CROATICA CHEMICA ACTA CCACAA 58 (4) 671—680 (1985)

YU ISSN 0011-1643
CCA-1614 UDC 547.9
Original Scientific Paper

Synthesis of Spiro-Ketal Pheromones*

Živorad Čeković and Jovan Bošnjak

Department of Chemistry, Faculty of Science, University of Belgrade, Studentski trg 16, 11001 Belgrade, Institute for Chemistry, Technology and Metallurgy, Belgrade, Yugoslavia

and

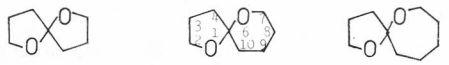
Dušan Mandić and Dimitar Ilijev

Faculty of Pedagogy, University of Osijek, Osijek, Yugoslavia

Received May 24, 1985

Pheromones possessing a spiro-ketal skeleton, such as 2--ethyl-1,6-dioxaspiro[4,4]nonane (chalcogran) and 7-methyl-1,6--dioxaspiro[4,5]decane, were synthesized by silver oxide-bromine and by lead tetraacetate oxidation of 1,7- and 1,8-nonanediols, respectively.

Since the identification of 2-ethyl-1,6-dioxaspiro[4,4]-nonane as the principal aggregation pheremone of the bark beetle *Pityogenes chalcographus L* (in 1977),[1] five different systems (*1*—*5*) possessing spiro-ketal skeleton have been found in insects, and fully characterized.[2] Since then, the interest in the isolation, structure elucidation and synthesis of spiro-ketal pheromones has been permanently increasing[2–7] and the following types of spiro-ketal pheromones have been discovered: 1,6-dioxaspiro[4,4]nonanes *1*,[1,5,8] 1,6-dioxaspiro-[4,5]decanes *2*,[9–11] 1,6-dioxaspiro[4,6]undecanes *3*,[3] 1,7-dioxaspiro[5,5]undecanes *4*,[6,8,10] and 1,7-dioxaspiro[5,6]dodecanes *5*.[12]



1 2 3

4 5

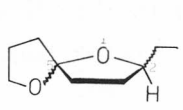
All hitherto known pheromones possessing spiro-ketal moiety contain unbranched carbon skeletons usually consisting of nine, eleven or thirteen carbon atoms, thus showing close relationships to a large number of other

* Dedicated to Professor Mihailo Lj. Mihailović on the occasion of his 60th birthday.

pheromones which presumably derive from fatty acids.[13] Most of these compounds appear as mixtures of enantiomers, diastereomers or geometrical enantiomers.

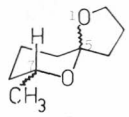
The spiro-ketal moietyl plays a very important role as a structural element not only of insect pheromones,[2] but also of many other biologically active natural products, such as polyether antibiotics,[14] hence, new and efficient synthetic methods for the construction of such skeletons are becoming increasingly important.[2,5-7]

In this paper we wish to report a new and facile method for the construction of spiro-ketal pheromones of type *1* and *2* by silver oxide-bromine and by lead tetraacetate oxidation of the corresponding diols. By applying this methodology we decided to prepare the following two spiro-ketal insect pheromones: 2-ethyl-1,6-dioxaspiro[4,4]nonane named — chalcogran *6*, known as the principal aggregation pheromone od *Pityogenes chalcographus L*,[1,5,15] and 7-methyl-1,6-dioxaspiro[4,5]decane *7*, a common wasp pheromone from *Paravespula vulgaris L.*[9,16,17]



6

2R, 5R
2R, 5S
2S, 5R
2S, 5S

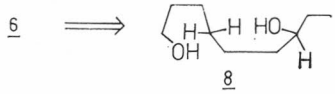


7

5R, 7R
5R, 7S
5S, 7R
5S, 7S

Spiro-ketal pheromones of type *1* and *2*, deriving from an unbranched aliphatic chain, suggest that bifunctional compounds may be used as synthetic precursors of the 1,6-dioxaspiro skeleton function, which could be formed by intramolecular regioselective double functionalization of the δ-carbon atom. It is known that cyclic ether functional group can be easily introduced by lead tetraacetate or silver oxide-bromine oxidation of aliphatic alcohols.[18-21] Since these oxidative cyclizations of alcohols to cyclic ethers are simple and mild reactions, we used them as the key synthetic step in the synthesis of spiro-ketal pheromones *6* and 7.

