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CYCLOCARBONYLATION OF UNSATURATED TOSYLATES AS A METHOD OF CYCLANONE SYNTHESIS[1]

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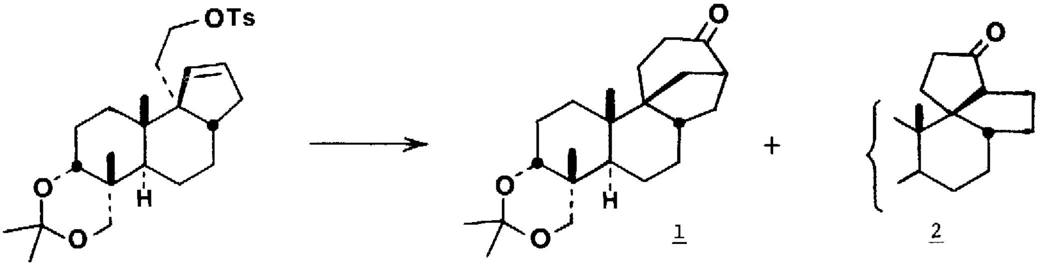
Abstract. A study has been made to determine the scope of the cyclocarbonylation reaction of olefinic tosylates with $Na_2Fe(CO)_4$.

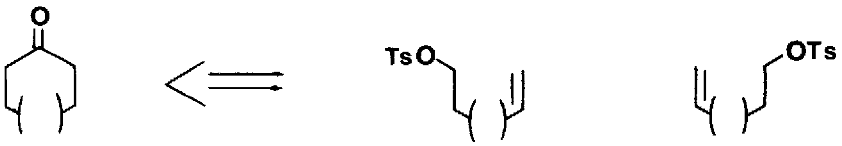
Our recently reported synthesis of aphidicolin[2] employed, as the key step, the cyclocarbonylation of olefinic tosylate 1 with Collman's reagent, $Na_2Fe(CO)_4$.



1

2

This interesting and potentially useful reaction was first reported by Merour[3,4] and subsequently by Collman,[5] but had not previously been used in synthesis. Its potential value stems from the fact that it allows chemists a fundamentally new and different way of preparing cycloalkanones. For planning purposes, one can disconnect the cycloalkanone into two different olefinic tosylates which might serve as simple precursors to more complex targets.



We have now undertaken a brief study of the scope of the cyclocarbonylation reaction and wish to report the results illustrated in the Table.

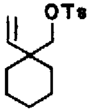
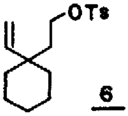
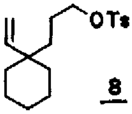
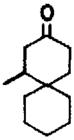
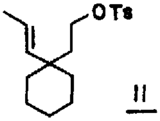
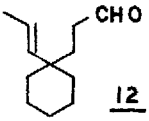
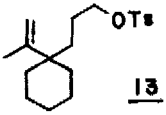
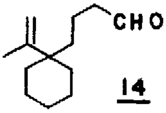
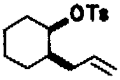
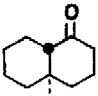
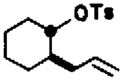
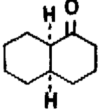
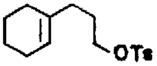
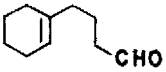
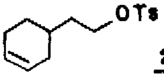
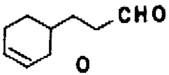
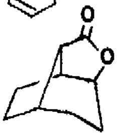
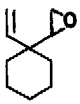
Reaction No.	Unsaturated Tosylate	Product(s)	Isolated Yield (%)
1	 **4**	 **5**	65
2	 **6**	 **7**	70
3	 **8**	 **9** +  **10** 1.8:1	70
4	 **11**	 **12**	
5	 **13**	 **14**	51
6	 **15**	 **16**	30
7	 **17**	 **18**	45
8	 **19**	 **20**	75
9	 **21**	 **22**	70
10	 **23**	 **24**	56
11	 **25**	 **7** +  **26** 1:1.5	61

Table. Cyclocarbonylation of Some Olefinic Tosylates with $Na_2Fe(CO)_4$

As the first two examples in the Table indicate, the cyclocarbonylation reaction is an effective means of preparing five and six-membered rings, and works well in the preparation of difficulty accessible spiro compounds. Seven-membered rings can also be prepared (reaction 3) but the reaction is not regioselective and a mixture of products results.

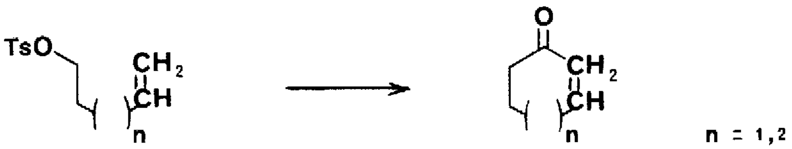
Unfortunately, the reaction appears to be limited to monosubstituted olefins since addition of a second substituent on either carbon of the double bond prevents cyclization. Attempted cyclocarbonylation of disubstituted olefins (reactions 4 and 5) led only to aldehydes. Evidently the intermediate acylferrates are formed normally in these cases, but further olefin insertion to the more hindered double bonds does not occur.

