloride led to bisnoradamantane sulfites in very good yields. The reaction has also been applied to related polycyclic scaffolds. The compounds have been tested for antiviral activity but none of them showed to be active. Several attempts to generate and trap SO from these polycyclic sulfites have been unsuccessful.

Keywords: Antiviral activity, bisnoradamantanes, polycyclic compounds, sulfites, sulfur monoxide, vesicular stomatitis virus.

INTRODUCTION

Derivatives of adamantane are of significant interest in medicinal chemistry. Amantadine and rimantadine have been used for years as anti-influenza A agents [1], and a dimethyl derivative of amantadine, memantine, is a NMDA receptor antagonist clinically used for the treatment of Alzheimer's disease [2]. Recently, structurally more complex adamantane derivatives have been introduced into the clinic, such as the dipeptidil peptidase IV (DPP-IV) inhibitors vildagliptin and saxagliptin, of interest for the treatment of type 2 diabetes (Fig. **1**) [3].

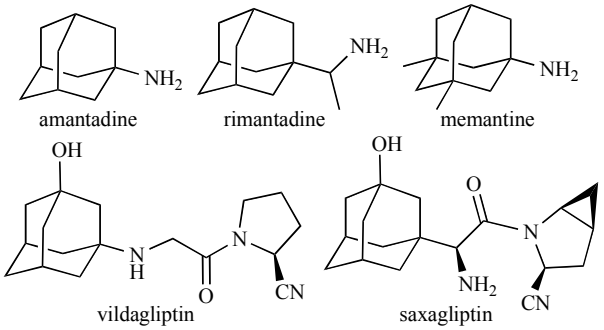
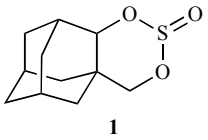


Fig. (1). Adamantanes of clinical interest.

It is well-known in medicinal chemistry that when drugs contain cyclic systems, it is generally worth synthesizing analogues where the ring is opened, expanded or contracted by one unit, because these analogues show similar activity to the parent compound [4]. For this reason, some time ago we started a program aimed to synthesize and pharmacologically evaluate a series of ring-contracted analogs of amantadine, memantine and rimantadine. We have already found that several bisnoradamantane and noradamantane amines showed an interesting activity as NMDA receptor antagonists [5].

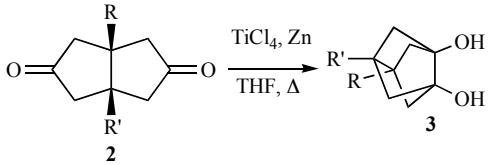
Very recently, Kolocouris *et al.* found that racemic adamantane sulfite **1**, is markedly active against vesicular stomatitis virus, its potency being 2.5-fold higher than that of the reference compound, (*S*)-9-(2,3-dihydroxypropyl)adenine (Fig. **2**) [6].



1

Fig. (2). Antiviral adamantane sulfite **1**.

Some time ago, we described a short, inexpensive, high-yielding synthesis of a series of bisnoradamantane pinacols of general structure **3** by pinacol coupling of diketones of general structure **2** (Scheme **1**) [7].



2 **3**

Scheme 1. Synthesis of bisnoradamantane pinacols **3** from easily available diketones **2**.

Taking into account the easy access to pinacols of structure **3** and the potent anti-viral activity displayed by adamantane sulfite **1**, we undertook the synthesis and antiviral evaluation of sulfites derived from **3** and related pinacols as ring-contracted analogs of adamantane sulfite **1**.

