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Synthesis, ^{17}O NMR spectroscopy and structure of 2-trifluoroacetyl-1-methoxycycloalkenes

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Abstract

Among the synthesis of a series of five well-known 2-trifluoroacetyl-1-methoxycycloalkenes derived from cyclopentanone and substituted cyclohexanones, this paper describes the synthesis of three new 2-trifluoroacetyl-1-methoxycycloalkenes derived from cycloheptanone, cyclooctanone and cyclododecanone in 60–68% yield. Subsequently, the ^{17}O NMR chemical shift analysis of the carbonyl and the methoxy groups for these cyclic molecules clearly showed the electron *push–pull* phenomenon and revealed large and irregular variations of ^{17}O NMR chemical shifts with the ring size. Finally, a more stable conformation of these trifluoroacetyl-containing cycloalkenes was determined by energy minimization calculations using Austin Model 1 (AM1) semi-empirical method and correlations between ^{17}O NMR data and torsion angles or oxygen net charge calculated by AM1 semi-empirical method were performed.

Keywords: ^{17}O NMR; NMR; Trifluoroacetylcycloalkenes; Cycloalkanones; Methoxycycloalkenes; Enones

1. Introduction

Historically, β-alkoxyvinyl trihalomethyl ketones derivated from cyclopentanone and cyclohexanone have been developed by our research group [1a]. The results obtained from the reaction of these carbocyclic trihaloacetylated enolethers with some dinucleophiles are very interesting [1–5]. Parallel to the synthetic works, some publications have reported studies about the molecular structure of some heterocyclic compounds derived from 2-trihaloacetyl-1-methoxycyclohexen using ^{1}H and ^{13}C NMR spectroscopy, X-ray diffraction and semi-empirical MO calculation tools [6,7].

On the other hand, since the 60s, ^{17}O NMR spectroscopy is becoming an increasing important method in organic chemistry for examining a wide variety of structural problems [8] and it provides insights into the understanding of chemical reactivity [9].

Recently, it was reported that the cyclization reactions between acyclic β-alkoxyvinyl trifluoromethyl ketone, derived from phenones and urea, to obtain phenyl substituted 2(1*H*)-pyrimidinones [10], strongly depended on the conformation of the enone precursors. The MO calculations carried out by the Austin Model 1 (AM1) semi-empirical method demonstrated that the conformation of these acyclic β-alkoxyvinyl trifluoromethyl ketones is the main factor to explain the yields of these reactions. In fact, when electron *push–pull* structures are available, the electronic density of each atom of this system is directly related to conformation. In β-alkoxyvinyl trifluoromethyl ketones, due to the possibility of p-π electronic conjugation, the ^{17}O NMR chemical shifts of the carbonyl and methoxy oxygen's are related to the electronic density of both oxygens; moreover, the value of the chemical shift depends essentially on the efficiency of this conjugative interaction. Considering the

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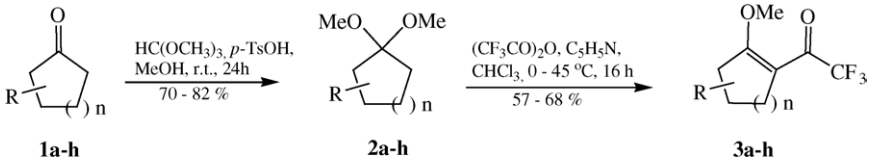


1-3	a	b	c	d	e	f	g	h
R	H	H	6-Me	4-Me	4-*t*-Bu	H	H	H
n	1	2	2	2	2	3	4	8

Scheme 1. Synthetic route for trifluoroacetylcycloalkenes.

electron *push–pull* structure of these substrates, where there is a donor group (OMe) and an acceptor group (CO), they can be used as good models to study the relationships between the ^{17}O NMR chemical shifts and the conformations with the advantage of allowing direct observation of the two oxygen sites involved.