By applying these reactions to primary and secondary diols, *e. g.* 1,7-nonanediol, a spiro-ketal pheromone-chalcogran *6* could be prepared in several steps from easily available starting materials (Scheme 1.).



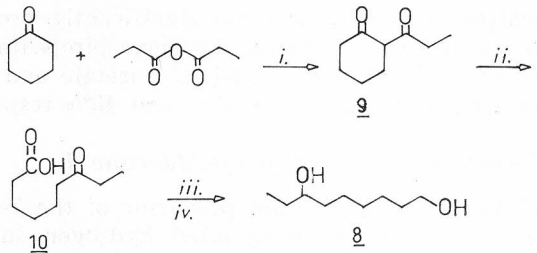
6 ⟹ 8

Scheme 1.

i. Synthesis of 2-Ethyl-1,6-dioxaspiro[4,4]nonane-Chalcogran 6

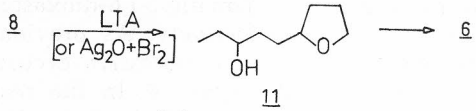
As already pointed out, the synthetic precursor in our methodology for the construction of the 2-ethyl-1,6-dioxaspiro[4,4]nonane *6* was 1,7-nonanediol *8*. The diol *8* was obtained by the reduction of methyl 7-ketononanoate with

lithiumaluminium hydride. 7-Ketononanoic acid *10*, was prepared by the ring opening of 2-propionyl cyclohexanone *9* with sodium hydroxide.[22] This cleavage reaction was followed by esterification of the keto-acid *10* to the corresponding methyl ester. 2-Propionyl cyclohexanone *9* was prepared by acylation of cyclohexanone with propionic acid anhydride in the presence of an excess of borontrifluoride etherate (Scheme 2.).[23]

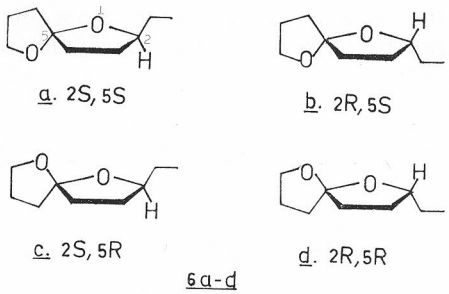


Scheme 2.

The key step in our approach to spiro-ketal skeleton synthesis is the spiroketalisation of 1,7-nonanediol *8* by silver oxide-bromine or by lead tetraacetate oxidation. The bicyclic ether ring closure occurs successively. The rate of cyclization of a primary alcoholic group to a monosubstituted tetrahydrofuran was found to be several times higher than that of a secondary hydroxylic group.[18,19] The progress of the reaction of lead tetraacetate with 1,7-nonanediol *8* was monitored by gas chromatography. It was expected that also in this case the oxidation of the primary hydroxyl group would be much faster than that of the secondary one, and that the detection of the intermediary tetrahydrofuran derivative *11* might be possible. However, no full selective oxidation of the primary hydroxyl group was achieved, because the alkoxy radical generated from the secondary hydroxyl group reacts with the



Scheme 3.