RESULTS AND DISCUSSION

Chemistry

Reaction of known pinacol **3a** with an excess of thionyl chloride led to sulfite **4a** in 89% yield. The same procedure

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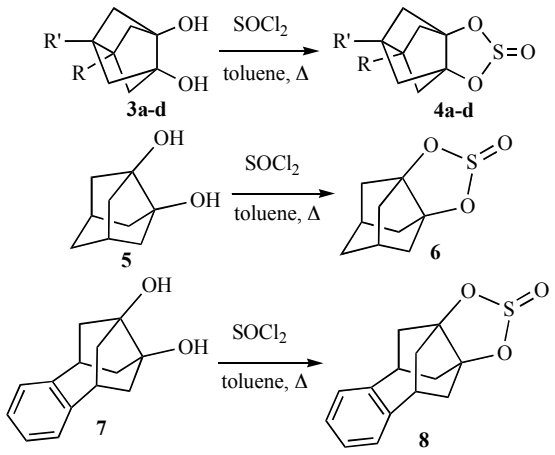
was used for bisnoradamantane pinacols **3b-d**, the corresponding sulfites **4b-d** being obtained. Moreover, starting from pinacols **5** and **7**, sulfites **6** and **8** were obtained in quantitative yield (Scheme **2**). Worthy of note, although pinacols **5** and **7** were known compounds [8], their previously described syntheses were somehow problematic and low-yielding. We have now found that both compounds are also easily available in essentially quantitative yield by the pinacol coupling of their corresponding diketones applying the same methodology that we had previously used for the syntesis of pinacols **3** (see experimental part for details).



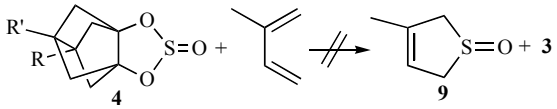
Scheme 2. Synthesis of new bisnoradamantane sulfites **4a-d**, noradamantane derivative **6** (65%) and related compound **8** (65% yield). **4a** (R=R'=CH_3; 89% yield), **4b** (R,R'=-$(CH_2)_4$-; 66% yield), **4c** (R=CH_3, R'=C_6H_5; 71% yield), **4d** (R,R'=2,2'-biphenylene; 67% yield).

The new polycyclic sulfites described herein are easily accessible and, with the only exception of **4c**, achiral compounds, thus avoiding issues related to the different pharmacological activity that may be associated with the two enantiomers of chiral compounds, such as sulfite **1**. The structure of all new compounds was confirmed by elemental analysis or accurate mass measurement, IR, ^{1}H NMR, ^{13}C NMR and mass spectral data.

We have previously found that bisnoradamantane pinacols **3** were not very stable, undergoing ring-opening processes to bicyclic derivatives. These processes were explained taking into account the large strain released during the opening of the strained bisnoradamantane skeleton to a bicyclo[3.3.0]octane derivative [9].

Taking into account these precedents we wondered about the possibility of using these new sulfites as a potential source of sulfur monoxide, SO, a very reactive species. Although there are several methods for SO production, the search for an effective source has proven to be a challenging problem as most of the reported procedures only lead to trapped products in very low yields [10]. In 2001, Grainger and coworkers reported a convenient method for its generation and trapping, although the yield of the synthesis of the precursor, a naphthalene-derived trisulfide oxide, was modest [11].

Interestingly, adsorption of sulfite **4b** in silica gel for 24 hours at room temperature, followed by elution with hexane/EtOAc led to a mixture of the starting sulfite and diketone **2b**. Besides, refluxing overnight a toluene solution of sulfite **4b** furnished a mixture of diketone **2b**, **4b** and several minor impurities. Encouraged by these results, we investigated the potential of sulfites **4** to act as a source of sulfur monoxide in trapping experiments with dienes. However, refluxing a solution of sulfite **4b** in chlorobenzene with excess isoprene gave no evidence for the formation of sulfoxide **9**, although formation of diketone **2b** was again observed. Although several attempts involving thermal and acidic conditions were explored, no evidences for the generation of SO were found. Sulfoxide **9** was not detected even when the thermally induced decomposition was carried out in isoprene as a solvent (Scheme **3**).



Scheme 3. Unsuccessful attempt to generate and trap SO from sulfites **4**.

So far, we do not have a conclusive explanation for the opening of the sulfites to the corresponding diketones. Perhaps, the decomposition of these sulfites involves oxidation to their corresponding sulfates, followed by SO_2 extrusion. In fact, we have previously found that the sulfate derived from pinacol **4a** underwent thermally induced conversion to the corresponding diketone [12].