On the other hand, the effect of the ring size and its conformations on ^{17}O NMR of the carbonyl and methoxy chemical shifts for 2-trifluoroacetyl-1-methoxycycloalkenes (cyclic β-alkoxyvinyl trifluoromethyl ketones) have not been systematically studied and in due to the importance of such systems to synthetic chemistry, the additional information which may be obtained on the electronic distribution of these compounds, by employing ^{17}O NMR spectroscopy methodology, seems likely to be valuable.

The influence of electronic and steric effects, torsion angles, electron density on ^{17}O NMR chemical shifts of anthraquinones and flavones [11], methyleneindanones [12], aromatic carbonyl [13] and nitro compounds [14] has also recently been well documented and various correlation analyses have produced quantitative relationship between carbonyl ^{17}O NMR chemical shifts and the substituent constants for aryl carbonyl derivatives including substituted aromatic ketones [15], benzoic esters [16] and aldehydes [17], and chalcones [18]. However, despite the interest in the molecular structure of cyclic β-alkoxyvinyl trifluoromethyl ketones, no systematic effort to correlate these molecular structures with ^{17}O chemical shifts has appeared.

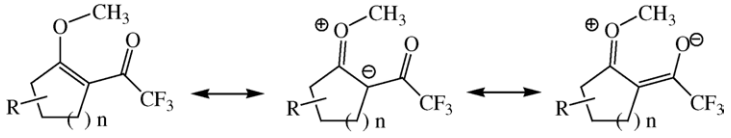
Thus, considering the importance of β-alkoxyvinyl trihalomethyl ketones, as 1,3-dielectrophile precursor and, despite our extensive studies on the NMR spectroscopy of acyclic β-alkoxyvinyl trihalomethyl ketones, we now wish to report the synthesis, ^{17}O NMR study and conformational analysis of a series of eight 4(6)-alkyl-2-trifluoroacetyl-1-methoxycycloalkenes derived from one cyclopentanone, four substituted cyclohexanones and three new larger cycloalkanones.

2. Results and discussion

According to Scheme 1, the cycloalkanone dimethyl acetals **2a–h** were synthesized from the reaction of the respective cycloalkanones **1a–h** with trimethyl orthoformate in molar ratio 1:1.5 and in the presence of *p*-toluenesulfonic acid as catalyst and using anhydrous methanol as solvent by similar procedure described in the literature [1a–d] (Scheme 1). The acylation of **2a–h** with trifluoroacetic anhydride in pyridine, in molar ratio 1:2:2, was carried out in anhydrous chloroform as solvent. Two equivalents of the acylating reagent per dimethyl acetal were necessary to obtain the cyclic β-methoxyvinyl trifluoromethyl ketones **3a–h** since one molecule of the acylating promotes the acylation and a second traps the methoxy group liberated by the ketone dimethyl acetal and to give methyl trifluoroacetate. A mixture of distilled ketone dimethyl acetals, pyridine and anhydrous chloroform is added to pure trifluoroacetic anhydride at 0 °C with cooling in an ice bath. After the addition, the optimal reaction time and reaction temperature for trifluoroacetylation were found to be 16 h at 40–45 °C. Under the conditions employed, ketone dimethyl acetals reacted with trifluoroacetic anhydride to give the cyclic trifluoroacetyl vinyl enones **3a–h** in good yields. In all reactions, we have not found polymerization products and all crude products were purified by distillation. More satisfactory results of these reactions, selected physical (b.p.), NMR and mass spectral data of **3a–h** are presented in the experimental part.

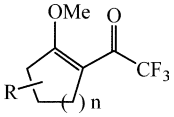
The present compounds **3a–h** can be considered not just as α,β-unsaturated olefinic ethers but also as α,β-unsaturated ketones and, therefore, they can be characterized as possible model for p-π conjugation in the β-methoxyvinyl ketone system (Scheme 2).

In 1994, Taskinen [19] reported the ^{1}H, ^{13}C and ^{17}O NMR data in chloroform-d_1 solution, force field and MNDO calculations of 4- to 9-membered 1-methoxycycloalkenes. The ^{17}O NMR chemical shifts revealed unexpected large and



Scheme 2. The p-π conjugation in the β-methoxyvinyl trifluoromethyl ketone system **3a–h**.

