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Synthetic studies related to pentalenolactones , Part II [1]
Cyclopentanation with 2-chloromethyl-allyl phenylsulfone.

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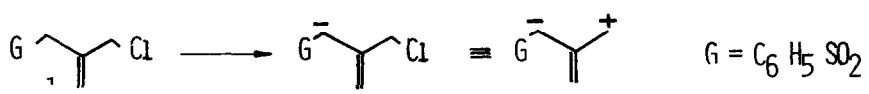
Summary · *The title sulfone was cyclocondensed with cyclopentenones under palladium catalysis in a biphasic system (1N KOH-TEBA/CH_2Cl_2) to give methylene-bicyclo [3,3,0] octanones in 39-43% yield.*

We recently reported[1] a convenient preparation of Tsuji's conjunctive reagent 2 [2] using the readily available chloro-sulfone 1 and its condensation with 5,5-disubstituted cyclopent-2-enones to prepare some bicyclo [3,3,0] octanones The anionization of the sulfone 1 itself would lead to an anionic species embodying both a nucleophilic and an electrophilic centers (Scheme 1), precisely the feature displayed by conjunctive reagents [3] It seemed

Scheme 1 

therefore promising to directly use the sulfone 1 as a cyclopentanation reagent.

The ability of compound 1 to be anionized was ascertained by treatment with butyllithium in THF. The corresponding anion, as evidenced by a trapping experiment (D_2SO_4, 98% monodeuteration), proved stable provided the temperature was kept low (~ -95°C)[4] and could be condensed with electrophiles (Table 1).

With cycloalkenones, in presence of HMPT, Michael additions took place but no bicyclic products could be detected, a prolonged contact between reagents just resulting in an isomerization of the allylic chloride moiety into the chloro-vinylic form Other conditions (potassium t-butoxide, 50% NaOH-TEBA/CH_2Cl_2) were tried without success. The 1,4-addition product 3 was isolated in high yield under phase transfer conditions with methyl acrylate (Scheme 2).

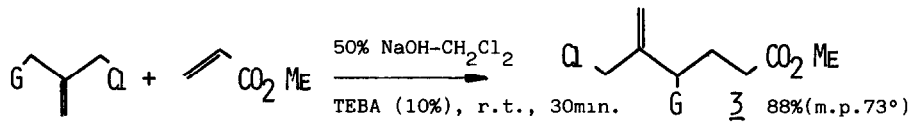
Table 1 Condensation of the lithio derivative of sulfone 1 with electrophiles

Electrophile	Products,	% yield	(Mp°C)
allyl bromide	4	93	(oil)
acetaldehyde	5	80*	(70-72)
cyclohex-2-enone	6	6**	(104)
methyl-3-cyclopent-2-enone	7 + 8	64**	(112-113)
10b	9	61**	(138-140)
methyl acrylate	—		

notes * after oxidation with Jones's reagent

** In presence of 2 mol. eq. of HMPT

Scheme 2



Palladium catalysis was then examined. Methallyl chloride has been shown to react with Ishi's catalyst (Pd_2 (DBA)$_3$ - $CHCl_3$, 15) [6] in the presence of phosphines to give a cationic π-allyl complex and it could be expected that 1 would react with 15 to give such a cationic species which then would react with a base to give a trimethylenemethane derivative [2] or conversely that the enolate resulting from the conjugated addition would be activated by oxidative insertion of the zerovalent palladium reagent into the carbon-chlorine bond

Indeed a yellow solution formed adding the deep purple catalyst 15 to the sulfone 1 in methylene chloride but again no cyclization could be observed on treatment by 15 of a mixture of sulfone 1 with the ketone 10a in presence of bis-diphenylphosphinoethane (DPPE) and of an excess of sodium ethoxide in T H F. Other bases (triethylamine, potassium t-butoxide, KOH on alumina, K_2CO_3) were also disappointing but we were delighted to find out that adding first the catalyst (1 mole %) to a solution of the chlorosulfone 1, the cyclopentenone (two fold excess) the phase transfer agent (triethylbenzylammonium chloride, TEBA) and DPPE in CH_2Cl_2 then, as soon as the yellow colour had well developped (c.a 10mn), a 1N aqueous KOH solution the expected cyclized product 11a was formed in fair yield after 2 days stirring at room temperature under argon (Scheme 3).

Scheme 3

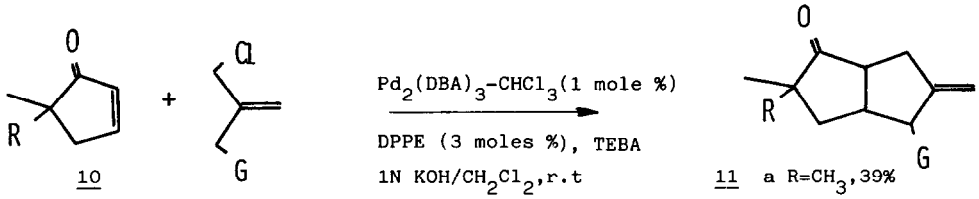
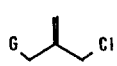