a. 2S, 5S b. 2R, 5S

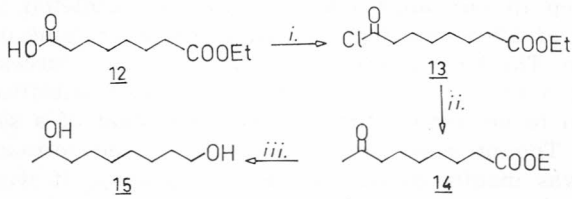
c. 2S, 5R d. 2R, 5R

6a-d

activated C—H bond, adjacent to ether oxygen, thus forming a spiro-ketal bicyclic ether *6*. The ether oxygen atom activates the adjacent C—H bond and the abstraction of such hydrogen is a preferable reaction of the intermediary alkoxy radical.[24] In the first cyclization reaction, equal amounts of the two diastereomeric pairs of 2-(3-hydroxypentyl-)-tetrahydrofuran *11* were obtained. In the second cyclization step, the stereochemical difference between the two transition states, deriving from diastereomeric pairs of alkoxy radical generated from hydroxy-ether *11*, was not significantly pronounced, so that a mixture of four diastereomeric 2-ethyl-1,6-dioxaspiro[4,4]nonanes *6a-d* was obtained. The yield of chalcogran *6* in lead tetraacetate and silver oxide-bromine oxidations of 1,7-nonanediol *8* was 61% and 48% respectively.

ii. Synthesis of 7-methyl-1,6-dioxaspiro[4,5]decane 7

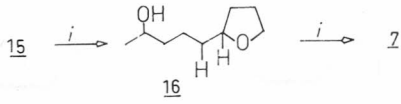
1,8-Nonanediol *15*, as an open chain precursor of the 7-methyl-1,6-dioxaspiro[4,5]decane was prepared by using ethyl hydrogen suberate *12* as the starting material.[25] The free carboxylic group was transformed to the corresponding acyl chloride *13*, which was methylated by dimethyl cadmium[26] and ethyl 8-ketononanoate *14* was obtained in a fair yield. The keto-ester *14* was reduced by lithiumaluminium hydride and 1,8-nonanediol *15* was obtained (Scheme 4.).



i. $SOCl_2$, *ii.* $(CH_3MgJ \rightarrow) Cd(CH_3)_2$, *iii.* $LiAlH_4$

Scheme 4.

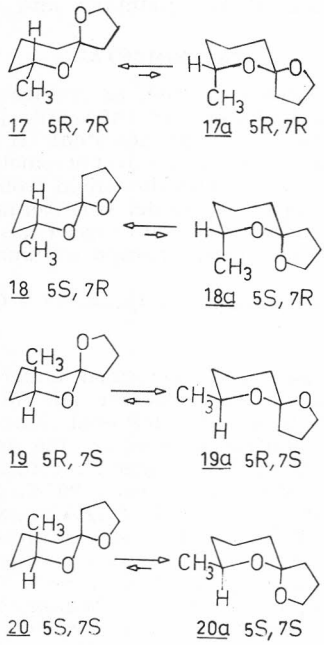
By treatment of 1,8-nonanediol *15*, either with silver oxide-bromine reagent or with lead tetraacetate, the 7-methyl-1,6-dioxaspiro[4,5]decane was obtained in 49% and 60% yields, respectively. As previously discussed, the formation of spiro-ketal moiety involves a successive cyclization to the intermediary 2-(4-hydroxypentyl)-tetrahydrofuran *16*. In the reaction of hydroxy--ether *16* with oxidants, the 1,6-transfer of hydrogen, adjacent to the ether oxygen, to the radicalic oxygen is energetically more favourable than hydrogen abstraction from the non-activated carbon atom in position 1 of the side chain of the intermediate *16*; thus, the six-membered cyclic ether ring is closed (Scheme 5.).[21,24]



i. LTA or Ag_2O+Br_2

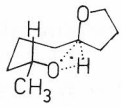
Seheme 5.

