Pergamon

Tetrahedron Letters, Vol. 35, No. 13, pp. 1985-1988, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $6.00+0.00

0040-4039(94)E0217-L

Fluorinated Ketene Dithioacetals.
3. A Radical Entry to α-Perfluoroalkyl Ketene Dithioacetals. Application to Sugar Derivatives.

S. Bergeron, T. Brigaud, G. Foulard, R. Plantier-Royon, C. Portella*

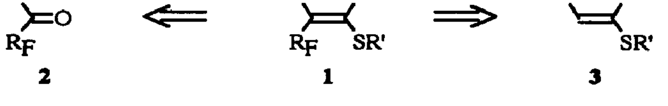
Laboratoire des Réarrangements Thermiques et Photochimiques, Associé au CNRS,
U.F.R. Sciences, B.P. 347, 51062 Reims Cedex, France

Key-words: ketene dithioacetals, radical perfluoroalkylation, perfluoroalkylated sugars.

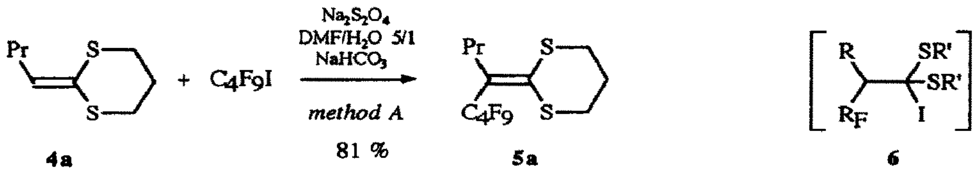
Abstract : α-Perfluoroalkyl ketene dithioacetals were synthesized by radical perfluoroalkylation of ketene dithioacetals with perfluoroalkyl iodide and sodium dithionite in a basic medium. Application to sugar derived ketene dithioacetals gave results depending strongly on the sugar structure.

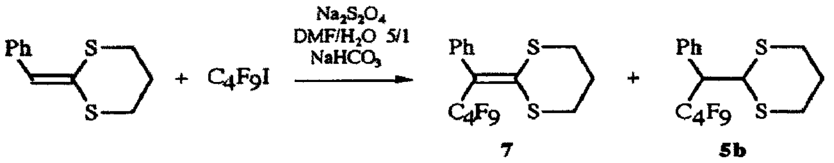
Radical perfluoroakylation is a widely used methodology in organofluorine chemistry. The electrophilic character of the perfluoroalkyl radical makes it well adapted to electron rich olefinic substrates, although other types of substrates may be suitable. Among electron rich olefins, enol ether[1], enol ester[2], silyl enol ether[3] and enamines[4] are excellent candidates. To our knowledge, enol thioethers and ketene dithioacetals have not been submitted to such perfluoroalkylation, except the addition of the trifluoromethyl radical to phenyl vinyl sulfides.[5]

Owing to their versatility as intermediates in organic synthesis[6], ketene dithioacetals were also recently considered to synthesize various types of organofluorine compounds[7]. Particularly, we have proposed a general approach to α-trifluoromethyl carbonyl and carboxyl derivatives via α-trifluoromethylketene dithioacetals **1** ($R_F = CF_3$) prepared from trifluoromethylketones **2** by a Peterson reaction[7d]. Considering functionalized substrates, this methodology could present some limitations. Hence, in the area of fluorine derivatives of carbohydrates synthesis, we have considered another possible disconnection to have access to compounds **1** in which R could be a sugar residue. We describe in this paper the preliminary results related to the radical addition of perfluoroalkyl iodide to ketene dithioacetals **3** and application to the grafting of a perfluoroalkyl chain to sugar derivatives.



Among the various ways of initiation we have chosen sodium dithionite[8], known as a very cheap and efficient initiator[9] acting as a single electron transfer donor. As model substrates, 2-propyliden-1,3-dithiane **4a** and 2-benzylidene-1,3-dithiane **4b**[10] were treated with 1.2 equivalent of perfluorobutyliodide in a mixture DMF/H$_2$O (5/1) containing Na$_2$S$_2$O$_4$ (1.3 eq.) and NaHCO$_3$ (1.3 eq.). When all reactants are added to the solvent mixture DMF-H$_2$O (method A),[11] perfluoroalkylated dithioacetal **5a**[12] was obtained in a good yield. No trace of the iodide adduct **6** was observed, indicating a spontaneous hydrogen iodide elimination in the reaction medium. Replacement of sodium dithionite by rongalite[9] (HOCH$_2$SO$_2$Na) which allows to carry out the reaction in a more homogeneous organic medium gave no better results. The benzylic derivative **4b** had a somewhat curious behaviour giving, following the conditions A[11], the hydroperfluoroalkylation product **7** beside **5b**[12] with Na$_2$S$_2$O$_4$ or rongalite as the initiator. The formation of **7** could be avoided when Na$_2$S$_2$O$_4$ was added as a solution in water to a solution of the other reactants in DMF (method B). Owing to the heterogeneous medium and the varying time of induction, it is difficult to estimate the concentration effect and to rationalize this behaviour. We have observed that when they are produced together, **5b** and **7** are always found in a ratio approaching 50/50. This is consistent with the occurence of a disproportionation favoured by the presence of a labile benzylic hydrogen.