Antiviral Assays

None of the six tested sulfites displayed activity against the enveloped DNA viruses herpes simplex virus (type 1 or type 2) or vaccinia virus; the enveloped RNA viruses feline coronavirus, parainfluenza-3 virus, respiratory syncytial virus, vesicular stomatitis virus, sindbis virus or Punta Toro virus; or the non-enveloped RNA viruses Coxsackievirus B4 and Reovirus-1. Also, none of the compounds was found to be active against influenza virus A/H1N1, A/H3N2 or B.

CONCLUSIONS

Six new polycyclic sulfites have been synthesized from easily available pinacols. Several attempts to trap sulfur monoxide from the decomposition of these sulfites met with failure. None of the sulfites displayed antiviral activity. Taking into account that the precursor of biologically active sulfite **1** features a primary and a secondary alcohol group and that the new sulfites reported herein are derived from tertiary alcohols, it seems that less steric congestion around the sulfite group is required for antiviral activity. The syntheses of this kind of sulfite from bisnoradamantane derivatives are currently in progress.

EXPERIMENTAL SECTION

Chemistry

General

Melting points were determined in open capillary tubes. Unless otherwise stated, NMR spectra were recorded in CD_3OD in the following spectrometers: ^{1}H NMR (500 MHz), ^{13}C NMR (75.4 MHz). Chemical shits (δ) are reported in ppm related to internal tetramethylsilane (TMS). Assign-

ments given for the NMR spectra are based on DEPT, COSY $^1H/^1H$, HETCOR $^1H/^{13}C$ (HSQC and HMBC sequences for one bond and long range $^1H/^{13}C$ heterocorrelations, respectively) and NOESY experiments for selected compounds. For the MS and GC/MS analyses the sample was introduced directly or through a gas chromatograph. For GC/MS analyses a 30−meter column [5% diphenyl−95% dimethylpolysiloxane, conditions: 10 psi, initial temperature: 35 ºC (2 min), then heating at a range of 8 ºC/min till 300 ºC, then isothermic at 300 ºC] was used. The electron impact (70 eV) or chemical ionization (CH_4) techniques were used. Only significant ions are given: those with higher relative ratio, except for the ions with higher *m/z* values. Accurate mass measurements were obtained using ESI technic. Absorption values in the IR spectra (KBr) are given as wave-numbers (cm^{-1}). Only the more intense bands are given. Column chromatography was performed on silica gel 60 Å (35−70 mesh). For the thin layer chromatography (TLC) aluminum-backed sheets with silica gel 60 F_{254} were used and spots were visualized with UV light and/or 1% aqueous solution of $KMnO_4$.

Tricyclo[3.3.1.0^{3,7}]nonane-3,7-diol, (5)

Powdered Zn (6.54 g, 100 mmol) was added portionwise at room temperature to a solution of $TiCl_4$ (9.48 g, 50 mmol) in anhydrous 1,4-dioxane (75 mL). Pyridine (2.5 mL) was added and the mixture was heated at reflux for 1 h in an argon atmosphere. A solution of bicyclo[3.3.1]nonan-3,7-dione (761 mg, 5 mmol) in anhydrous 1,4-dioxane (25 mL) was added dropwise with stirring and the mixture was heated at reflux for 18 h. The mixture was allowed to cool to room temperature and was slowly added to 30% aqueous solution of K_2CO_3 (250 mL), the final aqueous phase being alkaline. CH_2Cl_2 (300 mL) was added to the dark blue mixture, which was then filtered through Celite®. The two phases of the filtrate were separated and the aqueous one was extracted once with CH_2Cl_2 (300 mL). The combined organic phase and extract was washed with water, aqueous 2N HCl and brine, dried with anhydrous $MgSO_4$, filtered and concentrated in vacuo to give a semisolid residue that was crystallized from CH_2Cl_2 to give pinacol **5** (732 mg, 95% yield). The spectroscopic data of **5** were identical to those previously published [8].