Due to the presence of two chiral carbon atoms (positions 5 and 7), 7-methyl-1,6-dioxyspiro[4,5]decane can exist in two diastereomeric pairs, *17*—*20*, which can be in equilibrium with their four conformational isomers *17a*—*20a*. The most favourable are the conformers possessing the equatorial methyl group in position 7 (*17*, *18*, *19a* and *20a*). The axial ether oxygen in position 1 (*e. g. 17* and *20a*) is preferred by 3.35 kJ/mole, since the equatorial oxygen (*e. g.* in *18* and *19a*) may cause a considerable polar interaction between the two oxygen atoms.[27,28] From these considerations it follows that the isomer *17* (with 5*R* and 7*R* configuration) and its energetical equivalent *20a* (with 5*S* and 7*S* configuration) are the most stable conformers. The conformer *18* (having 5*S* and 7*R* configuration) is enantiomeric and energetically equivalent to the conformer *19a* (with 5*R* and 7*S* configuration), but they are less stable (by about 3.35 kJ/mole) than the isomers *17* and *20a*, having the oxygen atom

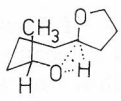


in position 1 in equatorial orientation. The isomers *19* and *20* and their energetical equivalents *18a* and *17a* are not favourable because of a strong 1,3-diaxial interaction between the methyl group and ether oxygen (1) in *19* and *18a* and between the methyl group and methylene (4) in *20* and *17a*.

The transition state for the intramolecular 1,6-hydrogen abstraction of type *21* (5*S*,7*R*) leading to the tetrahydropyran ring closure, is preferable when the methyl group is in a quasi-equatorial position and isomers *17* (5*R*,7*R*) and *20a* (5*S*,7*S*) can easily be formed. Quite similar transition states are involved when enantiomers *18* and *19a* are formed. However, the transition state of type *22*, in which the methyl group is in a quasi-axial position, is unfavourable and isomers *19* and *20* cannot be formed; and only their conformational isomers may be present in the reaction mixture. By the Dreiding model inspection and by applying the conformational parameters on final



21 5S, 7R



22

products and transition states, we assumed that in both applied reactions the diastereomers *17* and *20* predominate, while the formations of isomers *18* and *19a* are less favourable.

This approach to the synthesis of 7-methyl-1,6-dioxaspiro[4,5]decane can be also applied to the preparation of other spiro-ketals of type *2*, possessing an alkyl substituent in position 7; however, spiro-ketals of the same skeleton but with an alkyl group in position 2, *i. e.* attached to the five-membered cyclic ether ring, cannot be prepared by this sequence of reactions because of different oxidation rates of the primary and the secondary hydroxylic groups.

EXPERIMENTAL

Boling points have not been corrected, IR spectra (CCl_4 solution, if not stated otherwise) were taken on a Perkin-Elmer Infracord spectrophotometer, model 337 (only strong and characteristic bands are indicated). ^1H NMR spectra were recorded on a Varian FT-80A (80 mHz in $CDCl_3$) spectrophotometer with TMS as the internal standard; shifts are given in ppm values downfield from TMS. Gas chromatography was performed on a Varian apparatus, model 1400 (column, 10% XE-60, 2 m × 2 mm at 70—200 °C, temperature gradient 6 °C/min, carrier gas H_2), while separations were performed on a Varian 90-P gas chromatograph (column, XE-60, 2 m × 5 mm).

i. Synthesis of 2-Ethyl-1,6-dioxaspiro[4,4]nonane - Chalcogarn

2-Propionyl cyclohexanone 9

Acylation of cyclohexanone was performed under acidic conditions.[23] A cold mixture of 29.5 g (0.3 mole) of cyclohexanone and 78.1 g (0.6 mole) of propionic acid anhydride was added from an additional funnel to cold borontrifluoride etherate (84.8 g, 0.6 mole) during 5 minutes, the temperature of the reaction mixture being kept below 10 °C. The reaction mixture was stirred for additional 4 hrs and the temperature allowed to reach 20 °C. Hydrolysis was carried out by pouring the reaction mixture into 1.2 l of 13% aqueous sodium acetate solution. Ether was removed by distillation under reduced pressure, and the mixture was then heated to reflux for 30 min. The mixture was then treated with sodium bicarbonate and extracted with petrolether (40—70 °C). The organic layer was washed successively with aqueous saturated sodium bicarbonate and water, and then dried over anh. $MgSO_4$. Petrolether was removed by distillation in vacuo and the residue was distilled at 123—125 °C/22 mm Hg, giving 27 g (58%) of 2-propionyl cyclohexanone. Satisfactory IR and NMR spectra were obtained.