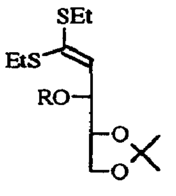




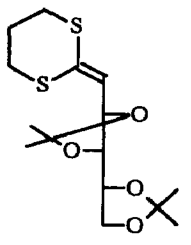
	7	5b
method A	37%	31%
method B	80 %	0 %

The application of this methodology to sugar derivatives was more or less successful according to their structures. No reaction was observed when dithioacetals **8**[14] and **9**[10,15] derived from D-xylose were treated as above[11]. On the other hand, the 3-O-benzyl derivative **10a**[10,16] gave the perfluoroalkyl grafted derivative **11a**[12] in 37% yield. The compound **11b** was obtained from the 3-O-methyl analogue **10b**[17] showing that an hypothetic hydrogen transfer from the benzylic methylene does not occur. More interesting is the case of compound **10c**[10,18] which is not protected at the 3 position. The 3,6-anhydro derivative **12**[12] was obtained in a fairly good yield, resulting from an intramolecular trapping of the iodide adduct by the 3-hydroxy group with hydrogen iodide elimination. This result is to be linked to the formation of perfluoroalkyl tetrahydrofuran by radical addition of perfluoroalkyliodide to penten-4-ol[19].

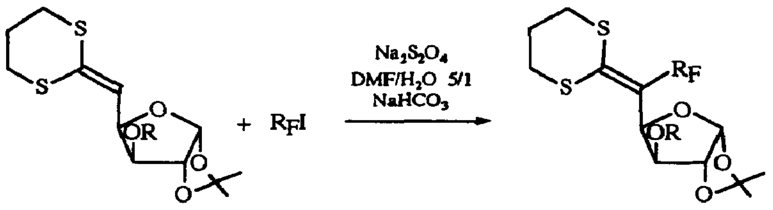
In summary, radical perfluoroalkylation of simple ketene dithioacetals is efficient. With sugar derived ketene dithioacetals, it depends strongly on the structure of the substrate, the better results being obtained when intramolecular trapping of the adduct occurs. Owing to the interest in fluorinated surfactants derived from carbohydrates,[20] these preliminary results prompt us to carry on this research with new substrates and with further transformation of the grafted products.



8 (R = H or Bn)

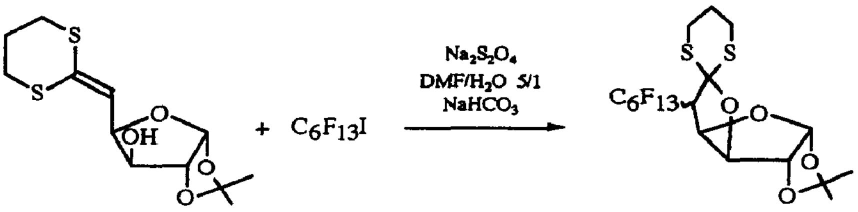


9



10a (R=Bn)
10b (R=Me)

11a(R_F=C_6F_{13}) 37%
11b(R_F=C_4F_9) 44%



10c

12 60 % (50/50)

Acknowledgements.

We thank the "*Agence Régionale pour la Recherche-Développement*" for a post-doctoral fellowship (R. P.-R.), the "*Conseil Général de la Marne*" for a doctoral fellowship (S. B.), and *ATOCHEM* for the gift of perfluoroalkyl iodides.

References and notes

1 a) Huang, W.; Lu, L.; Zhang, Y. *Chin. J. Chem.* **1990**, *8*, 281-8. b) Huang, W.; Xie, Y.; Lu, L. *Chin. J. Chem.* **1991**, *9*, 167-173. c) Huang, W.,-Y; Lu, L. *Chin. J. Chem.* **1991**, *9*, 174-80. d) Sasahoka, S.-I.; Uno, M.; Joh, T.; Imazaki, H.; Takahashi, S. *J. Chem. Soc. Chem. Commun.* **1991**, 86-7. e) Uneyama, K.; Kitagawa, K. .*Tetrahedron Lett* . **1991**, *32*, 3385-6.

