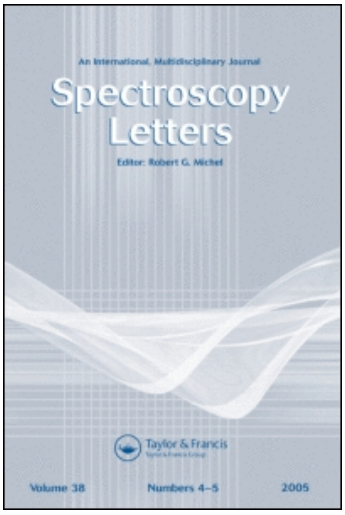

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FUNCTIONALIZED PINOLS: ^{13}C AND ^{1}H NMR SPECTRA ASSIGNMENTS AND STRUCTURES

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ABSTRACT

Aqueous cohalogenation reactions of *cis*-carveol and of α-terpineol afford respectively the 2,6-dimethyl-6-iodomethyl-7-oxabicyclo[3.2.1]oct-2-ene and 2,6,6-trimethyl-7-oxabicyclo [3.2.1]octan-2-ol. Previous structural analysis involving such functionalized pinols have lacked justification of the proposed relative configuration of the substituents and detail of the ^{1}H and ^{13}C NMR spectra assignments. Thus, a full structure and NMR analysis for these two bicyclic compounds are presented by way of 2D NMR experiments, ^{1}H spectra simulations and AM1 calculations.

Key Words: Functionalized pinols; ^{1}H and ^{13}C NMR; ^{13}C-Pendant; COSY-45; COSY-DQF; HMQC; HMBC; NOESY; ^{1}H spectra simulations.

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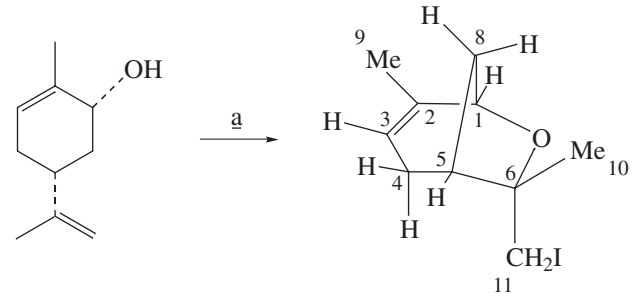
INTRODUCTION

Electrophilic halogenation of alkenes to produce vicinal dihaloalkanes is a well-known reaction in organic chemistry (1). However, when the halogenation of the alkene is carried out in a nucleophilic solvent (water, alcohols, etc), difunctionalized products (halohydrins, β-halo ethers, etc) are obtained (2). This process, termed 'cohalogenation', is useful for diverse synthetic applications (3) and we found that cohalogenation of diverse olefins is easily achieved in the presence of metal salts (4). Thus, the reaction of *cis*-carveol (1) and α-terpineol (3) with I_2 / H_2O / Cu(II) produced the pinol bicyclic ethers (2) and (4), respectively, through an intramolecular cohalogenation process as shown in the following scheme (5).



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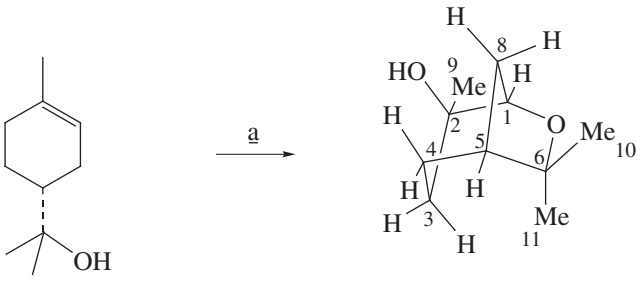

3 **4**

a = I_2/H_2O/Dioxane/$Cu(OAc)_2.H_2O$/rt

The only reported data for compound (2), 2,6-dimethyl-6-iodomethyl-7-oxabicyclo[3.2.1]oct-2-ene, include IR and a low field ^{1}H NMR (60 MHz) (6). The relative configuration of the C-6 substituents were not established despite its