Table 1
^{17}O NMR data for 4(6)-alkyl-2-trifluoroacetyl-1-methoxycycloalkenes (**3a–h**)



No.	*n*	No. of ring atoms	R	C=O (ppm)	*W* 1/2 (Hz)[a]	OCH_3 (ppm)	*W* 1/2 (Hz)[a]
3a	1	5	H	508.45	(550)	92.45	(410)
3b	2	6	H	532.0	(500)	80.0	(430)
3c	2	6	6-Me	545.0	(590)	64.5	(470)
3d	2	6	4-Me	534.03	(710)	79.09	(560)
3e	2	6	4-*t*-Bu	536.77	(900)	79.08	(820)
3f	3	7	H	535.60	(595)	76.89	(590)
3g	4	8	H	486.77	(630)	114.53	(520)
3h	8	12	H	567.0	(900)	55.0	(1700)

[a] Values in parentheses are for peak widths at half-height.

irregular variations with the ring size (14 ppm). According to the author, since the oxygen atom is exocyclic to the cycloalkene ring, the irregularities in the ^{17}O NMR chemical shifts of these compounds was not explainable by variations in the inductive and shielding effects of the different ring sizes. These variations were attributed due to the differences in the relative amounts of planar and non-planar conformers about the CH_3–O–C=C bonds. Taskinen concluded that in addition to the s-*cis* and possibly the planar s-*trans* conformers, varying amounts of non-planar conformers (*gauche*) exist for the methoxy group in the cyclic 1-methoxycycloalkenes [19].

Table 1 contains ^{17}O NMR spectroscopy data for 4(6)-alkyl-2-trifluoroacetyl-1-methoxycycloalkenes (**3a–h**) obtained, at natural abundance, also in chloroform-d_1 solution at 27 °C. The ^{17}O NMR signals for the carbonyl group of these compounds appear between 487 and 567 ppm, a range of 80 ppm and for the methoxy group between 55 and 114 ppm, a range of 59 ppm. In comparison with non-substituted 1-methoxycycloalkenes [19], one can observe that the introduction of a trifluoroacetyl group at the 2-position increased the range of the ^{17}O NMR chemical shifts of the methoxy group of the 5- to 8-membered 1-methoxycycloalkenes from 11 to 22 ppm. According to Table 1, the electron *push–pull* phenomenon can also clearly observed. It is observed for each compound that when the ^{17}O NMR chemical shifts of the carbonyl oxygen increase, the chemical shifts of the methoxy oxygen decrease. The intensity of this phenomenon is variable and may be attributed to different conformations of the CH_3–O–C=C–C=O system resulting in planar and non-planar structures for the Me–O–C=C and C=C–C=O moieties. Accordingly, the variations on the ^{17}O NMR data of **3a–h** may be indicative of varying strengths of p-π conjugation in these compounds. In this case, the highest contribution of p-π interaction is found for compound **3g** (8-membered ring size) and the lowest for **3h** (12-membered ring size). This fact can be proved by the ^{13}C NMR data analysis when the ^{13}C NMR chemical shifts of **3a–b** and **3f–g** are compared with those of the respective

Table 2
^{13}C NMR chemical shifts of 5- to 8-membered 1-methoxycycloalkenes and 2-trifluoroacetyl derivatives (**3**)

1-Methoxycycloalkenes[a]			2-Trifluoroacetyl-1-methoxycycloalkenes (**3**)		
Ring size	C-1	C-2	Ring size	C-1	C-2
5	161.1	93.3	5	177.8	108.1
6	155.4	93.1	6	170.0	110.4
7	162.0	96.0	7	175.4	116.7
8	158.3	94.0	8	185.5	118.3
12	[b]	[b]	12	178.8	109.5

[a] Data from reference [19].
[b] No ^{13}C NMR data.

