^{1}H NMR study of inclusion of substituted bicyclo[3.3.1]nonanes in α- and β-cyclodextrins

E. P. Butkus[a]* *and J. C. Martins*[b]

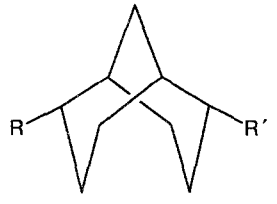
[a]*Vilnius University, 3 ul. Universiteto, 2734 Vilnius, Lithuania. Fax: (0 122) 263 417*
[b]*Vrije Universiteit Brussel, 2 Pleinlaan, B-1050 Brussel, Belgium. Fax: (322) 629 3304*

The interaction of 2,6-disubstituted bicyclo[3.3.1]nonanes with α- and β-cyclodextrins has been investigated by ^{1}H NMR spectroscopy and the formation of (1:1) "host—guest" complexes has been established.

Key words: bicyclo[3.3.1]nonane, cyclodextrin, complex formation, ^{1}H NMR.

The property of cyclodextrins (CD) to form complexes of the "host—guest" type with organic compounds makes it possible to use them in studies of intermolecular interactions related to supramolecular chemistry.[1] A great number of aromatic compounds manifesting themselves as "guests" in such complexes with CD have been studied.[2] However, one of the strongest interactions with CD is characteristic of compounds of adamantane series.[3] Chiral molecules are of particular interest, because enantiomers can react with CD to give diastereometric complexes with various properties.[4] In this connection, it is important to study complex formation of compounds of the bicyclo[3.3.1]nonane series with CD. These compounds have one carbon atom less than the adamantane molecule and possess conformationally mobile structures. In addition, 2,6-derivatives of this bridged bicyclic system are chiral, which allows one to distinguish enantiomers.

We studied the formation of complexes of bicyclononanes **1**—**3** with α- and β-cyclodextrins using ^{1}H NMR spectroscopy. NMR titration of substrates **1**—**3** was carried out by adding increasing amounts of α- and β-CD. Changes in chemical shifts of proton signals both for CD and substrates **1**—**3** were thereby observed.



1—**3**

1: R = R′ = O
2: R = R′ = OH
3: R = OH, R′ = OAc

When organic molecules are included in the cavity of CD, the signals for H-3 and H-5 protons, which are localized in the inner cavity of CD, undergo the strongest shift. The interaction of diketone **1** and *endo*-diol **2** with α- and β-CD proceeds variously. When α-CD is added to a solution of diketone **1** in D_2O, an upfield shift of a signal for H-3, which is placed close to the larger cavity of the truncated cone of α-CD occurs (Δδ, 0.064) and the chemical shift of a signal for H-5 (proton at a narrower cavity of the CD cone) remaines practically unchanged. The signals for protons of substrates, *e.g.*, H-1 and H-9, are downfield shifted by 0.04 and 0.02 ppm, respectively (Fig. 1). These data indicate that molecules of diketone **1** do not penetrate deep into the cavity of α-CD. Therefore, complex formation with β-CD was studied, the diameter of cavity of the latter being ~7 Å. In this case, greater shifts of signals for the substrate (Δδ, 0.11—0.12) and CD (H-5: Δδ, −0.12; H-3: Δδ, −0.064) are registered (see Fig. 1).

Inclusion of diol **2** in β-CD exerts a larger effect on the shift of the signal for H-3 (Δδ, −0.054) in comparison with H-5 (Δδ, −0.03). Downfield shifts by 0.02—0.16 ppm are observed for the proton signals of the bicyclic fragment (Table 1). It is most likely that in the case of substrate **2** the reaction with β-CD has a more complicated character than simple inclusion. Another type of complex formation is documented: when alkanediols and other bifunctional compounds react with CD, they cover the cavity of the CD.[5] In the case of diol **2**, the "guest" molecule is partially included in the cavity of the CD, while its other part covers this cavity. This assumption is confirmed by results of complex formation of β-CD with monoacetate **3**, which is more hydrophobic than diol **2**.

A much stronger upfield shift (induced by complex formation with β-CD) of proton H-5 of CD (Δδ, −0.13) in comparison with the shift of proton H-3 (Δδ, −0.07) is characteristic of ^{1}H NMR spectra of monoacetate **3**. Hence, the molecule of monoacetate **3** penetrates more

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 12, pp. 2523—2525, December, 1995.
1066-5285/95/4412-2420 $12.50