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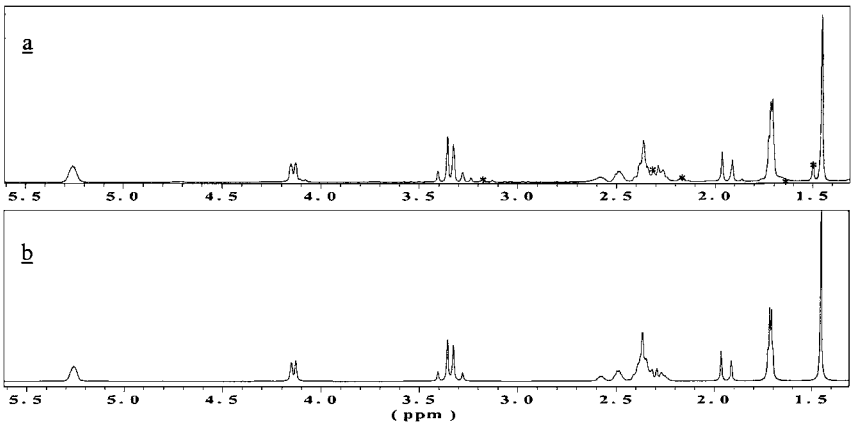

Figure 1. 200.13 MHz experimental a and simulated b ^{1}H NMR spectrum of compound (2) in $CDCl_3$, (*) impurities.

importance in view of mechanistic considerations involved in the reaction process. The compound (4), 2,6,6-trimethyl-7- oxabicyclo[3.2.1]octan-2-ol, has been analyzed previously in some detail, mainly with respect to the ^{13}C NMR spectrum (7,8). Nevertheless the relative configuration of the C-2 substituents and why it

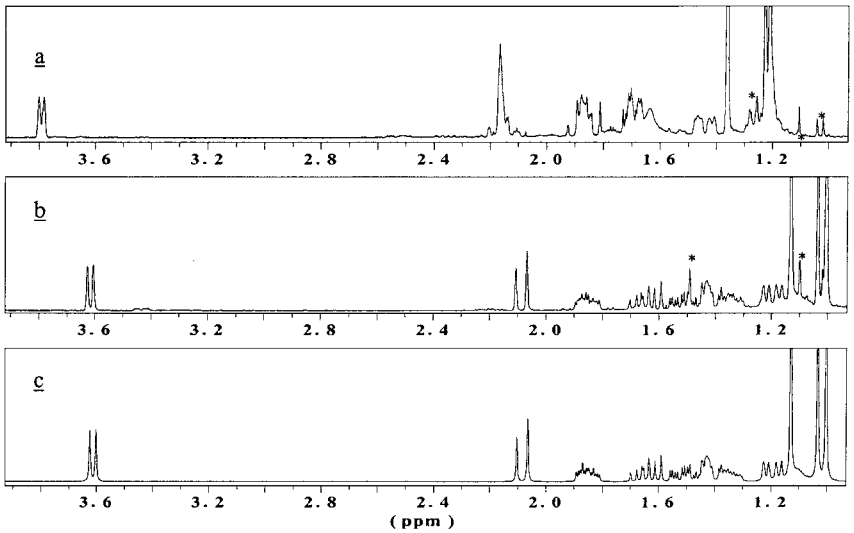

Figure 2. 300.13 MHz experimental a ($CDCl_3$) and b ($C_6D_6/CDCl_3$ 4:1) and simulated c ($C_6D_6/CDCl_3$ 4:1) ^{1}H NMR spectrum of compound (4), (*) impurities.

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was assumed (intuitively) that the six membered ring adopts a chair conformation was not justified. The ^{1}H data, even at 400 MHz, is limited and the ^{13}C spectra assignments are mainly supported by empirical considerations.

In fact, the main problems in analyzing the bicyclic systems (2) and (4) are with respect to the ^{1}H NMR spectra assignments. As shown in Fig. 1a and 2a several signals are overlapped and involved not only in geminal and/or vicinal couplings but also in long range couplings (9). Thus, in this work we present the complete spectra analysis for these two compounds. The study was supported by 2D NMR experiments (10), AM1 calculations and ^{1}H spectra simulations. The most suitable solvent for improving the dispersion of the signals in the ^{1}H spectrum for compound (4) was also determined.

RESULTS AND DISCUSSION

FT-IR of compound (2) indicates the presence of C═C, C–O and C–I bonds and HRGC-MS leads to the molecular formula $C_{10}H_{15}IO$. A rapid inspection of the ^{13}C-Pendant (11) spectrum shows the following groups: one CH═C (δ 120.72 and 139.77), one C–O (δ 84.08), one CH–O (δ 77.56), one methyne (δ 40.73), three methylenes (δ 14.21, 29.72 and 35.07) and two methyls (δ 21.36 and 27.89). The above data confirm that the structure of compound (2) must be the proposed iodobicyclic ether (a pinol derivative). At this point it is of prior importance to assign the ^{1}H NMR spectrum in such a manner to avoid extensive comparisons with data of related structures described earlier (that could have eventual errors due to limitations of the equipment and techniques available).