2 a) Laurent, P.; Blancou, J.; Commeyras, A. *Tetrahedron Lett.* **1992**, *33*, 2489-92. b) Napoli, M.; Fraccaro, C.; Conti, L.; Gambaretto, G.P.; Legnaro, E. *J. Fluorine Chem.* **1992**, *57*, 219-27. Langlois, B.R.; Laurent, E.; Roidot, N. Tetrahedron Lett. **1992**, *33*, 1291-4.

3 a) Miura, K.; Taniguchi, M.; Nozaki, K.; Oshima, K.; Utimoto, K. *Tetrahedron Lett.* **1990**, *31*, 6391-4. b) Miura, K.; Takeyama, Y.; Oshima, K.; Utimoto, K. *Bull. Chem. Soc. Jpn* **1991**, *64*, 1542-53. c) Ge, W.; Wu, Y.; Huang, W. *Chin. J. Chem.* **1991**, *9*, 527-35. d) Huang, W.-Y.; Wu, Y. *J. Fluorine Chem.* **1992**, *59*, 179-83.

4 Cantacuzène, D.; Wakselman, C.; Dorme, R. *J. Chem. Soc.Perkin Trans I*, **1977**, 1365-71.

5 Langlois, B, R. *Private communication.*

6 a) Gröbel, B.T.; Seebach, D. *Synthesis* **1977**, 357-402. b) Kolb, M. *Synthesis* **1990**, 171-90.

7 a) Tanaka, K.; Nakai, T.; Ishikawa, N. *Chem. Lett.* **1979**, 175-8. b) Purrington, S.T.; Samaha, N.F. *J. Fluorine Chem.* **1989**, *43*, 229-34. c) Solberg, J.; Benneche, T.; Undheim, K. *Acta Chemica Scand.* **1989**, *43*, 69-73. d) Muzard, M.; Portella, C. *Synthesis* **1992**, 965-8. e) Muzard, M.; Portella, C. *J. Org. Chem.* **1993**, *58*, 29-31.

8 Louis-André, O.; Gelbard, G. *Bull. Soc. Chim. Fr.* **1986**, 565-76.

9 Huang, W.-Y. *J. Fluorine Chem.* **1992**, *58*, 1-8, and references therein.

10 Prepared from the corresponding aldehyde and 2-lithio-2-trimethylsilyl-1,3-dithiane in THF.

11 Compound **4a** (2.4 mmol), $NaHCO_3$ (3.1 mmol), $Na_2S_2O_4$ (3.1 mmol) and perfluorobutyl iodide (2.88 mmol) are added at O°C to a mixture of DMF (1.6 ml) and water (0.3 ml). The mixture is allowed to stirr in the dark at rt. The reaction is monitored by GLC. The reaction mixture is then diluted with 10 ml of water and extracted with light petroleum (25 ml). The organic layer is washed with brine, dried over $MgSO_4$. Evaporation gave **5a** which can be purified by flash chromatography (CH_2Cl_2/light petroleum: 10/90).

12 All new products gave satisfactory spectral characteristics and microanalysis.

13 No trace was detected by ^1H NMR spectroscopy.

14 Wong, M.Y.H.; Gray, G.R. *J. Am. Chem. Soc.* **1978**, *100*, 3548-53.

15 Corresponding aldehyde prepared by deprotection ($Hg(ClO_4)_2$ in $THF-H_2O$) of the parent diethylthioacetal, which was obtained according to: Horton, D.; Varela, O. *Carbohydr. Res.* **1984**, *134*, 205-14.

16 Corresponding aldehyde: Anderson, R.C.; Fraser-Reid, B.J. *J. Org. Chem.* 1985, *50*, 4781-6.

17 Prepared in 90% yield from **12** (NaH, THF, MeI).

18 Prepared from the lithium salt of 1,2-O-isopropylidene-α-D-xylopentodialdo-1,4 furanose: Wolfrom, M. L.; Thomas, G. H. S. Methods in Carbohydrate Chemistry; Whistler, R. L., Wolfrom, M. L., Eds.; Academic Press: New York, 1963; Vol. 2, p 32.

19 Greiner, J.; Milius, A.; Riess, J.G. *J. Fluorine Chem.* **1992**, *56*, 285-93.

20 a) Zarif, L.; Greiner, J.; Pace, S.; Riess, J.G. *J. Med. Chem.* **1990**, *33*, 1262-9. b) Milius, A.; Greiner, J.; Riess, J.G. *New J. Chem.* **1991**, *15*, 337-44. c) Manfredi, A.; Abouhilale, J.; Riess, J.G. *Bull. Soc. Chim..Fr.* **1989**, *6*, 872-8. d) El Ghoul, M.; Escoula, B.; Rico, I.; Lattes, A. *J. Fluorine Chem.* **1992**, *59*, 107-12. e) Huang, W.-Y.; Wie, Y. *Chin. J. Chem.* **1991**, *9*, 351-9.

(*Received in France* 6 *January* 1994; *accepted* 20 *January* 1994)