5- to 8-membered 1-methoxycycloalkenes [19] in Table 2. One can observe that the trifluoroacetyl group at the position 2 induces a remarkable deshielding effect on C-1 (∼18 ppm) and C-2 (∼19.3 ppm). Considering the series **3a–b** and **3f–g**, the deshielding effect is highest at C-1 (27.2 ppm) and C-2 (24.3 ppm) for the 8-membered ring **3g**.

According to Table 1, it is also observed that the ^{17}O NMR data for the methoxy group of **3b–e** (cyclohexen derivatives) show a deshielding effect only for **3c**. We noted that the chemical shift of 6-methyl-2-trifluoroacetyl-1-methoxycyclohexene (**3c**) was downfield from the non-substituted 2-trifluoroacetyl-1-methoxycyclohexene (**3b**) by 15.5 ppm. This shift is presumably, mostly, a result of steric inhibition of p-π electronic conjugation of the methoxy group with the carbonyl group. As expected, we do not observe a deshielding effect when a methyl- or *t*-butyl-substituent is attached at the 4-position for 2-trifluoroacetyl-1-methoxycyclohexenes (**3d**, **3e**). Similar deshielding effect due to the steric effect of a *vicinal* methyl group has been reported in rigid planar molecules, as nitrotoluene [14] and methylanthraquinone [11] derivatives.

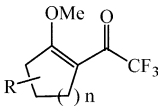
Considering also the work reported by Taskinen [19], we agree that in addition to the s-*cis* and possibly s-*trans* conformers on the Me–O–C=C moiety, varying amounts of non-planar conformers may exist for compounds **3a–h**, when in solution. Moreover, from our point of view, the planarity or non-planarity of the C=C–C=O moiety and the strong electron withdrawing effect of the trifluoromethyl group are also responsible for the variations on both ^{17}O NMR chemical shift values.

The ^{17}O NMR data for compounds **3a–h** presented in Table 1 suggested quantitative relationships between the chemical shifts of the carbonyl oxygen and the oxygen of the methoxy group. A good relationship with $r = 0.9856$ and 95% confidence limits for error in slope was obtained (Eq. (1)). When substituted cyclohexen derivatives (**3c–e**) are not evaluated, a better relationship with $r = 0.9940$ involving non-substituted 5-, 6-, 7-, 8- and 12-membered carbocycles (**3a**, **3b**, **3f–h**) was found (Eq. (2)).

$$\delta_{C=O} = (-1.32 \pm 7.61)\delta_{OMe} + 636.98 \qquad (\mathbf{3a}-\mathbf{h}) \qquad (1)$$

$$\delta_{C=O} = (-1.37 \pm 7.51)\delta_{OMe} + 641.15 \qquad (\mathbf{3a}-\mathbf{b}, \mathbf{3f}-\mathbf{h}) \qquad (2)$$

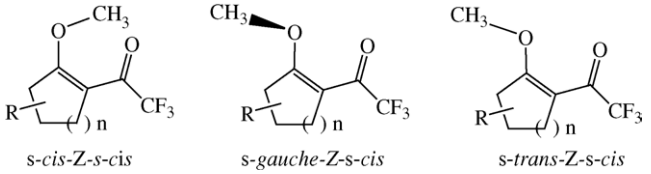
Table 3
Selected structural parameters calculated by AM1 for 4(6)-alkyl-2-trifluoroacetyl-1-methoxycycloalkenes (**3a–h**)



No.	*n*	No. of ring atoms	R	C=C–O (°)	C=C–C=O (°)	C=C–O–C (°)	Oxygen net charges C=O/OCH$_3$	Energy (kcal mol^{-1})
3a	1	5	H	134.73	24.82	1.42	−0.222/−0.172	−74832.26
3b	2	6	H	116.84	35.45	6.68	−0.222/−0.187	−78428.15
3c	2	6	6-Me	127.66	73.89	1.16	−0.219/−0.208	−82018.24
3d	2	6	4-Me	116.90	37.64	7.37	−0.229/−0.213	−82.020.16
3e	2	6	4-*t*-Bu	117.04	38.23	6.54	−0.218/−0240	−92791.69
3f	3	7	H	128.69	72.81	0.15	−0.215/−0.245	−82015.94
3g	4	8	H	127.80	76.27	0.03	−0.212/−0.223	−85607.20
3h	8	12	H	127.03	75.00	1.45	−0.220/−0.225	−99980.33