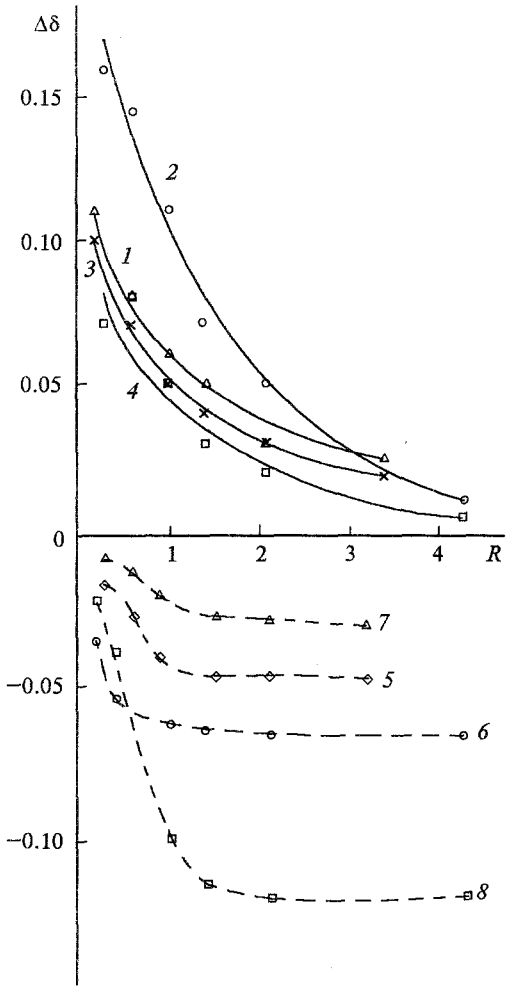


Fig. 1. Dependence of induced chemical shifts of protons H-1 (*1*, *2*) and H-9 (*3*, *4*) of diketone **1** (*1*, *3*) and diol **2** (*2*, *4*) and chemical shifts of protons H-3 (*5*, *6*) and H-5 (*7*, *8*) of CD for complexes **1** · CD (*5*, *7*) and **2** · CD (*6*, *8*) on the substrate-to-CD molar ratio (*R*).

deeply into the cavity of β-CD in comparison with diol **2** to give a common complex of the "host—guest" type. The greatest changes in the induced chemical shifts of signals for protons H-3 and H-5 of CD take place at a 1:1 "host—guest" molar ratio (see Fig. 1). No changes in induced chemical shifts occur at higher substrate—CD ratios.

With the examples studied, no splitting of proton signals of substrates **1**—**3** was observed in the ^{1}H NMR spectra, although these molecules are chiral. This may be explained by the fact that total chirality of CD is considered to be insignificant due to their symmetry C_n. Besides, molecules of substrates **1** and **2** have symmetry C_2, that results in a decrease in enantiodifferentiating ability of CD during complex formation with 2,6-disubstituted bicyclo[3.3.1]nonanes. From coupling constants it follows that the conformation of bicyclononanes **1**—**3** in complexes with CD is not changed, and a form of double chair, which has been established earlier for these compounds,[6] remains. The position of molecules of compounds **1**—**3** in the cavity of CD is given in Fig. 2.

Table 1. Induced chemical shift values (Δδ) in ^{1}H NMR spectra for proton signals of compounds **1**—**3** in relation to substrate-to-β-CD concentration ratios (*R*)

Compound	Atom	*R*						
		0.2	0.3	0.6	1.0	1.4	2.1	4.3
1	H-1	0.11	—	0.08	0.06	0.05	0.03	0.02
	H-9	0.10	—	0.07	0.05	0.04	0.03	0.02
2	H-1	—	0.16	0.15	0.11	0.07	0.05	0.01
	H-9	—	0.07	0.08	0.05	0.03	0.02	0.00
3	H-2	—	0.07	0.07	0.07	0.06	—	0.03
	H-6	—	0.08	0.07	0.07	0.06	—	0.03

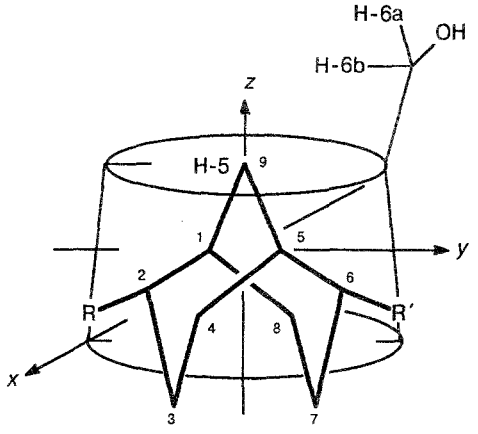


Fig. 2. Position of bicyclononanes **1**—**3** in the cavity of β-CD with indication of numeration of carbon atoms.

