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Vinyl Cyclobutanol Strategy for Halogenated Cyclopentanoids

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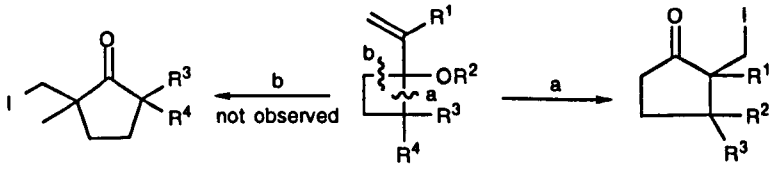
Abstract: The iodonium ion mediated ring expansion of the olefinic cyclobutanols **19**, **20**, and **22** gave the mixture of iodoalkylated cyclopentanones **27a-c** and **28a-c**, respectively. On the other hand, the same reaction of **24** - **26** afforded stereoselectively the iodoalkylated cyclopentanones **27d** and **27e**.

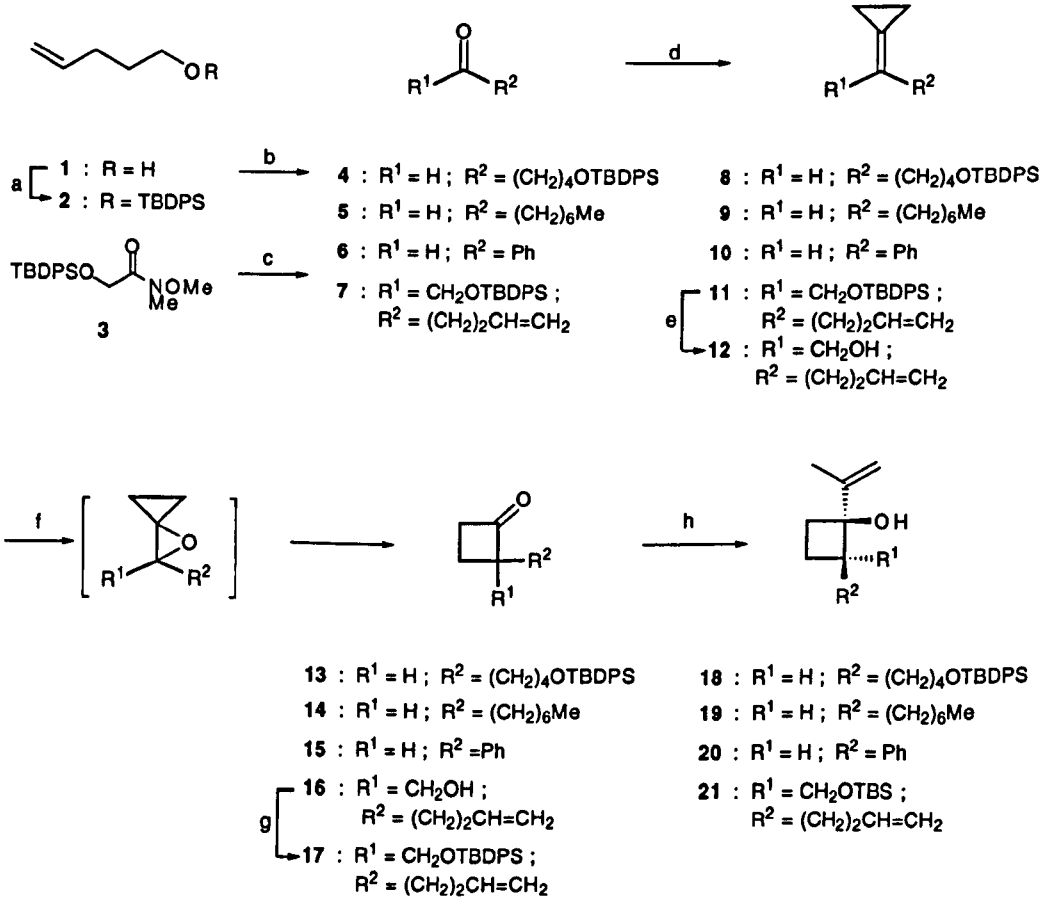
The ubiquity of cyclopentane rings[1] justifies the recent activities[2] of organic chemists in the synthesis of mono- as well as polycyclic cyclopentanoid derivatives. Of these, the cyclopentanoids containing iodoalkyl substituents are particularly attractive since the iodides play an important role in the organic synthesis as the sources of organometallics[3] and radicals.[4] We now communicate a novel strategy for the synthesis of iodoalkylated cyclopentanones **B** based on the iodonium ion-mediated ring expansion of olefinic cyclobutanols **A**.