The predominant conformational structures of compounds **3a–h** were determined by energy minimization calculations using AM1 semi-empirical method. The calculated AM1 data listed in Table 3 show dihedral angles C=C–C=O and C=C–O–Me different of zero and because of this fact, the resonance in the all conjugated system for **3a–h** is not 100%. With the exception of compound **3c** (74°), which present a *vicinal* methyl substituent to the methoxy group, the compounds derived from cyclopentanone or other substituted cyclohexanone show the carbonyl group between 25 and 38° out of C=C–OCH$_3$ plane and the best resonance in this conjugated system. For compound **3c** and cyclic β-alkoxyvinyl trifluoromethyl ketones derived from larger cycloalkanones (**3f–h**), the carbonyl group is between 73 and 77° out of the C=C–OCH$_3$ plane. The AM1 calculations reveals also that the dihedral angle of the C=C–O–Me moiety varies from 0.03° for **3g** and 7.37° for **3d**, as well, that the s-*cis*-*Z*-s-*cis* is the main conformation for compounds **3a**, **3c–h** while that the s-*trans*-*Z*-s-*cis* is the preferred conformation for **3b**, in gas phase. Thus, in this case, the p-π conjugation is more efficient for C=C–O–Me moiety than for C=C–C=O moiety in the molecules **3a–h** (Scheme 3).

Unfortunately, quantitative relationships between the ^{17}O NMR chemical shifts of the carbonyl oxygen and the dihedral angles and the oxygen net charge (Table 1) of compounds **3a–h** show unsatisfactory correlations ($r \leq 0.2000$). However, from our point of view, some other factor(s) must be involved to explain the irregularities in the ^{17}O NMR shift values and the disagreement between the ^{17}O NMR data and some parameters deduced via AM1 calculations.



Scheme 3. Conformers for the β-methoxyvinyl trifluoromethyl ketone system **3a–h**.

The solvent effect on the conformations of **3a–h** could be suggested as an important factor for disagreement between the ^{17}O NMR data obtained in chloroform solution and the parameters obtained via AM1 calculations in gas phase. However, in a recent publication [20], we have reported a multi-linear regression analysis using the Kamlet-Abboud-Taft (KAT) solvatochromic parameters in order to elucidate and quantify the solvent effect on the ^{17}O NMR chemical shifts of two acyclic β-methoxyvinyl trichloromethyl ketones, which presented the resonance in the conjugated system equal and different of 100% (planar and non-planar structures). The chemical shifts of carbonyl group of these molecules showed similar and very low dependencies on the solvent polarity-polarizability, solvent hydrogen-bond-donor acidities (HBD) and hydrogen-bond-acceptor basicities (HBA) and showed a negligible effect on the chemical shifts of the methoxy group. It was observed that the influence of the solvent is weakly considerable on the ^{17}O NMR chemical shifts when an acyclic β-methoxyvinyl trichloromethyl ketone has dihedral angles C=C–C=O and C=C–O–Me equal zero when the resonance in the conjugated system is ∼100% (planar) and slightly for the non-planar structure. In the case related to the cyclic **3a–h**, the dihedral angles C=C–C=O and C=C–O–Me are different of zero and the resonance in the conjugated system is not 100%. Thus, due to the low polarity-polarizability and hydrogen-bond-donor acidity of the chloroform-d_1 (solvent of the NMR experiments), we suggest that the solvent effect is not the main factor for the disagreement between the ^{17}O NMR data and parameters obtained via AM1 calculations in gas phase.