Experimental

^{1}H NMR spectra were recorded on a Bruker AMX-500 (500.13 MHz) instrument in D_2O solution at 303 K. NMR titration was carried out by adding CD portionwise to solutions of substrates **1**—**3**. Concentrations of the substrates and CD varied within a $(1—5) \cdot 10^{-3}$ mol L^{-1} range. The solutions obtained were stirred thoroughly and left to reach equilibrium. α- and β-CD were dried *in vacuo* before use. Synthesis of compounds **1**—**3** has been described earlier.[7,8]

References

1. J.-M. Lehn, *Angew. Chem., Int. Ed. Engl.*, 1988, **27**, 89.
2. O. S. Tee, *Adv. Phys. Org. Chem.*, 1994, **29**, 1.

3. M. T. Shortreed, S. Wylie, and D. H. Macartney, *Inorg. Chem.*, 1993, **32**, 1824 (see also references cited therein).
4. Yu. A. Zhdanov, Yu. E. Alekseev, E. V. Kompantseva, and E. N. Vergeichik, *Usp. Khim.*, 1992, **61**, 1025 [*Russ. Chem. Rev.*, 1992, **61** (Engl Transl.)].
5. S. Andiini, G. Gastrunuovo, V. Elia, and E. Gallota, *Carbohydr. Res.*, 1991, **217**, 87.
6. E. P. Butkus, P. P. Kadziauskas, and M. Yu. Kornilov, *Zh. Org. Khim.*, 1980, **16**, 2446 [*J. Org. Chem. USSR*, 1980, **16** (Engl. Transl.)].
7. E Butkus, J. Malinauskiene, and P. Kadziauskas, *Z. Chem.*, 1980, **20**, 123.
8. E. P. Butkus, R. V. Verkauskaite, and P. P. Kadzyauskas, *Nauchn. Tr. Vyssh. Uchebn. Zaved., Lit. SSR, Khim. Khim. Tekhnol.* [*Proceedings of Higher Educational Establishments of Lit. SSR, Chemistry and Chemical Technology*], 1981, **22**, 23 (in Russian).

Received May 5, 1995;
in revised form June 26, 1995

Polyfluorinated hydrazones in organic syntheses
3.* Reactions of poly- and perfluoroaldehyde hydrazones with hydrazine hydrate

G. G. Bargamov* and M. D. Bargamova

A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences,
28 ul. Vavilova, 117813 Moscow, Russian Federation.
Fax: +7 (095) 135 5085

The reaction of poly- and perfluoroaldehyde hydrazones with hydrazine hydrate was studied. A new preparative method for obtaining the hitherto inaccessible *N,N*-unsubstituted bis-hydrazones of polyfluorinated α-oxoaldehydes was developed based on this reaction.

Key words: hydrazine hydrate, 7-H-dodecafluoroheptanal, poly- and perfluoroaldehyde hydrazones, polyfluorinated α-oxoaldehyde bis-hydrazones.

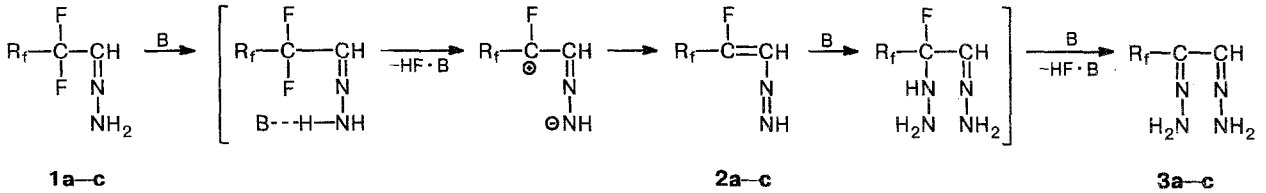
The interaction of *N,N*-unsubstituted hydrazones of monocarbonyl compounds with hydrazine hydrate usually results in their reduction to hydrocarbons.[1] We have studied for the first time the behavior of fluorine-containing analogs in this reaction, with perfluoropentanal hydrazone as an example, and have obtained, in a low yield, *N,N*-unsubstituted perfluoropropylglyoxal bis-hydrazone, the first fluorine-containing representative of such compounds.[2]

* For Part 2, see *Izv. Akad. Nauk, Ser. Khim.*, 1995, 2465 [*Russ. Chem. Bull.*, 1995, **44**, 2360 (Engl. Transl.)].

The present work deals with the reaction of poly- and perfluoroaldehyde hydrazones with hydrazine hydrate with the purpose of synthesizing new compounds belonging to this class.

The reactions of perfluoro- (**1b**) and 7-H-dodecafluoroheptanal hydrazone (**1c**) with hydrazine hydrate gave hitherto unknown perfluoro- (**3b**) and 5-H-decafluoropentylglyoxal bis-hydrazones (**3c**) in high yields (Scheme 1). The reaction occurred in methanol; no less than 3 mol.-equiv. hydrazine hydrate was used, of which 2 mol.-equiv. were consumed to bind HF. The transformation of hydrazone (**1a**) into bis-hydrazone

Scheme 1



1a–c **2a–c** **3a–c**

$R_f = C_3F_7$ (**a**), C_5F_{11} (**b**), $CHF_2(CF_2)_4$ (**c**); B = $N_2H_4 \cdot H_2O$

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 12, pp. 2526–2527, December, 1995.