The COSY-45 experiment of compound (2) shows that one of the C-4 hydrogens is located at δ2.52 (broad doublet, 17.90 Hz) and the other between δ 2.20-2.45 (both show cross signals with the H-3 broad singlet at δ 5.26), and that one of the C-8 hydrogens is located at δ 1.94 (doublet, 10.77 Hz) and the other also between δ 2.20-2.45 (both show cross signals with the H-1 broad doublet at δ 4.14). The last methylene group C-11 appears as AB doublets (9.75 Hz) at δ 3.37 and 3.31 where both show correlation with the H-10 singlet at δ 1.45 due to $^{4}J_{H,H}$. Long range couplings are readily detected in the COSY-45 experiment and can be measured directly (e.g. for the H-9 broad quartet at δ 1.71 with the C-3 and C-4 hydrogens, $^{4}J_{H,H}$ 1.75 Hz and $^{5}J_{H,H}$ 1.83 and 2.01 Hz) or not (e.g. H-11 at δ 3.31 with H-8a at δ 1.94, thus resulting in additional line broadening of the signals) in the ^{1}H spectrum. As expected from the AM1 calculations H-8a (δ 1.94) appears only as a doublet due to geminal coupling with H-8e and no $^{3}J_{H,H}$ with H-1 or H-5 is observed in the ^{1}H spectrum due to unfavorable dihedral angles ($\phi \sim 90^{\circ}$). All these informations were used in the ^{1}H spectrum simulation (Fig. 1b) and are also described in the ^{1}H data of Table 1.

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Table 1. ^{1}H and ^{13}C Chemical Shifts and ^{1}H Coupling Constants for Compound (2)

C	H	δ_C	δ_H(J/Hz)*
1	1	77.56	4.14 bd (4.91, 0.88, 0.62, 0,53)
2	–	139.77	-
3	3	120.72	5.26 bs (3.11, 3.02, 1.75, 0.53)
4	*pax*	29.72	2.31 m (17.90, 3.20, 3.02, 1.83)
	peq		2.52 bd (17.90, 3.11, 2.51, 2.01, 0.96)
5	5	40.73	2.38 m (4.46, 3.20, 2.51, 1.24, 0.88, 0.60)
6	–	84.08	–
8	eq	35.07	2.32 m (10.77, 4.91, 4.46, 0.96)
	ax		1.94 d (10.77, 0.62, 0.60, 0.41)
9	9	14.21	1.71 bq (2.01, 1.83, 1.75, 0.41)
10	10	27.89	1.45 s (0.63)
11	A	21.36	3.37 d (9.75)
	B		3.31 d (9.75, 0.63)

$(*)^{n} J_{H,H} < 1.5$ Hz were estimated from the signal linewidths and/or by the ^{1}H spectrum simulation.

The HMQC spectrum confirms the pairs of hydrogen atoms in each methylene group as each methylene carbon atom shows two distinct cross signals with respect to the ^{1}H axis (F2). The H-5 chemical shift was located by this experiment as part of the multiplets between δ 2.20-2.45 as in the case of H-8e and one of the C-4 hydrogens. In fact, the δ_H assignments (Table 1) for these three overlapped hydrogens were measured by such correlations and also used in the ^{1}H spectrum simulation (Fig. 1b).

With the aid of a NOESY experiment it was feasible to establish the relative configuration of the C-6 substituents and also to distinguish between the C-4 hydrogens. Thus, the experiment revealed that C-10 occupies the *exo* position due to correlation of H-10 with H-8e, and that C-11 occupies the *endo* position due to correlation with one of the C-4 hydrogens that can only be the H-4pe (δ 2.52). The *pseudo* (p) notation was used for the former in view that due to the double bond (C-2/C-3) and the bridge (C-1/C-5/C-8) the six membered ring being nearly planar from C-1 to C-5.