3. Conclusion

In summary, this work demonstrated a single and useful method for the synthesis of new 2-trifluoroacetyl-1-methoxycycloalkenes derived from large cycloalkanones under mild conditions and good yields, as well as the ^{17}O

NMR data for a series of eight new 4(6)-alkyl-2-trifluoroacetyl-1-methoxycycloalkenes. The electron *push–pull* phenomenon by the conjugation of the system O=C–C–C–O–Me could also be clearly observed and shows that there is an extensive p-π conjugation for these new non-planar molecules. Finally, possibly in addition to the s-*cis* and s-*trans* conformers on the Me–O–C=C moiety, varying amounts of non-planar conformers (s-*gauche*) exist for compounds **3a–h** when in solution. Moreover, from our point of view, the planarity or non-planarity of the C=C–C=O moiety, as well the CF_3 group is also responsible for the variations on both ^{17}O NMR chemical shift values. Until the present moment, we cannot manage to qualify or quantify some other factor(s), which furnished unsatisfactory correlations involving ^{17}O NMR data and dihedral angles (conformational analysis) or the oxygen net charge calculated by AM1 semi-empirical method.

4. Experimental

Unless otherwise indicated, all common reagents and solvents were used as obtained from commercial suppliers without further purification. Mass spectra were registered in a HP 6890 GC connected to a HP 5973 MSD and interfaced by a Pentium PC. The GC was equipped with a split–splitless injector, autosampler, cross-linked HP-5 capillary column (30 m, 0.32 mm of internal diameter), and helium was used as the carrier gas.

4.1. Semi-empirical molecular orbital calculations

The MO calculations were carried out by the Austin Model 1 (AM1) semi-empirical method [21], implemented in the Hyperchem 4.5 Package (1999) [22]. Geometries were completely optimized without fixing any parameter, thus bringing all geometric variables to their equilibrium values. The energy minimization protocol employs the Polak–Ribiere algorithm, a conjugated gradient method [22]. Convergence to a local minimum is achieved when the energy gradient is <0.01 kcal mol^{-1}. The calculations were performed on a PC Pentium-IV 2.4 GHz Dell.

4.2. NMR spectroscopy

^1H and ^{13}C NMR spectra were acquired on a Bruker DPX 400 spectrometer (^1H at 400.13 MHz and ^{13}C at 100.62 MHz), 5 mm sample tubes, 298 K, digital resolution ±0.01 ppm, in $CDCl_3$ and using TMS as internal reference.

^{17}O NMR spectra were acquired on a Bruker DPX 400 spectrometer at 54.24 MHz. The sample temperature was set at 300 ± 1 K. The instrumental settings were as follows: spectral width 38 kHz (705 ppm), 8 K data points, pulse width 12 μs, acquisition time 54 ms, peak acquisition delay 10 ms, 16,000–90,000 scans. LB of 100 Hz, sample spinning 20 Hz. The spectra were recorded with a RIDE (Ring Down Eliminate) sequence for suppression of acoustic ringing [23–25]. The general reproducibility of chemical shift data is estimated to be better than ±1.0 ppm (±0.2 within the same series). The half-height widths were in the range 400–900 Hz. All spectra were acquires in a 10 mm tube, at natural abundance in chloroform-d_1 as solvent. The concentration of the compounds used in these experiments was 0.5 M and the signal was referenced to external water (in a capillary coaxial tube).

4.3. Compounds

All ketone dimethyl acetals were synthesized by similar procedure described in the literature [1] and purified by distillation under reduced pressure.

The β-methoxyvinyl trifluoromethyl ketones **3a–e** derived from cyclohexanones (**1a–d**) and cyclopentanone (**1e**) were prepared previously [1a,1d]. Herein, the new β-methoxyvinyl trifluoromethyl ketones **3f–h** derived from cycloheptanone (**1f**), cyclooctanone (**1g**) and cyclododecanone (**1h**) were synthesized from the reaction of the respective 1,1-dimethylcycloalkanone acetals with trifluoroacetic anhydride by similar procedure described in the literature [1d] furnishing acceptable yields.

4.4. 2-Trifluoroacetyl-1-methoxycyclopentene (*3a*)

Yellow oil; yield 65%; bp 49–50 °C/3.2 mbar. [Ref. 1(a)]: yield 70%; bp 97–99 °C/10 mbar.