Table 2 Condensation of chloro-sulfone 1 with 5,5-disubstituted cyclopentenones *

chlorosulfone 1	ketone	KOH	palladium catalyst	ligand	Phase transfer agent	products (% Yield)
10mmol	10a(20mmol)	1N(13ml) 1N(13ml)	$Pd_2(DBA)_3CHCl_3$ (0 1mmol)	DPPE(0 326mmol)	TEBA 300mg	11a (39 - Mp 148°C)
"	" "	0 4N(25ml)	"	"	"	11a (20) + 13 (12)
"	" "	2N (13ml)	"	"	"	11a (16) + 13 (12 5)
"	" (10mmol)	1N(13ml)	"	"	"	11a (18)
"	" (20mmol)	"	"	"	Aliquat 336 300mg	12 (16)
"	" "	"	"	"	0	11a(trace) 13 (29)
"	" "	"	(0 2mmol)	"	TEBA 300mg	12 + 11a (27)
"	" "	"	(0 1mmol)	2 2'-Bypiridine(0 1mmol)	"	13 (trace)
"	" "	"	$Pd(PPh_3)_4$ 0 1mmol	PPh_3 (0 4mmol)	"	starting materials
"	10b(20mmol)	1N(13ml)	$Pd_2(DBA)_3CHCl_3$ (0 1mmol)	DPPE (0 35mmol)	TEBA 300mg	11b (43, 2 isomers)

* Solvent CH_2Cl_2 (50ml) 2 days stirring under argon at r t

Formula



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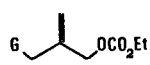

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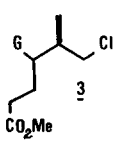

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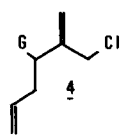

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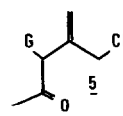

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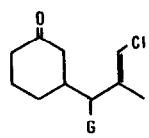

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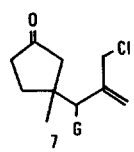

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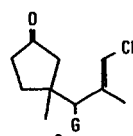

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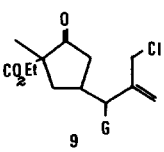

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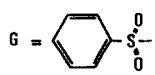
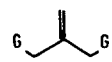
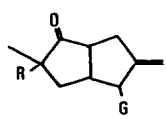


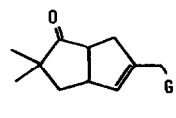


13

10a R = CH_3
10b R = CO_2Et



11a R = CH_3
11b R = CO_2Et



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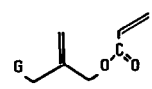

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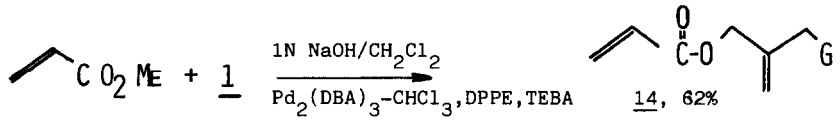
The yield proved very sensitive to the reaction conditions, especially to the ratio of reagents (Table 2). In some cases the disulfone 13 could be isolated [7].

The compound 11a formed from 5,5-dimethyl-cyclopent-2 enone proved identical (M.p. 148°C) with the product we previously prepared using Tsuji's reagent [9].

Using the carboethoxy derivative 10b a mixture of two isomers resulted and was fractionnated by flash-chromatography on silica gel. One of the component was identical (n m.r.) with the product we already obtained [1] by Tsuji's protocole. Both isomers did not equilibrate when separatly submitted to the condensation medium, nor did the corresponding ketones they formed upon ozonolysis. Consequently, that mixture of stereoisomers has been formed under kinetic control. Cyclohexenone and 3-methylcyclopent-2-enone did not react at all under these conditions. Curiously methyl acrylate led to a new acrylate ester 14 (Scheme 4).

Scheme 4



14, 62%

CONCLUSION A substantially simplified procedure to convert cyclopentenones into methylene-bicyclo [3,3,0] -octanones has been set up. A stereochemical discrepancy using either Tsuji's reagent or the present one has been observed and clearly further experiments (currently under investigation) are need to get insight into both mechanisms.

Acknowledgments We thank Professor M. Julia for encouragements and C.N.R S for support.

References

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2 I. Shimizu, Y. Ohashi and J. Tsuji, Tetrahedron Lett., 25, 5183 (1984)
3. B.M. Trost, Angew. Chem. Intern. Ed., 25, 1 (1986) , M D. Jones, R.D.W. Kemmitt and A.W G. Flatt, J. Chem. Soc Dalton Trans., 1411 (1986) , M.D. Jones and R.D.W. Kemmitt, J. Chem. Soc., Chem. Commun., 1201 (1986) , see also I. Shimizu, Y. Ohashi and J. Tsuji, Tetrahedron Lett., 26, 3825 (1985).
4. The stability of the anionized species was dramatically reduced on addition of two molar-equivalents of HMPT at -78°C but much less at -95°C.
5. The failure of the transient enolate eventually formed in the 1,4-addition step to cyclize is surprising considering Knapp's results (S. Knapp, U. O'Connor and D. Mobilio, Tetrahedron Lett., 21, 4557 (1980)) We attribute the low reactivity of the allylic chloride moiety in 1 to the deactivating effect of the electron withdrawing phenylsulfonyl group
6. T. Ukai, H. Kawazura, Y. Ishii, J.J. Bonnet and J A. Ibers, J. Organomet. Chem., 65, 253 (1974).
7. The formation of the disulfone could be viewed as resulting from a nucleophilic substitution of the chlorine atom in 1 by a phenylsulfinate anion which would result from a palladium catalyzed elimination process in 11 [8]. This has not yet been clearly demonstrated.
8. B.M Trost, N.R. Schmuff and M.J. Miller, J. Am. Chem Soc., 102, 5979 (1980).
9. Without palladium catalyst no reaction took place at all ! Two main hypotheses then arise 1- The formation of a cationic π-allyl complex from 1 renders the methylene bearing the sulfonyl group more acidic than in sulfone 1 itself (for examples of increased acidity of C-H bonds adjacent to π-allyl complexes, see M.F. Semmelhack and E J. Fewkes, Tetrahedron Lett., 28, 1497 (1987) and references therein) and/or 2- The hydroxide ion associated with a cationic palladium complex is a stronger base than the alkyl ammonium hydroxide Experiments are currently designed to enlight this point.

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