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TosMIC IN THE PREPARATION OF SPIROACETALS : SYNTHESIS OF PHEROMONE COMPONENTS OF OLIVE FRUIT FLY

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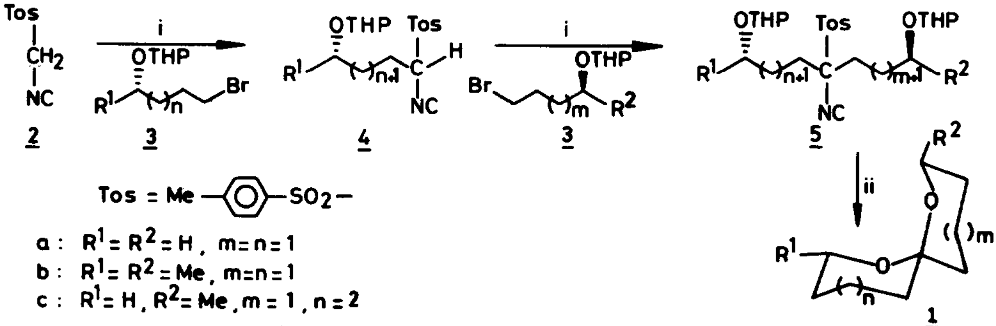
Abstract: The dialkylated tosylmethyl isocyanide derivatives obtained by alkylation of TosMIC with halohydrin derivatives, on hydrolysis lead to the formation of 1,7-dioxaspiroalkanes.

Spiroacetals[1] constitute important structural features of naturally occurring compounds from widespread sources like insects, plants, microbes, marine organisms etc. and any attempt to synthesize these useful compounds is appreciated, provided the reaction sequences are highly simplified. One of the widely accepted procedures, to synthesise these spiroacetals involves intramolecular cyclization of suitably placed dihydroxyketones which in turn could be obtained[2] by alkylation of active methylene compounds in the presence of bases such as n-BuLi, LDA, etc. In addition spiroacetalization of keto-olefins by using salts of palladium[3], selenium[4] and mercury[5] have also been demonstrated to prepare racemic spiroacetal derivatives. In this communication we report a simple strategy for obtaining spiroacetals by taking advantage of tosylmethyl isocyanide (2)[6] undergoing readily, alkylation with desired bromohydrin derivatives 3 in presence of milder base such as sodium hydroxide.



a : $R^1 = R^2 = H$, m = n = 1
b : $R^1 = R^2 = Me$, m = n = 1
c : $R^1 = H$, $R^2 = Me$, m = 1, n = 2

i) 40% aq.NaOH, $n\text{-}Bu_4N^+Br^-$, CH_2Cl_2 ; ii) 2N H_2SO_4 in 1:4 H_2O-MeOH

In order to illustrate the efficacy of this strategy the sytnthesis of spiroacetal components (1a-1c) of pheromone isolated from olive fruit fly were undertaken (see Table). For instance, alkylation[6] of 2 with 2 eq. of alkyl bromide 3a in the presence of 40% aq. NaOH-CH_2Cl_2 (1:2) containing a catalytic amount of tetra-n-butylammonium bromide at 25°C provided 5a which on treatment with dil.acid (2N H_2SO_4 in 1:4 H_2O-MeOH) furnished 1,7-dioxaspiro[5,5]undecane (1a)[7], a major constituent of the pheromone.

The chiral synthesis of (2S,6R,8S)-2,8-dimethyl-1,7-dioxaspiro[5,5]undecane (1b)[9], component of pheromone of Andrena wilkella was achieved from 2 by dialkylation with (2S)-5-bromo-2-tetra-

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Table : Preparation of Spiroacetals (1)

Entry	Halides (3)	Monoalkylated TosMIC (4);(%)	Halides (3)	Dialkylated TosMIC (5),(%)	Spiroacetals (1) (%)*
1	**3a** R^1=H n=1	-	**3a** R^2=H m=1	85	**1a** (75)
2	**3b** R^1=Me n=1	-	**3b** R^2=Me m=1	82	**1b** (67)
3	**3c** R^1=H n=2	92	**3b** R^2=Me m=1	77	**1c** (55)

* Yields from **2** are given in parenthesis.