^{13}C NMR ($CDCl_3$) $\delta = 177.8$ (C-1); 175.8 (C=O, $^2J_{CF} = 36.0$ Hz); 116.8 (CF_3, $^1J_{CF} = 290$ Hz); 108.1 (C-2); 58.6 (OCH_3); 31.8 (CH_2); 28.5 (CH_2); 19.4 (CH_2). MS [*m/z* (%)] for $C_8H_9F_3O_2$ (194.15): 194 (M^+,17), 125 (100), 95 (7), 67 (22).

4.5. 2-Trifluoroacetyl-1-methoxycyclohexene (*3b*)

Yellow oil; yield 65%; bp 44–46 °C/3.0 mbar. [Ref. 1(a)]: yield 65%; bp 106–109 /10 mbar.

^{13}C NMR ($CDCl_3$) $\delta = 181.4$ (C=O, $^2J_{CF} = 35$ Hz); 170.0 (C-1); 116.8 (CF_3, $^1J_{CF} = 289$ Hz); 110.4 (C-2); 54.8 (OCH_3); 26.0 (CH_2); 24.0 (CH_2); 22.0 (CH_2); 21.6 (CH_2). MS [*m/z* (%)] for $C_9H_{11}F_3O_2$ (208.18): 208 (M^+, 42), 139 (100), 79 (66), 69 (31).

4.6. 6-Methyl-2-trifluoroacetyl-1-methoxycyclohexene (*3c*)

Yellow oil; yield 58%; bp 80–82 °C/4.0 mbar. [Ref. 1(d)]: yield 60%; bp 79–81 °C/3.5 mbar. ^{13}C NMR ($CDCl_3$) $\delta = 183.0$ (C=O, $^2J_{CF} = 37$ Hz); 172.7 (C-1); 116.5 (CF_3, $^1J_{CF} = 289$ Hz); 112.0 (C-2); 55.4 (OCH_3); 30.0 (CH_2); 29.0 (CH_2); 24.4 (CH_2); 18.0 (CH_2); 17.5 (CH_3). MS [*m/z* (%)] for $C_{10}H_{13}F_3O_2$ (222.20): 222 (M^+, 24), 153 (100), 93 (33), 69 (15).

4.7. 4-Methyl-2-trifluoroacetyl-1-methoxycyclohexene (**3d**)

Yellow oil; yield 61%; bp 87–89 °C/3.0 mbar. [Ref. 1(d)]: yield 60%; bp 89–92 °C/3.4 mbar.

^{13}C NMR ($CDCl_3$) δ = 181.5 (C=O, $^2J_{CF}$ = 35 Hz); 170.0 (C-1); 116.9 (CF_3, $^1J_{CF}$ = 290 Hz); 110.0 (C-2); 54.8 (OCH_3); 32.0 (CH_2); 30.0 (CH_2); 27.9 (CH_2); 25.9 (CH_2); 20.8 (CH_3). MS [*m*/*z* (%)] for $C_{10}H_{13}F_3O_2$ (222.20): 222 (M^+, 8), 153 (100), 69 (9).

4.8. 4-(1,1-Dimethyethyl)-2-trifluoroacetyl-1-methoxycyclohexene (**3e**)

Yellow oil; yield 57%; bp 90–92 °C/2.4 mbar. [Ref. 1(d)]: yield 60%; bp 84–86 °C/1.5 mbar.

^{13}C NMR ($CDCl_3$) δ = 181.8 (C=O, $^2J_{CF}$ = 35 Hz); 170.3 (C-1); 117.0 (CF_3, $^1J_{CF}$ = 290 Hz); 110.6 (C-2); 55.0 (OCH_3); 43.8 (CH_2); 32.3 (CH_2); 27.5 ($3CH_3$), 27.3 (C_{quat}); 25.8 (CH_2); 23.6 (CH_2). MS [*m*/*z* (%)] for $C_{13}H_{19}F_3O_2$ (264.28): 264 (M^+, 21), 249 (66), 111 (50), 57 (100).