5,6,9,10-Tetrahydro-5,8:7,10-dimethanobenzocyclooctene-7,8-diol, (7)

As described for **5**, starting from 5,6,8,9,-tetrahydro-5,9-propano-7*H*-benzocycloheptene-7,11-dione (1.50 g, 7.0 mmol), pinacol **7** was obtained as a white solid (1.46 g, 96.3% yield). The spectroscopic data of **7** were identical to those previously published [8].

3,7-Dimethyl-1,5-sulfinyldioxytricyclo[3.3.0.0^{3,7}]octane, (4a)

Pinacol **3a** (592 mg, 3.52 mmol) was solved in CH_2Cl_2 (12 mL) at room temperature and thionyl chloride (0.42 mL, 5.77 mmol) in CH_2Cl_2 (4.2 mL) was added dropwise. The solution was stirred at room temperature for 1 h and concentrated under reduced pressure to give a dark solid (754 mg) that was purified by column chromatography (pentane) to give sulfite **4a** as a white solid (673 mg, 89% yield). An analytical sample of **4a** was obtained by crystallization from EtOAc/hexane, mp 49-50 ºC (EtOAc/hexane); IR (KBr) ν 2943, 2929, 2366, 1478, 1380, 1293, 1260, 1225, 1206, 1168, 1033, 1010, 838, 794, 691, 519, 460 cm^{-1}; ^1H NMR δ: 1.11 (s, 3 H) and 1.12 (s, 3H) [C$\underline{H}_3$-C(3) and C$\underline{H}_3$-C(7)], 1.75 (dd, J = 7.5 Hz, J' = 3.5 Hz, 2 H) [2(4)-H_α or 6(8)-H_α], 1.92 (d, J = 7.5 Hz, 2 H) [2(4)-H_β or 6(8)-H_β], 2.00 (d, J = 8.0 Hz, 2 H) [6(8)-H_β or 2(4)-H_β], 2.08 (dd, J = 8.0 Hz, J' = 3.5 Hz, 2 H) [6(8)-H_α or 2(4)-H_α]; ^{13}C NMR δ: 16.4 (CH_3) and 16.5 (CH_3) [$\underline{C}H_3$-C(3) and $\underline{C}H_3$-C(7)], 46.7 (C) and 46.9 (C), (C3 and C7), 54.9 (CH_2) and 56.2 (CH_2) [C2(4) and C6(8)], 94.6 [C, C1(5)]. MS (EI), m/z (%): 214 ($[M]^+$, 1), 150 ($[M-SO_2]^+$, 86), 135 (31), 133 (31), 132 (62), 131 (13), 123 (18), 122 (16), 121 (20), 117 (50), 110 (10), 109 (24), 108 (53), 107 (97), 105 (26), 95 (27), 94 (22), 93 (41), 91 (42), 83 (37), 82 (28), 81 (26), 80 (12), 79 (41), 77 (21), 69 (10), 68 (55), 67 (30), 65 (11), 55 (100), 52 (21), 77 (41), 69 (100). Accurate mass measurement: calcd for $C_{10}H_{15}O_3S$ ($[M+H]^+$): 215.0736; found: 215.0740.

3,7-Tetramethylene-1,5-sulfinyldioxytricyclo[3.3.0.0^{3,7}]octane, (4b)