A FT-IR of compound (4) indicates the presence of O−H and C−O bonds and the HRGC-MS leads to the molecular formula $C_{10}H_{17}O_2$. Inspection of the ^{13}C-Pendant (11) spectrum reveals the following groups: two C–O (δ 80.83 and 70.54), one CH–O (δ 81.50), one methyne (δ 40.32), three methylenes (δ 32.02, 30.73 and 23.33) and three methyls (29.09, 27.51 and 22.22). The above data confirms that compound (4) structure has the proposed hydroxypinol. Following the same line of analysis as applied to compound (2) it was imperative to resolve all signals in

the ^{1}H spectrum. However, as can be seen in Fig. 2a, this is unfeasible in $CDCl_3$ solution. At this point it was necessary to find a better solvent media, to allow greater dispersion of the signals at 300 MHz (unfortunately, a test at 600 MHz did not show significant improvement in the signal dispersion). The result of this solvent media trial, pure and mixtures, lead to a mixture of 4:1 of C_6D_6 and $CDCl_3$ in which all eleven groups of each equivalent hydrogens present are adequately separated (Fig. 2b). At prior importance was the separation gained between the two more shielded methyls, approximately 0.1 ppm (∼30 Hz) separation in $CDCl_3$ and approximately 0.3 ppm (∼90 Hz) in the solvent mixture, thus allowing a perfect configurational analysis using the NOESY technique, *vide infra*.

A *gs*-DQF-COSY experiment (*gs*, gradient selected) of compound (4) shows similar features to the COSY-45 experiment for compound (2): correlations due to geminal and vicinal couplings and several due to long range couplings. The assignment of the methylene groups is easily done by the *gs*-HMQC experiment in the same way. Long range H,H couplings are really detected in the *gs*-DQF-COSY experiment and can be measured directly (e.g. for the H-4e triple triplet at δ 1.35 with the H-8e multiplet at 1.86, $^4J_{H,H}$ 2.45 Hz) or not (e.g. H-10 at δ 1.01 with H-11 at δ 1.13, resulting in additional line broadening of the signals) in the ^{1}H spectrum. As expected from the AM1 calculations H-8a (δ 2.09) also appears, as for compound (2), like a doublet in the ^{1}H spectrum due to unfavorable dihedral angles ($\phi \sim 90^\circ$) with H-1 or H-5 ($^3J_{H,H}$), showing only a measurable coupling with H-8e (δ 1.86, 11.70 Hz). The same structural feature also explains why the H-3e (δ 1.20) appears only as a broad double doublet (couplings with H-3a and H-4a, 14.45 and 6.50 Hz) and does not present measurable additional splitting due to coupling with H-4e (δ 1.35). The hydroxyl hydrogen appears as a very broad singlet at δ 1.12 as determined by an exchange ^{1}H NMR experiment with D_2O. All this information was used in the ^{1}H spectrum simulation (Fig. 2c) and is also described in the ^{1}H data of Table 2.

The *gs*-HMBC experiment ratifies all the ^{13}C spectrum assignments and mainly allows the distinction between C-2 and C-6 due to different cross signals in the spectrum. The former shows correlation with the C-9 methyl hydrogens (δ 1.04) and the second shows correlations with both the C-10 and C-11 methyls hydrogens (δ 1.01 and δ 1.13). The NOESY experiment was very helpful to discern between the H-10 and H-11 methyls and mainly to determine the relative configuration of C-2. Thus, the C-10 hydrogens (δ 1.01) show correlation with H-8e (δ 1.86) and the C-11 hydrogens (δ 1.13) show correlations with H-3a (δ 1.64). The latter correlation is very significant for confirming the chair conformation of the six membered ring and is further ratified by complete absence of corelations between any of C-3 hydrogens and H-8a (the chair conformation is also preferred to the boat by AM1 calculations). Finally, the absence of a signal between the C-9 methyl hydrogens and H-8a show that H-9 can only occupy an equatorial position.

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Table 2. ^{1}H and ^{13}C Chemical Shifts and ^{1}H Coupling Constants for Compound (4)

C	H	δ_C	δ_H(J/Hz)*
1	1	81.50	3.62 bd (6.50, 0.50, 0.40)
2	–	70.54	–
3	ax	32.02	1.64 ddd (14.545, 12.96, 6.90)
	eq		1.20 bdd (14.45, 6.50, 0.80, 0.60)
4	ax	23.33	1.51 dddd (13.98, 12.96, 6.50, 2.84)
	eq		1.35 tt (13.98, 6.90, 3.05, 2.45, 0.80)
5	5	40.32	1.43 m (4.50, 3.05, 2.84, 0.61, 0.60, 0,50)
6	–	80.83	–
8	eq	30.73	1.86 m (11.70, 6.50, 4.50, 2.45)
	ax		2.09 bd (11.70, 0.61, 0.42, 0.40)
9	9	27.51	1.04 s
10	10	29.09	1.01 bs (0.62)
11	11	22.22	1.13 bs (0.62, 0.42)
–	OH	–	1.12 bs

$(*)^{n} J_{H,H} < 1.5$ Hz were estimated from the signal linewidths and/or by the ^{1}H spectrum simulation.