Reactions 6 and 7 indicate that secondary olefinic tosylates can be cyclocarbonylated although in diminished yields. Both *cis* and *trans* 1-decalones can be prepared, depending on the stereochemistry of the starting tosylate. Once again, however, reaction of a more hindered olefin (reaction 8) fails to give cyclized product.

A further limitation is the apparent inability of the reaction to form bicyclo[3.2.2]nonanones or bicyclo[3.2.1]octanones (reactions 9 and 10). In the former case only aldehyde is formed, while in the latter case, an unusual double carbonylation occurs to give a product for which we propose the lactone structure 24.[6] This is particularly surprising in view of our successful cyclocarbonylation of the cyclopentenylethyl tosylate 1 in the aphidicolin synthesis.[2] Clearly, 23 serves as a poor model for the aphidicolin work.

The last entry in the Table shows the result of cyclocarbonylating an epoxy olefin (25).[7] The idea in this instance was to extend the cyclocarbonylation reaction for enone synthesis, since one would expect to obtain a β-hydroxyketone product. In practice, treatment of 25 with $Na_2Fe(CO)_4$ gave a mixture of saturated ketone 7 and desired enone 26. Presumably, enone 26 is formed during reaction but undergoes a rapid reduction by hydridoiron species during protonolytic work-up.[8] All attempts to eliminate this side reaction have thus far failed.[9]

The results presented in the Table can be summarized by saying that the cyclocarbonylation of an olefinic tosylate is an effective means of preparing cyclopentanones and cyclohexanones from olefinic tosylate precursors in which the double bond is monosubstituted:



In a representative procedure, a mixture of 1-vinyl-1-(2-tosyloxyethyl)-cyclohexane (6, 0.142 gm, 0.460 mmoles), disodium iron tetracarbonyl dioxane complex (0.363 gm, 1.05 mmoles) and 30 ml of dry tetrahydrofuran were refluxed for three hours under nitrogen. The reaction was then quenched by addition of 0.5 ml acetic acid. After filtration through a short column of alumina, the solvent was removed under reduced pressure. Kugelrohr distillation gave spiro-[5.5]undecan-3-one (7, 0.054 gm, 0.32 mmoles, 70%); bp $_{.5mm}$ 62°; ir ($CHCl_3$) 2940, 1700 cm^{-1};

^{1}H nmr: (CDCl$_3$) δ 2.30 (t, 4H, J=7 Hz), 1.68 (t, 4H, J=7 Hz), 1.46 (br s, 10 H); ^{13}C nmr: (CDCl$_3$) δ 210.7, 36.2, 35.3, 35.0, 31.2, 25.9, 21.2; MS (19 ev) 166 (M$^+$).

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Notes and References

1. This work was carried out at the University of California, Santa Cruz, California 95064.
2. J. E. McMurry, A. Andrus, G. M. Ksander, J. H. Musser, and M. A. Johnson, *J. Amer. Chem. Soc.*, *101*, 1330 (1979).
3. J. Y. Merour, J. L. Roustan, C. Charrier, J. Collin, and J. Benaim, *J. Organomet. Chem.*, *51*, C24 (1973).
4. J. L. Roustan, J. Y. Merour, C. Charrier, J. Benaim, and P. Cadiot, *J. Organomet. Chem.*, *169*, 39 (1979) and references therein.
5. J. P. Collman, *Acc. Chem. Res.*, *8*, 342 (1975).
6. Lactone structure 24 was assigned based on the following spectroscopic evidence: ir (CHCl$_3$) 1760 cm^{-1}; ^{1}H nmr (CDCl$_3$) δ 4.8 (m, 1H), 1.2-3.2 (m, 11H); ^{13}C nmr (CDCl$_3$) δ 180.2, 84.3, 50.8, 46.2, 45.4, 34.7, 32.1(2), 29.2; MS (19 ev), 152 (M$^+$), 124, 108, 93, 80, 78, 67.
7. The reaction of epoxides with acyltetracarbonylferrates has been reported: M. Yamashita, S. Yamamura, M. Kurimoto, R. Suemitsu, *Chem. Lett.*, 1067 (1979).
8. *cf.* R. Noyori, I. Umeda, and T. Ishigami, *J. Org. Chem.*, *37*, 1542 (1972).
9. It occurred to us that protonolytic work-up *in the presence of an excess of an added enone* might serve to suppress reduction of the desired enone, but this was only partially successful. When reaction 11 was worked up in the presence of 5 equiv. 3-buten-2-one, compounds 7 and 26 were formed in a 1:1:5 ratio (as opposed to 4:1 without added enone).

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