As described for **4a**, starting from pinacol **3b** (500 mg, 2.57 mmol), sulfite **4b** was obtained as a white solid (408 mg, 66% yield). An analytical sample of **4b** was obtained by crystallization from EtOAc/hexane, mp 69-70 ºC (EtOAc/hexane); IR (KBr) ν 2986, 2941, 2855, 1740, 1477, 1457, 1289, 1264, 1225, 1203, 1116, 1080, 1010, 932, 799, 693, 654, 528, 515 cm^{-1}; ^1H NMR δ: 1.57 (complex signal, 4 H) [C$\underline{H}_2$CH$_2$-C(3) and C$\underline{H}_2$CH$_2$-C(7)], 1.65 (complex signal, 4 H) [C$\underline{H}_2$-C(3) and C$\underline{H}_2$-C(7)], 1.78 (dd, J = 7.5 Hz, J' = 3.5 Hz, 2 H) [2(4)-H_α or 6(8)-H_α], 2.06-2.12 (complex signal, 4 H) [2(4)-H_β or 6(8)-H_β and 6(8)-H_α or 2(4)-H_α], 2.19 (d, J = 8.0 Hz, 2 H) [6(8)-H_β or 2(4)-H_β]; ^{13}C NMR δ: 17.9 (CH_2) and 18.0 (CH_2) [$\underline{C}H_2$CH$_2$-C(3) and $\underline{C}H_2$CH$_2$-C(7)], 25.0 (CH_2) and 25.1 (CH_2) [$\underline{C}H_2$-C(3) and $\underline{C}H_2$-C(7)], 46.6 (C) and 46.8 (C), (C3 and C7), 52.5 (CH_2) and 53.8 (CH_2) [C2(4) and C6(8)], 94.4 [C, C1(5)]. MS (EI), m/z (%): 240 ($[M]^+$, 2), 192 ($[M-SO]^+$, 14), 176 ($[M-SO_2]^+$, 40), 175 (17), 164 (14), 162 (11), 161 (90), 150 (20), 149 (31), 148 (48), 147 (48), 144 (11), 143 (10), 136 (17), 135 (27), 134 (46), 133 (82), 131 (11), 122 (18), 121 (34), 120 (39), 119 (38), 118 (13), 117 (14), 109 (12), 108 (54), 107 (58), 106 (34), 105 (56), 96 (12), 95 (41), 94 (19), 93 (66), 92 (30), 91 (100), 82 (15), 81 (23), 80 (24), 79 (89), 78 (14), 77 (51), 68 (24), 67 (32), 65 (21), 55 (16), 53 (25).

3-Methyl-7-phenyl-1,5-sulfinyldioxytricyclo[3.3.0.0^{3,7}]octane, (4c)

As described for **4a**, starting from pinacol **3c** (539 mg, 2.34 mmol), sulfite **4c** was obtained as a white solid (460 mg, 71% yield). An analytical sample of **4c** was obtained by crystallization from EtOAc/hexane, mp 109-110 ºC (EtOAc/hexane); IR (KBr) ν 3037, 2997, 2956, 2919, 2897, 2862, 1958, 1604, 1500, 1476, 1449, 1376, 1331, 1294, 1262, 1206, 182, 1157, 1137, 1058, 1021, 992, 976, 913, 840, 791, 757, 697, 687, 663, 583, 532, 511, 477 cm^{-1}; ^1H NMR δ: 0.77 [s, 3 H, CH$_3$-C(3)], 1.90 (dd, *J* = 8.0 Hz, *J'* = 3.5 Hz, 2 H) [2(4)-H_α or 6(8)-H_α], 2.06 (d, *J* = 8.0 Hz, 2 H) [2(4)-H_β or 6(8)-H_β], 2.33 (dd, *J* = 8.0 Hz, *J'* = 3.5 Hz, 2 H) [6(8)-H_α or 2(4)-H_α], 2.69 (d, *J* = 8.0 Hz, 2 H) [6(8)-H_β or 2(4)-H_β], 7.20 (m, 2 H, Ar-H_{ortho}), 7.27 (tt, 1 H, *J* = 7.5 Hz, *J'* = 1.5 Hz, Ar-H_{para}), 7.36 (m, 2 H, Ar-H_{meta}); ^{13}C NMR δ: 18.4 [CH$_3$, CH$_3$-C(3)], 49.7 (C, C3), 54.2 (CH_2) and 54.7

(CH_2) [C2(4) and C6(8)], 55.0 [C, C1(5)], 94.5 (C, C7), 126.8 (CH, C_{para}), 127.9 (CH, C_{ortho}), 128.2 (CH, C_{meta}), 139.0 (C, C_{ipso}). MS (EI), *m*/*z* (%): 276 ($[M]^{\cdot+}$, 1), 228 ($[M-SO]^{\cdot+}$, 1), 212 ($[M-SO_2]^{\cdot+}$, 4), 195 (31), 194 (100), 193 (11), 179 (24), 170 (14), 169 (20), 141 (12), 129 (11), 128 (14), 117 (22), 115 (31), 91 (20), 77 (10), 55 (13). Anal. Calcd for $C_{15}H_{16}O_3S$ (276.35): C 65.19, H 5.84, S 11.60. Found: C 65.26, H 5.81, S 11.43.