EXPERIMENTAL

Compounds (1) and (3) were purchased from Aldrich and compounds (2) and (4) were synthesized as described (5) and purified by radial chromatography (kieselgel/$CHCl_3$). Infrared spectra were recorded on a PE1600 FTIR spectrometer and the mass spectra were recorded on a HP5896-A HRGC-MS spectrometer.

NMR spectra were recorded at 200.13 MHz (^{1}H) and 50.33 MHz (^{13}C) in $CDCl_3$ solution (14 mg/ml in 5mm tubes) for compound (2) and at 300.13 MHz (^{1}H) and 75.47 MHz (^{13}C) in $C_6D_6/CDCl_3$ 4:1 solution (10 mg/ml in 5mm tubes) for compound (4), respectively with spectral widths of 1.5KHz/8.0KHz for the former and of 2.2KHz/12.0KHz for the second, using TMS as internal reference at 298K for both. All experiments were run with a relaxation delay of 1.8 s, 32K (^{1}H) and 64K (^{13}C) data points for 1D experiments and 2048 × 256 data matrixes for COSY-45, NOESY(mixing time of 800 ms), COSY-DQF, HMQC and HMBC. Gradient selections were used in the three last 2D techniques for compound (4). Zero filling and/or linear predictions were used in all 2D experiments. Pulse programs and data processings were performing using Xwin-Nmr 1.3/9 software from Bruker A. M. GMBH. The AM1 calculations were done with Spartan Plus software from Wavefunction Inc. The ^{1}H simulations were executed with the WinDasy 2.0/WinNmr 5.1 package from Bruker A. M. GMBH.

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REFERENCES

1. De La Mare P.B.D. *Electrophilic Halogenation*, London: Cambridge University Press, 1976.
2. Rodriguez J. M., Dulcère J. P. *Cohalogenation in Organic Synthesis*, Synthesis 1993: 1177–1205.
3. Spargo P. L.*Organic Halides*, Comtemp. Org. Synthesis 1995, 2: 85–105.
4. de Mattos M. C. S., Sanseverino A. M. *An Easy and Efficient Synthesis of Iodohydrins from Alkenes*, J.Chem Res.(S) 1994: 440–441.
5. da Silva F.M., Jones Jr. J, de Matto M.C.S., *Reaction of Terpenic Unsaturated Alcohols with I_2/H_2O in the Presence of $Cu(OAc)_2$*, VII Brazilian Meeting on Organic Synthesis, Rio de Janeiro 1996, Abstracts 146.
6. Yasui K., Fugami K., Tanaka S., Tamaru Y. *Unsymmetrical Ketone Synthesis via a Three-Component Connection Reaction of Organozincs, Allylating Agents and Carbon Monoxide*, J. Org. Chem. 1995, 60: 1365–1380.
7. Carman R. M., Fletcher M. T. *Halogenated Terpenoids. XX The Seven Monochlorocineoles*, Aust. J. Chem 1983, 36:1483–1493.
8. Carman R. M., Fletcher M. T., Lambert L. K. *NMR Assignments for Some 2-substituted 2,6,6-Trimethyl-7-oxa-bicyclo[3.2.1]octanes (Dihydropinols)*, Magn. Reson. Chem. 1988, 26: 271–272.
9. Barfield M., Chakrabarti B. *Long-Range Proton Spin-Spin Coupling*, Chem. Rev. 1969, 69: 757–778.
10. Croasmun W. R., Carlson R. M. K. (Eds.) *Two-Dimensional NMR Spectroscopy*, 2nd ed. New York: VCH, 1994.
11. Homer J., Perry M. C. *New Method for NMR Signal Enhancement by Polarization Transfer, and Attached Nucleus Testing*, J. Chem. Soc. Chem. Commun. 1994: 373–374.

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