7-Ketononanoic acid 10[22]

A mixture containing 88 ml of 5% aqueous sodium hydroxide (4.4 g, 0.11 mole) and 15.4 g (0.1 mole) of 2-propionyl cyclohexanone was stirred and refluxed during 2 hrs. The cold reaction mixture was acidified with conc. hydrochloric acid and saturated with sodium chloride. From a white suspension the keto-acid *10* was extracted with ether (3 × 30 ml), and the ethereal solution was washed with water and dried. The solvent was removed by distillation under reduced pressure and the oily residue was distilled in vacuo (7-ketononanoic acid boils at 150—151 °C/2 mm Hg). The yield of the keto-acid *10* was 10.5 g (61%). Satisfactory spectral data were obtained.

Methyl 7-ketononanoate

A solution of 8.6 g (0.05 mole) of 7-ketononanoic acid dissolved in 10 ml of ether was treated with dry ethereal solution of diazomethane until the solution

became pale yellow. The excess of diazomethane and ether was removed by distillation in vacuo and the ester was then distilled at 106—108 °C/2 mm Hg. Methyl 7-ketononanoate was obtained in quantitative yield. IR (film): 2925, 2850, 1730, 1705, 1455, 1430, 1410, 1355, 1250, 1190, 1170, 1110 and 1010 cm^{-1}; NMR δ: 0.95 (3H, t), 1.25—1.75 (6H, m), 2.10—2.50 (6H, m), 3.60 (3H, s).

Methyl 7-ketononanoate was also obtained directly from 2-propionyl cyclohexanone by using sodium methoxide as the base for the cyclohexanone ring opening. The yield of methyl 7-ketononanoate was also satisfactory, but its purification was troublesome.

1,7-Nonanediol 8

To a suspension of 0.4 g of lithium-aluminium hydride in 50 ml of dry ether, a solution of 1.88 g (0.01 mole) of methyl 7-ketononanoate in 20 ml of dry ether was added from the dropping funnel during 15 min. The mixture was then heated to reflux with stirring for 2 hrs. The cold mixture was then successively treated with 0.5 ml of ethyl acetate, 5 ml of cold water and 10% sulfuric acid to make the mixture acidic. Ethereal solution was separated and water solution was extracted with ether (5 × 25 ml). Combined ethereal solutions were then washed with water, aqueous sodium bicarbonate and dried over anh. $MgSO_4$. Ether was removed in vacuo and the oily residue was distilled at 134—135 °C/2 mm Hg. The yield of 1,7-nonanediol *8* was 1.4 g (75%). IR (film): 3320, 2910, 2840, 1450, 1430, 1370, 1110, 1050, 955 cm^{-1}; NMR: δ 0.90 (3H, t), 1.25—1.70 (10H, m) 3.25—3.50 (2H, b), 3.55—3.70 (3H, m).

2-Ethyl-1,6-dioxaspiro[4,4]nanone — Chalcogram 6a-d

i. By Lead Tetraacetate

A heterogeneous mixture containing 11.0 g (0.022 mole) of lead tetraacetate (92% purity), 2.2 g of dry calcium carbonate, 40 ml of dry benzene and 1.6 g (0.01 mole) of 1.7-nonanediol was stirred under reflux during 4.5 hrs. The formation of the intermediary ether *11* and the final product *6* was controlled by gas chromatography, while the consumption of lead tetraacetate was checked by the KI-starch testing paper. The cold mixture was filtered off and the precipitated salts were washed with ether. Combined solutions were washed with aqueous saturated sodium bicarbonate and water, and then dried over anh. sodium sulfate. Ether was removed by distillation while the residue was analyzed and separated by gas chromatography. The chalcogran *6,* was obtained in 61% yield. IR: 2960, 2920, 2870, 1460, 1440, 1380, 1345, 1240, 1175, 1155, 1115, 1050, 1020, 960, 930, 920, 870 and 830 cm^{-1}; NMR δ: 0.92 (3H t), 1.25—1.70 (4H, m), 1.80—2.15 (6H, m), and 3.75—4.19 (3H, m).