3,7-(2,2'-Biphenylene)-1,5-sulfinyldioxytricyclo[3.3.0.0^{3,7}] octane, (4d)

As described for **4a**, starting from pinacol **3d** (700 mg, 2.41 mmol), sulfite **4d** was obtained as a white solid (543 mg, 67% yield). An analytical sample of **4d** was obtained by crystallization from EtOAc/hexane, mp 178-179 ºC (EtOAc/hexane); IR (KBr) ν 2925, 1442, 1275, 1257, 1205, 1153, 1109, 1078, 998, 928, 794, 757, 728, 690, 546, 507 cm^{-1}; ^1H NMR δ: 2.38 (dd, *J* = 8.0 Hz, *J'* = 4.0 Hz, 2 H) [2(4)-H_α or 6(8)-H_α], 2.44 (d, *J* = 8.0 Hz, 2 H) [2(4)-H_β or 6(8)-H_β], 2.53 (d, *J* = 8.0 Hz, 2 H) [6(8)-H_β or 2(4)-H_β], 2.71 (dd, *J* = 8.0 Hz, *J'* = 4.0 Hz, 2 H) [6(8)-H_α or 2(4)-H_α], 7.14-7.23 (complex signal, 6 H, Ar-H), 7.83-7.88 (complex signal, 2 H, Ar-H); ^{13}C NMR δ: 47.9 (C) and 48.1 (C), (C3 and C7), 56.4 (CH_2) and 57.7 (CH_2) [C2(4) and C6(8)], 93.7 [C, C1(5)], 123.1 (CH), 123.2 (CH), 127.2 (CH), 127.3 (CH), 127.5 (CH), 127.6 (CH), 128.4 (CH) and 128.6 (CH) (Ar-CH), 130.4 (C), 130.6 (C), 134.6 (C) and 134.7 (C) (Ar-C). MS (EI), *m*/*z* (%): 288 ($[M-SO]^{\cdot+}$, 72), 232 (20), 231 (100), 215 (10), 204 (30), 203 (77), 202 (45), 189 (10), 101 (10). Anal. Calcd for $C_{20}H_{16}O_3S{\cdot}0.5C_6H_{14}$ (379.49): C 72.80, H 6.11, S 8.45. Found: C 73.14, H 5.68, S 8.16.

3,7-Sulfinyldioxytricyclo[3.3.1.0^{3,7}]nonane, (6)

As described for **4a**, starting from pinacol **5** (299 mg, 1.94 mmol), sulfite **6** was obtained as a white solid (252 mg, 65% yield). An analytical sample of **6** was obtained by crystallization from EtOAc/hexane, mp 76-77 ºC (EtOAc/hexane); IR (KBr) ν 2949, 2880, 2858, 1459, 1340, 1304, 1205, 1129, 1098, 997, 967, 938, 857, 833, 803, 778, 705, 670, 627, 615, 486 cm^{-1}; ^1H NMR δ: 1.50 (tm, *J* = 2.5 Hz, 2 H, 9-H_2), 1.98-2.04 [complex signal, 4 H, 2(8)-H_2 or 4(6)-H_2], 2.18 [dt, J = 11.5 Hz, J' = 2.0 Hz, 2 H4(6)-H_α or 2(8)-H_α], 2.46 [dm, *J* = 11.5 Hz, 2 H, 4(6)-H_β or 2(8)-H_β], 2.62-2.67 (complex signal, 2 H, 1-H and 5-H); ^{13}C NMR δ: 33.4 (CH_2, C9), 40.6 (CH) and 41.8 (CH) (C1 and C5), 48.3 (CH_2) and 50.2 (CH_2) [C2(8) and C4(6)], 100.2 [C, C3(7)]. MS (EI), *m*/*z* (%): 200 ($[M]^{\cdot+}$, 1), 152 ($[M-SO]^{\cdot+}$, 5), 142 (12), 136 ($[M-SO_2]^{\cdot+}$, 57), 135 (100), 108 (14), 107 (10), 95 (69), 94 (26), 93 (19), 92 (14), 91 (12), 79 (21), 78 (20), 77 (11), 68 (18), 67 (33), 66 (11). Anal. Calcd for $C_9H_{12}O_3S$ (200.25): C 53.98, H 6.04, S 16.01. Found: C 54.30, H 6.08, S 15.65.