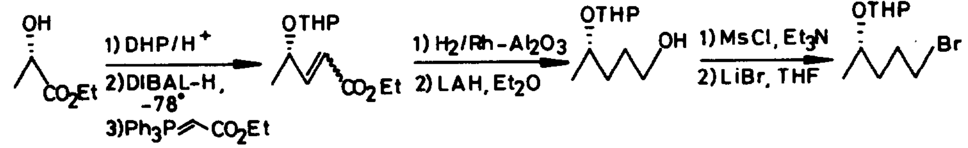
hydropyranyloxypentane (**3b**)[8] under the said conditions followed by hydrolysis { **1b**:$[\alpha]_D$ -61.7° (c 1.3, pentane), Lit.[9] $[\alpha]_D$ (antipode) +60.1° (c 1.14, pentane)}.

The methodology similarly was extended to the spiroacetals containing different ring sizes by successive alkylation[10] of **2** with different bromohydrin derivatives. For example **2** was alkylated with **3c** and then the monoalkylated product **4c** was further treated with **3b** in the presence of sodium hydroxide to afford the unsymmetrical dialkylated TosMIC **5c**. It was observed that the second alkylation of **4c** with **3b** could be effected using NaH as a base in Et_2O-DMSO (4:1) in a slightly improved yield (83%). The usual hydrolysis of **5c** with dil. acid provided (2S,6R)-2-methyl-1,7-dioxaspiro[5,6]dodecane (**1c**)[11], component of pheromone of Andrena haemorrhoa $[\alpha]_D$ -107° (c 1.7, pentane), Lit.[11] $[\alpha]_D$ -105° (c 1.1, pentane).

A general strategy for synthesis of spiroacetals[12] using TosMIC as the conjunctive reagent using milder bases for its alkylation is demonstrated.

REFERENCES

1. a) A.F. Kluge, Heterocycles, **24**, 1699 (1986); b) K.F. Alibizati and F. Perron, Chem. Rev., **89**, 161 (1989); c) K. Mori, Tetrahedron, **45**, 3233 (1989).
2. a) J.P. Ferezou, J. Gauchet-Prunet, M. Julia and A. Pancrazi, Tetrahedron Lett., **29**, 3667 (1988); b) M. Hirama, T. Nakamine and S. Ito, Tetrahedron Lett., **27**, 5281 (1986).
3. a) J.S. Yadav, E.S. Rao, C.S. Rao and B.M. Choudhary, J. Mol. Cat., **49**, L61 (1989); b) J.S. Yadav, E.S. Rao, V.S. Rao and B.M. Choudary, Tetrahedron Lett., **31**, 249 (1990) and references therein.
4. a) G. Mehta, G.S.P. Rao and K. Raja Reddy, J. Chem. Soc. Chem. Commun., 79 (1987); b) G. Pandey, V.J. Rao and U.T. Bhalerao, J. Chem. Soc. Chem. Commun., 416 (1989).
5. W. Kitching, A. Lewis, T. Fletcher, J. De Voss, A. I. Drew, J. Moore, J. Chem. Soc. Chem. Commun., 855 (1986).
6. a) A.M. van Leusen and J. Strating, Q. Rep. Sulfur. Chem., **5**, 67 (1970); b) A.M. van Leusen, R.J. Bauma and O. Possel, Tetrahedron Lett., 3487 (1975); c) O. Possel and A.M. van Leusen, Tetrahedron Lett., 4229 (1977); d) J.S. Yadav, P.S. Reddy and B.V. Joshi, Tetrahedron, **44**, 7243 (1988) and references cited therein.
7. K. Mori, H. Watanabe, K. Yanagi and M. Minobe, Tetrahedron, **41**, 3663 (1985).
8. **3b** was prepared as given below.



9. a) K. Mori and H. Watanabe, Tetrahedron, **42**, 295 (1986); b) K. Mori and K. Tanida, Tetrahedron, **37**, 3221 (1981).
10. a) A.M. van Leusen, J. Heterocyclic Chem., **17** (Suppl.5), 111 (1980); b) A.M. van Leusen, "The effect of sulfur substituents on chemistry of alkyl isocyanides, in the perspectives in the Org. Chem of Sulfur, p119 . (Eds B Zwanenburg and A.J.H. Klunder) Elsevier Science, Amsterdam (1987).
11. K. Mori and M. Katsurada, Liebigs Ann. Chem, 157 (1984).
12. All new compounds gave expected spectral data and exact mass (HRMS).

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