Synthesis of 5-Alkyl-Δ^2-cyclopentenones and 6-Alkyl-Δ^2-cyclohexenones

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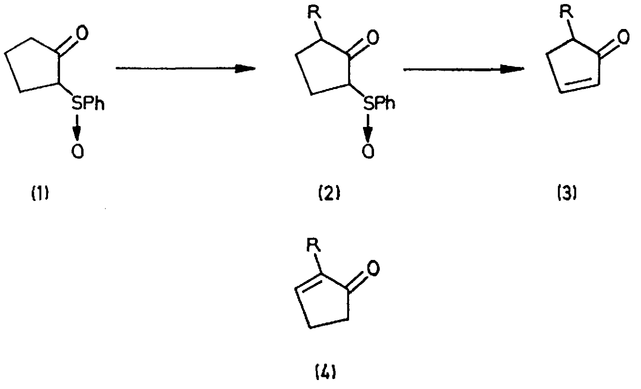
Summary The dianion of α-phenylsulphinyl cyclopentanone can be alkylated exclusively at the C-5 position; the resultant 5-alkyl-2-phenylsulphinyl cyclopentanone upon pyrolysis yields 5-alkyl-Δ^2-cyclopentenone with complete exclusion of the more stable 2-alkyl-Δ^2-cyclopentenone: similary α-phenylsulphinyl cyclohexanone provides access to 6-alkyl-Δ^2-cyclohexenones.

Δ^2-CYCLOPENTENONES possessing a substituent adjacent to the carbonyl in the C-5 position [*e.g.* (**3**)[1]] are potentially versatile intermediates in organic synthesis. We now report a general method (Scheme) for the synthesis of compounds of type (**3**) with exclusion of the more stable cyclopentenones of type (**4**), which is based on observations[2] that the dianion of phenylsulphinyl acetone undergoes exclusive γ-alkylation and on reports that α-phenylsulphinyl carbonyl systems readily eliminate benzenesulphenic acid on pyrolysis.[3]

Initial attempts used the Weiler dianion procedure[4] which proved successful in our dianion work.[2,5] β-Keto sulphoxide (**1**) was treated at 0° with 1·1 equiv. of sodium hydride followed by 1·1 equiv. of n-butyl-lithium in tetrahydrofuran (THF) containing 1·1 equiv of hexamethyl phosphoramide (HMPA). After dianion formation was assumed complete, the reaction was treated with allyl bromide. Work up followed by preparative t.l.c. afforded only a 15% isolated yield of (**2**) (R = allyl). Further analysis revealed 21% of unreacted starting material plus two other products X (15%) and Y (13%).†



SCHEME

TABLE. Preparation of 5-alkyl-Δ^2-cyclopentenones from α-phenylsulphinyl cyclopentanone

R-X	Yield (%)^c of (2)	R in (3)	Yield (%)^c of (3)
Bu^{n}I^a	65	Bu^n	43
$PhCH_2Br^b$	50	$PhCH_2$	55(82)^d
EtI^a	60	Et	46
$CH_2ClCH{=}CClMe^a$ ..	34	$MeCCl{=}CHCH_2$	60(77)^d

[a] Dianion formation at −20° (20 min) followed by addition of R-X at −20° with stirring for an additional 2—4 h.

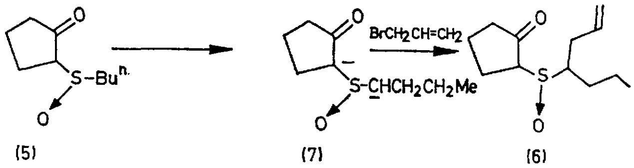
[b] Dianion formation (20 min) and addition of R–X were carried out at 0° followed by warming to room temperature (2 h).

[c] Reported yields are based on isolated analytically pure products.

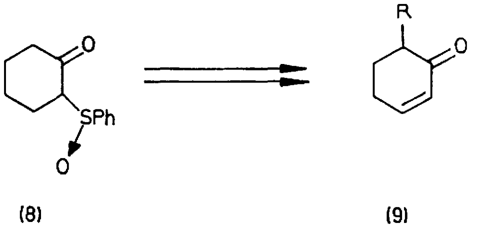
[d] Analysis by g.l.p.c.

After careful examination of the spectral data, the two structures (**5**) and (**6**) were assigned to X and Y respectively. The mono anion of (**1**) apparently undergoes a transmetallation reaction with n-butyl-lithium producing the new mono anion of the β-keto sulphoxide (**5**) which reacts further with the newly formed phenyl-lithium affording dianion (**7**). Treatment of the mono anion (NaH–THF) derived from (**1**) with 1·1 equiv. of n-butyl-lithium and usual work up resulted in a 45% yield of (**5**) along with an equal amount of (**1**) after preparative t.l.c.

To avoid these undesired side products, dianion formation was carried out using 2·2 equiv of the non-nucleophilic base lithium di-isopropylamide. A solution of (**1**) (1·0 mmol) in THF (1 ml) containing HMPA (1 equiv) at −20° under nitrogen was treated dropwise with lithium di-isopropylamide (2·2 equiv) in THF (2 ml). After 20 min dianion formation was complete and butyl iodide (2 equiv) was added. Stirring at −20° was continued for 4 h. The reaction was quenched with 5% hydrochloric acid. Usual work up followed by preparative t.l.c. (silica gel) gave a 65% yield of (**2**) (R = Bu^n). Based on recovered starting material, yields are generally greater than 90%.



Pyrolysis of the β-keto sulphoxide derivatives was carried out at *ca.* 75° under nitrogen for 4 h in CCl_4. The crude products were purified by preparative t.l.c. (silica gel). Yields are indicated in the Table. The absence of the 2-alkyl-Δ^2-cyclopentenones was clearly demonstrated by g.l.c. analysis of the crude reaction product.



The β-keto sulphoxide (**1**) is readily available *via* sulphenylation(diphenyldisulphide)[3a,b,6] of cyclopentanone with lithium di-isopropylamide followed by oxidation with periodate in aqueous methanol.[7] The application of the above method to α-phenylsulphinyl cyclohexanone provides a ready route to 6-alkyl-Δ^2-cyclohexenones [*e.g.* (**8**) → (**9**)].

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† Satisfactory analytical and/or spectral data have been obtained for all new compounds.

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