ii. By Silver Oxide-Bromine Reagent

To a heterogeneous mixture containing 1.6 g (0.01 mole) of 1,7-nonanediol *8,* 9.7 g (0.042 mole) of freshly prepared silver oxide and 40 ml of *n*-pentane, a solution of 6.4 g (0.04 mole) of bromine in 20 ml of *n*-pentane was slowly added (about 1.2 hrs) under vigorous stirring. When the addition of bromine solution was over, the mixture was stirred at room temperature for further 1.5 hrs. The precipitated silver salts were filtered off and the precipitate washed with *n*-pentane. The filtrate and the washing were united and washed successively with water, aqueous sodium thiosulfate and aquoeus sodium bicarbonate, and then dried over anh. sodium sulfate. The solvent was carefully removed by distillation through an efficient column and the residue analyzed and purified by gas chromatography, as described previously. The yield of chalcogran *6a—d* was 48%.

ii. Synthesis of 7-Methyl-1,6-dioxaspiro[4,5]decane 7

Ethyl Hydrogen Suberate 12[25]

The mixture of 17.4 g (0.1 mole) of suberic acid, 13.3 g (0.058 mole) of diethyl suberate, 10 ml of di-*n*-butyl ether, 2.5 ml of conc. hydrochloric acid and 8 ml of ethyl alcohol (95%) was refluxed for 5 hrs. The course of the reaction was monitored by TLC. When equilibrium was reached, the reaction mixture was cooled

to room temperature, and ether (100 ml) was added. The ethereal solution was washed with saturated aqueous sodium bicarbonate in order to remove acidic compounds. The alkaline solution, containing sodium ethyl suberate and di-sodium suberate, was acidified with dilute hydrochloric acid an extracted by ether. The ethereal solution was washed with water and dried. After removal of ether, the semi-solid residue was purified on silica gel (0.063—0.200 mesh) column by using chloroform as eluent. We obtained 10.8 g (53%) of pure ethyl hydrogen suberate, m. p. 25 °C, (b. p. 192 °C/17 mm Hg), displaying satisfactory spectral data.

Ethyl Suberoyl Chloride 13

To a solution of 10.8 g (0.044 mole) of ethyl hydrogen suberate in petrolether (40—70 °C) (50 ml), freshly distilled thionyl chloride (5.95 g, 0.05 mole) was added and the mixture was heated on a water bath to reflux gently for 20 hrs. The petrolether and the excess of thionyl chloride were removed by distillation under reduced pressure. It was shown by IR that the free carboxyl group was completely transformed into the corresponding acyl chloride, which was used in the following step without further purification.

Ethyl 8-ketononanoate 14[26]

To a solution of methyl magnesium iodide [prepared from 1.7 g (0.07 g/mole) of magnesium turnings and 10.9 (0.07 mole) of methyl iodide] cooled to —5 °C, 8.2 g (0.045 mole) of anh. cadmium chloride was added at once, in an inert atmosphere and with constant stirring. When the exothermic reaction ceased, the ice-bath was removed and ether was removed by distillation under reduced pressure. The oily residue was dissolved in dry benzene by gentle heating and stirring. When the oil was dissolved, the heating was stopped and a solution of ethyl suberoyl chloride (from previous step) in dry benzene was added from a dropping funnel. When the exothermic reaction ceased, the reaction mixture was heated for 1 h to reflux gently. To the cooled mixture, a solution of cold dilute sulfuric acid was added and the aqueous solution was extracted by benzene and the solution dried by anh. magnesium sulfate. After removal of solvents the oily residue was distilled under reduced pressure. The fraction collected at 132—135 °C/10 mm Hg was pure ketoester *14*; 7 g (70%) were obtained. IR (film): 2920, 2840, 1725, 1710, 1450—1400, 1360, 1290, 1250, 1170, 1080, 1020, 850, 810, 710 cm^{-1}. NMR: δ 1.20 (3H, t), 1.25—1.75 (8H, m), 2.10 (3H, s), 2.10—2.50 (4H, m), 3.95—4.25 (2H, q).