7,8-Sulfinyldioxy-5,6,9,10-tetrahydro-5,8:7,10-dimethanobenzocyclooctene, (8)

As described for **4a**, starting from pinacol **7** (1.46 g, 6.74 mmol), sulfite **8** was obtained as a white solid (1.15 g, 65% yield). An analytical sample of **8** was obtained by crystallization from EtOAc/hexane, mp 149-150 ºC (EtOAc/hexane); IR (KBr) ν 3062, 3018, 2978, 2867, 1488, 1454, 1312, 1281, 1228, 1205, 1125, 1053, 937, 920, 864, 810, 765, 712, 685, 671, 623, 597, 565, 526, 484, 465 cm^{-1}; ^1H NMR δ: 2.16 [dd, 2 H, *J* = 12.5 Hz, *J'* = 1.0 Hz, 6(12)-H_β or 9(11)-H_β], 2.30 [dd, 2 H, *J* = 12.5 Hz, *J'* = 1.0 Hz, 9(11)-H_β or 6(12)-H_β], 2.45 [ddd, 2 H, *J* = 12.5 Hz, *J'* = 6.5 Hz, *J''* = 3 Hz, 6(12)-H_α or 9(11)-H_α], 2.98 [ddd, 2 H, *J* = 12.5 Hz, *J'* = 6.5 Hz, *J''* = 3 Hz, 9(11)-H_α or 6(12)-H_α], 3.53 (t, 1 H, *J* = 6.5 Hz, 5-H or 10-H), 3.57 (t, 1 H, *J* = 6.5 Hz, 10-H or 5-H), 7.16-7.20 (complex signal, 4 H, Ar-H); ^{13}C NMR δ: 47.4 (CH) and 48.4 (CH) (C5 and C10), 48.1 (CH_2) and 49.9 (CH_2) [C6(12) and C9(11)], 105.5 [C, C7(8)], 127.0 (CH) and 127.1 (CH) (C1 and C4), 129.6 (CH) and 129.7 (CH) (C2 and C3), 142.6 (C) and 143.2 (C) (C4a and C10a). MS (EI), *m*/*z* (%): 262 ($[M]^{\cdot+}$, 62), 214 ($[M-SO]^{\cdot+}$, 6), 204 (37), 199 (12), 198 ($[M-SO_2]^{\cdot+}$, 56), 197 (57), 186 (12), 172 (22), 169 (14), 157 (47), 156 (27), 155 (73), 153 (12), 144 (30), 143 (15), 142 (17), 141 (56), 130 (37), 129 (100), 128 (92), 127 (28), 116 (20), 115 (66), 77 (11). Anal. Calcd for $C_{14}H_{14}O_3S$ (262.32): C 64.10, H 5.38, S 12.22. Found: C 64.08 H 5.41, S 12.03.

Antiviral Evaluation

The antiviral activity of the compounds was determined in established cell culture assays using a selection of DNA and RNA viruses, including three subtypes of influenza virus [A/Puerto Rico/8/34 (H1N1); A/Hong Kong/7/87 (H3N2) and B/Hong Kong/5/72] [13]. The compounds' inhibitory effect on virus replication as well as their cytotoxicity were monitored by microscopical examination, and confirmed by the colorimetric MTS cell viability assay.

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