4.9. Synthesis of 2-trifluoroacetyl-1-methoxycycloalkenes (**3f–h**)

To a stirred solution of dimethoxy acetals derived from cycloalkanones (30 mmol) and pyridine (60 mmol, 4.8 g) in chloroform (30 mL) kept at 0 °C (ice bath), trifluoroacetic anhydride (60 mmol) was added dropwise. The mixture was stirred for 16 h at 45 °C. The mixture was quenched and extracted with 0.1 M hydrochloric acid solution (3 mL × 15 mL) and after with water (1 mL × 15 mL). The organic layer was dried with magnesium sulfate and filtered. The solvent was evaporated and the products were obtained in high purity by distillation under reduced pressure.

4.10. 2-Trifluoroacetyl-1-methoxycycloheptene (**3f**)

Yellow oil; yield 68%; bp 83–85 °C/2.4 mbar.

^{1}H NMR ($CDCl_3$) δ = 3.7 (s, 3H, OCH_3); 2.61–2.58 (m, 2H, CH_2); 2.45–2.42 (m, 2H, CH_2); 1.80–1.77 (m, 2H, CH_2), 1.67–1.64 (m, 2H, CH_2); 1.55–1.54 (m, 2H, CH_2). ^{13}C NMR ($CDCl_3$) δ = 182.6 (C=O, $^2J_{CF}$ = 35 Hz); 175.4 (C-1); 116.8 (CF_3, $^1J_{CF}$ = 290 Hz); 116.7 (C-2); 55.9 (OCH_3); 31.4 (CH_2); 28.9 (CH_2); 26.7 (CH_2); 26.1 (CH_2); 24.2 (CH_2). MS [*m*/*z*(%)] for $C_{10}H_{13}F_3O_2$ (222.20): 222 (M^+,27), 153 (100), 93 (62), 69 (36).

4.11. 2-Trifluoroacetyl-1-methoxycyclooctene (**3g**)

Yellow oil; yield 65%; bp 70–71 °C/1.8 mbar.

^{1}H NMR ($CDCl_3$) δ = 3.8 (s, 3H, OCH_3); 2.82–2.78 (m, 2H, CH_2); 1.58–1.54 (m, 2H, CH_2); 1.36–1.34 (m, 2H, CH_2), 1.31–1.30 (m, 4H, CH_2); 0.89–0.87 (m, 2H, CH_2). ^{13}C NMR ($CDCl_3$) δ = 185.5 (C-1); 178.3 (C=O, $^2J_{CF}$ = 33 Hz); 118.3 (C-2); 116.7 (CF_3, $^1J_{CF}$ = 292 Hz); 56.3 (OCH_3); 33.8 (CH_2); 31.4 (CH_2); 28.9 (CH_2); 26.8 (CH_2); 22.4 (CH_2); 13.8 (CH_2) MS [*m*/*z* (%)] for $C_{11}H_{15}F_3O_2$ (236.23): 236 (M^+, 19), 167 (100), 79 (86), 69 (35).

4.12. 2-Trifluoroacetyl-1-methoxycyclododecene (**3h**)

Yellow oil; yield 60%; bp 118–120 °C/2.4 mbar.

^{1}H NMR ($CDCl_3$) δ = 3.98 (s, 3H, OCH_3); 2.50–2.44 (m, 2H, CH_2); 1.87–1.72 (m, 4H, CH_2); 1.3 (m, 14H, CH_2). ^{13}C NMR ($CDCl_3$) δ = 187.8 (C=O, $^2J_{CF}$ = 36 Hz); 178.8 (C-1); 109.5 (C-2); 119.2 (CF_3, $^1J_{CF}$ = 276 Hz); 60.0 (OCH_3); 32.4–23.0 (CH_2). MS [*m*/*z* (%)] for $C_{15}H_{23}F_3O_2$ (292.34): 292 (M^+,28), 223 (42), 111 (96), 69 (48), 55 (100).

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