Syntheses of the olefinic cyclobutanols **19**, **20**, **22**, **24**, **25**, and **26**, substrates for ring expansion, were straightforward. Aldehyde **4**, prepared by silylation (100%) of 4-pentenol (**1**) followed by hydroboration-oxidation (80%) and Swern oxidation (90%) of the resulting silyl ether **2**, was converted to cyclopropylidene ether **8** in 84% yield by the Wittig reaction with cyclopropylidenetriphenylphosphorane under the modified McMurry's conditions.[5] Aldehydes **5**, **6**, and ketone **7**, obtained by the Grignard reaction (95%) of hydroxamate **3**,[6] were also converted to cyclopropylidene derivatives **9** (88%), **10** (75%), and **11** (95%) by the same procedure described above. Cyclobutanones **13**, **14**, and **15**, prepared by oxidation of **8** (66%), **9** (34%), and **10** (35%) with MCPBA presumably *via* the oxaspiropentanes as intermediates, were subjected to the Grignard reaction to give cyclobutanols **18** (70%), **19** (79%), and **20** (63%). Cyclopropylidene alcohol **12**, derived by desilylation of **11** (100%), was also oxidized to give cyclobutanone **16** (53%), silyl ether **17** (94%) of which was then converted to cyclobutanol **21** (76%) (Scheme 1). The successive desilylation, Swern oxidation, and Wittig reaction of cyclobutanol **18** afforded unsaturated ester **22** (53%). Aldehyde **23**, obtained

(78%) by silylation and hydroboration-oxidation of cyclobutanol **21** followed by Swern oxidation of the resulting alcohol, was subjected to the Wittig reaction to give unsaturated ester **25** (93%) and also **24** (93%) after selective desilylation. Acetylenic ester **26** was prepared (81%) by the Wittig reaction of **23** followed by methoxycarbonylation of an *in situ* generated acetylide by base treatment of the resulting dibromoolefin (Scheme 2).

Scheme 1[a]