1,8-Nonanediol 15

Ethyl 8-ketononanoate *14* (5 g, 0.025 mole) was reduced with lithiumaluminium hydride (1.45 g) in dry ether. By distillation 3.7 g (92%) of 1,8-nonanediol was obtained, b. p. 142—145 °C/15 mm Hg. IR (film): 3300, 2910, 2840, 1450, 1365, 1050 cm^{-1}. NMR: δ 1.15 (3H, d), 1.20—1.70 (12H, m), 2.20 (2H), 3.45—3.70 (3H, m).

7-Methyl-1,6-dioxaspiro[4,5]decane 7

i. By Silver Oxide-Bromine Reagent

To a suspension of 1.6 g (0.01 mole) of 1,8-nonanediol and 10.2 g of silver oxide (freshly prepared) in 75 ml of *n*-pentane, 7.4 g (2.3 ml) of bromine in 20 ml of *n*-pentane was added from a dropping funnel during 3 hrs at room temperature with stirring of the mixture. After the bromine solution was added, the stirring of the mixture was continued for additional 1.5 hrs. The mixture was then filtered and the filtrate was successively washed with aqueous sodium thiosulfate, sodium bicarbonate solution and water, and then it was dried with anh. $MgSO_4$. Pentane was removed by distillation and the residue was purified by gas chromatography (column XE-60, 2 m). IR: 2930, 2860, 1450, 1435, 1370, 1365, 1350, 1305, 1280, 1265, 1210, 1150, 1105, 1075, 1035, 1005, 970, 935, 905, 890, 855 cm^{-1}. NMR: δ 1.20—1.90 (13H, m) and 3.50—3.90 (3H, m). ^{13}C NMR ($CDCl_3$): 20.41, 23.80, 25.39, 33.59, 37.76, 61.31, 66.98 and 105.67 ppm.

ii. By Lead Tetraacetate

A mixture containing 1.0 g (0.006 mole) of 1,8-nonanediol, 5.8 g (0.012 mole +10% excess) of lead tetraacetate in 30 ml of dry benzene was refluxed during 6 hrs with stirring, by which time the oxidant was completely consumed. The mixture was treated as described above. The yield of 7-methyl-1,6-dioxaspiro-[4,5]--decane was 60%. The spectral data were identical with those obtained from the mixture prepared by the silver oxide-bromine oxidation of diol *15*.