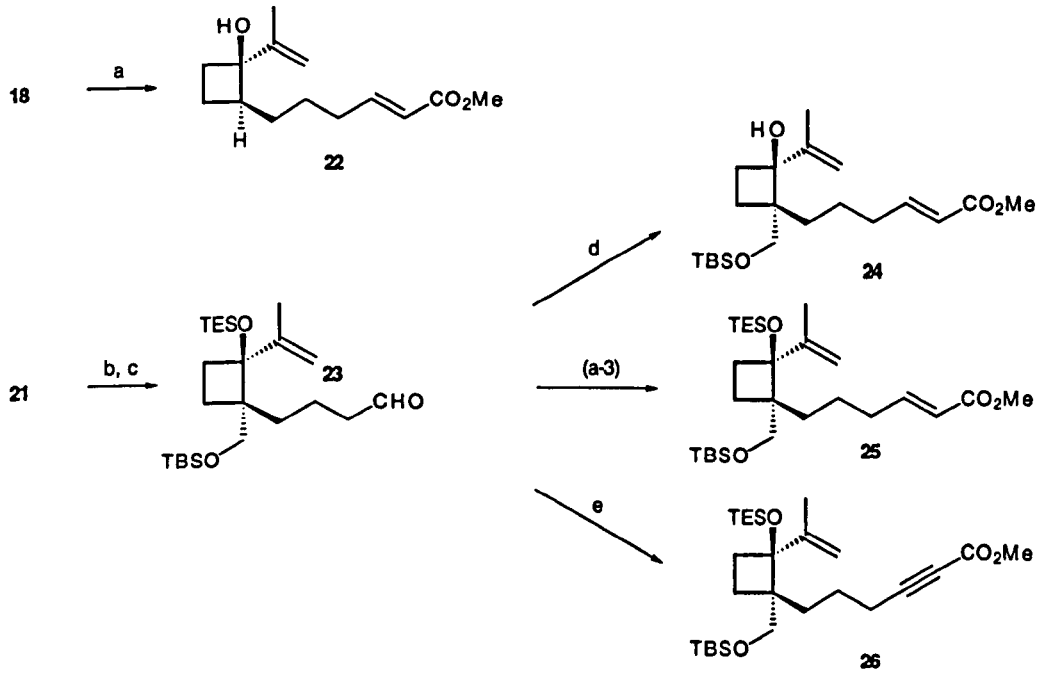


[a]Steps: (a) *tert*-butyldiphenylsilyl chloride (TBDPSCl), dimethylaminopyridine (DMAP), imidazole, DMF, rt, 19 h. (b) (1) BH_3·SMe_2, THF, rt, 2 h, then H_2O_2, NaOH, THF, rt, 1 h. (2) DMSO, $(COCl)_2$, CH_2Cl_2, -78 °C, 30 min, then Et_3N, -78 °C→0 °C. (c) $BrMgCH_2CH_2CH{=}CH_2$, THF, 0 °C, 1.5 h. (d) cyclopropyltriphenylphosphonium bromide, NaH, THF, 62 °C, 10 h, then **4-7**, tris[2-(2-methoxyethoxy)ethyl]amine (TDA-1), 62 °C, 4 h. (e) tetra-*n*-butylammonium fluoride (TBAF), THF, rt, 3.5 h; (f) *m*-chloroperbenzoic acid (MCPBA), CH_2Cl_2, 0 °C, 1 h. (g) *tert*-butyldimethylsilyl chloride (TBSCl), DMAP, imidazole, DMF, rt, 1.5 h.

The iodonium ion-mediated ring expansion of the olefinic cyclobutanols **19**, **20**, **22**, **24**, **25** and **26** was examined with iodine in the presence of $NaHCO_3$ or with N-iodosuccinimide (Table 1).

In all cases, the reaction proceeded in moderate to high yields and the silyl ether (entry 5) gave a slightly better result than the corresponding alcohol (entry 4). Although no stereoselectivity was found in the cases of monosubstituted substrates (entries 1 - 3) giving mixtures of diastereomers **27a-c** and **28a-c**, complete stereoselectivity was observed in the cases of geminally substituted substrates (entries 4 - 7) to afford **27d,e** as a sole product.

Scheme 2 [a]

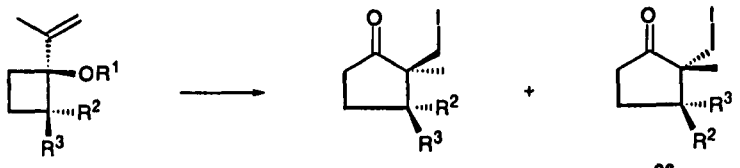


[a]Steps: (a) (1) TBAF, THF, rt, 3.5 h; (2) DMSO, $(COCl)_2$ CH_2Cl_2, –78 °C, 30 min, then Et_3N, –78 °C→0 °C; (3) $Ph_3P{=}CHCO_2Me$, MeCN, reflux, 1 h. (b) triethylsilyl trifluoromethanesulfonate (TESOTf), 2,6-lutidine, CH_2Cl_2, rt, 1 h; (c) (1) $BH_3{\cdot}SMe_2$, THF, rt, 2 h, then H_2O_2, NaOH, THF, rt, 1 h. (2) DMSO, $(COCl)_2$, CH_2Cl_2, –78 °C, 30 min, then Et_3N, -78 °C→0 °C. (d) (1) (a-3); (2) silica gel, CH_2Cl_2, rt, 13 h. (e) (1) CBr_4, PPh_3, CH_2Cl_2, rt, 10 h; (2) ^nBuLi, THF, -78 °C, 20 min, then $ClCO_2Me$, -78 °C, 10 min.

Thus,[7] we could disclose the new strategy for the synthesis of iodoalkylated cyclopentanoids based on the iodonium ion mediated ring expansion of olefinic cyclobutanols. We now continue to explore the synthetic usefulness of the iodoalkylated cyclopentanoids for biologically important compounds.

Table 1[a]

Iodonium Ion-Mediated Ring Expansion of Olefinic Cyclobutanols



27 28

entry	substrate	R^1	R^2	R^3	Product (%)[b]			
1	19	H	H	$(CH_2)_6Me$	27a	40	28a	39
2	20	H	H	Ph	27b	39	28b	55
3	22	H	H	$(CH_2)_3CH{=}CHCO_2Me$	27c	37	28c	36
4	24	H	CH_2OTBS	$(CH_2)_3CH{=}CHCO_2Me$	27d	88	28d	—
5	25	TES	CH_2OTBS	$(CH_2)_3CH{=}CHCO_2Me$	27d	96	28d	—
6	26	TES	CH_2OTBS	$(CH_2)_3C{\equiv}CCO_2Me$	27e	59	28e	—
7	26	TES	CH_2OTBS	$(CH_2)_3C{\equiv}CCO_2Me$	27e	100	28e	—

[a] All reactions were carried out in ether at 0 °C in the presence of iodine and $NaHCO_3$ except for entry 7 in which iodine and $NaHCO_3$ were replaced with N-iodosuccinimide.

[b] All were isolated yields.

References and Notes

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7. Details of the stereochemical assignments of all compounds appeared in this paper will be described in the article in due course.

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