REFERENCES

1. W. Francke, V. Heemann, B. Gerken, J. A. A. Renwick, and J. P. Vitè, *Naturwissenschaften* **64** (1977) 590.
2. K. Mori, *The Synthesis of Insect Pheromones,* in *The Total Synthesis of Natural Products,* Edited by J. ApSimon, Vol. **4** pp. 109, Wiley, New York, 1981.
3. G. Bergström, J. Tangö, W. Reith, and W. Francke, *Z. Naturforschung* **37c** (1982) 1124.
4. J. Tangö, G. Bergström, A.-K. Borg-Karlson, I. Groth, and W. Francke, *Z. Naturforschung* **37c** (1982) 376.
5. K. Mori, M. Sasaki, S. Tamada, T. Suguro, and S. Masuda, *Tetrahedron* **35** (1978) 1601; R. Jacobson, R. J. Taylor, H. J. Williams, and L. R. Smith, *J. Org. Chem.* **47** (1982) 3140; R. L. Smith, H. J. Williams, R. M. Silverstein, *Tetrahedron Letters* (1978) 3231.
6. K. Mori, K. Tanida, *Tetrahedron* **37** (1981) 3221.
7. K. Mori and M. Ikunaka, *Tetrahedron* **40** (1984) 3471.
8. F. Francke, W. Reith, G. Bergström and J. Tangö, *Naturwissenschaften* **67** (1980) 149.
9. W. Francke, G. Hindorf, and W. Reith, *Angew. Chem., Internat. Ed.* **17** (1978) 862; C. Phillips, R. Jacobson, B. Abrachams, H. J. Williams, and L. R. Smith, *J. Org. Chem.* **45** (1980) 1920.
10. S. V. Ley and B. Lygo, *Tetrahedron Letters* **23** (1982) 4625.
11. C. Iwata, K. Hattori, S. Uchida, and T. Imanishi, *Tetrahedron Letters* **25** (1984) 2995.
12. K. Mori, M. Katsureda, *Liebigs Ann. Chem.* (1984) 157.
13. M. Beroza, *Pest Management with Insect Sex Attractants,* Edited by M. Beroza, *ACS Symposium Ser.* **23**. Am. Chem. Soc., Washington, D. C. 1976.
14. W. Wierenga, *Total Synthesis of Ionophores,* in *The Total Synthesis of Natural Products,* Edited by J. ApSimon, Vol. **4**, pp. 263, Wiley, New York, 1981.
15. O. A. Kožič, G. M. Segalj, and I. V. Torgov, *Izvest. Akad. Nauk SSSR, ser. him.* (1982) 325.
16. S. V. Ley and B. Lygo, *Tetrahedron Letters* **25** (1984) 113.
17. T. Kožluk, L. Cottier, and G. Desotes, *Tetrahedron* **37** (1981) 1875.
18. M. Lj. Mihailović and Ž. Čeković, *Synthesis* (1970) 209.
19. M. Lj. Mihailović, Ž. Čeković, Z. Maksimović, D. Jeremić, Lj. Lorenc, and R. I. Mamuzić, *Tetrahedron* **21** (1965) 2799.
20. M. Lj. Mihailović, Ž. Čeković, and J. Stanković, *Chem. Commun.* (1969) 981.
21. V. M. Mićović, S. Stojčić, M. Bralović, S. Mladenović, D. Jeremić, and M. Stefanović, *Tetrahedron* **25** (1969) 985.
22. R. M. Menyik, F. C. Frostick, Jr., J. J. Sanderson, and C. R. Hauser, *J. Amer. Chem. Soc.* **75** (1965) 5030; C. R. Hauser, F. M. Swamer, and B. I. Ringler, *J. Amer. Chem. Soc.* **70** (1948) 4023.
23. J. T. Adams and C. R. Hauser, *J. Amer. Chem. Soc.* **67** (1945) 284.
24. M. Lj. Mihailović and M. Miloradović, *Tetrahedron* **22** (1966) 723.
25. S. Swann, Jr., R. Oehler, and R. J. Buswell, *Org. Synth., Coll. Vol.* **2** (1943) 276.
26. H. McKennis, Jr. and V. du Vigneaud, *J. Amer. Chem. Soc.* **68** (1946) 832; J. Cason and F. S. Prout, *J. Amer. Chem. Soc.* **66** (1944) 46.
27. E. L. Eliel and C. A. Giza, *J. Org. Chem.* **33** (1968) 3754.
28. S. Zefirov and N. M. Šehtman, *Uspehi himii* **40** (1971) 593.

IZVOD

Sinteze spiro-ketalnih feromona

Živorad Čeković, Jovan Bošnjak, Dušan Mandić i Dimitar Ilijev

Izvršene su sinteze nekih feromona koji sadrže spiro-ketalnu strukturu. Feromon izolovan iz insekta *Pityogenes chalcografus L*, 2-etil-1,6-dioksaspiro[4,4]nonan, sintetizovan je reakcijom 1,7-nonadiola sa srebro-oskid-bromnim reagensom ili s olovo-tetraacetaton. Spiro-ketalni feromon 7-methyl-1,6-dioksaspiro[4,5]dekan izolovan iz insekta *Paravespula vulgaris L.* dobiven je također dvostrukom intramolekulskom ciklizacijom 1,8-nonandiola pomoću navedenih reagenasa.