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2,3a,5,6,7,7a-HEXAHYDRO-3H,4H-BENZOTHIOPHENE-3,4-DIONE AND CYCLOPENTA [b]--TETRAHYDROTHIOPHENE-3,4-DIONE ENOLATE ANIONS AS SYNTHETIC EQUIVALENTS TO CYCLOHEX-2-ENONE AND CYCLOPENT-2-ENONE C-2-CARBANIONS.

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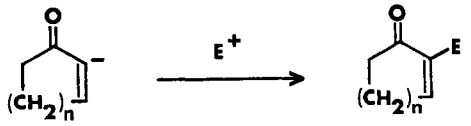
Summary. An efficient procedure for α-alkylation of cyclohex-2-enone and cyclopent-2-enone involving a base-promoted tandem of retrograde Dieckmann--Michael reactions of the C-alkylated derivatives of the title heterocycles is presented.

The importance of methodology for the introduction of a substituent at the α-position of five and six-membered αβ-unsaturated ketones is amply documented in reports of their utilization as starting materials in many significant synthetic strategies. The most straightforward method to accomplish this important operation would be the generation of the corresponding α-ketovinyl anions 1a or 1b followed by its capture with an appropriate electrophile[1].



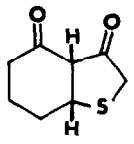
1a n=1

1b n=2

Difficulties in putting into practice this concise protocol, made the development of efficient synthetic equivalents of such anions a particularly important goal[2].

Herein we report on the employment of the bicyclic diketones 2[3] and 3, both readily available starting from cyclohex-2-enone and cyclopent-2-enone respec-

tively*, as latent α-ketovinyl anions equivalents of 1a and 1b, paving the way to a new interesting method for the preparation of both 2-substituted-cyclohexenones and -cyclopentenones[4].



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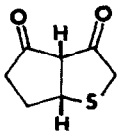

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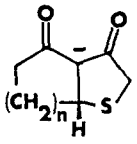
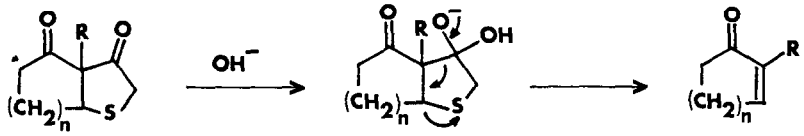


2a n=1

3a n=2

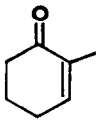
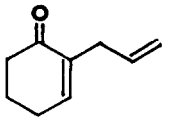
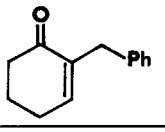
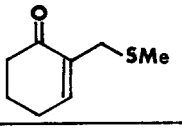
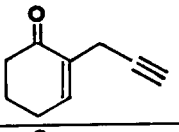
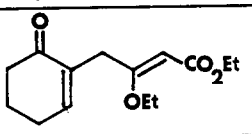
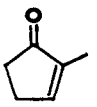
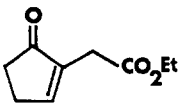
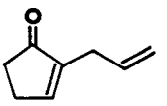
Central to the strategy was the assumption that the anions 2a and 3a derived from 2 and 3 could behave as synthetic equivalents of the C(2)-carbanions of cyclohex-2-enone and cyclopent-2-enone respectively, provided that the products arising by C-alkylation of their 1,3-diketone moiety underwent the anticipated[5] regioselective attack at C(3)carbonyl by hydroxide ions giving rise to 2-substituted-unsaturated cyclohexenones and cyclopentenones through a tandem of reversed Dieckmann-Michael reactions as outlined in the Scheme



Thus the alkylation of both 2 and 3 with reactive alkyl halides proceeded smoothly in the presence of anhydrous K_2CO_3 in refluxing acetone to afford the corresponding C-alkylated products, which were isolated by simple filtration from inorganic salts followed by removal of the solvent under reduced pressure. On subsequent exposure of the crude compounds to the action of 5% aqueous sodium hydroxide in a two phase, H_2O/Et_2O, system, the hydroxide ions-promoted fragmentation took place leading to the formation of 2-substituted-cyclohexenones and -cyclopentenones. Our results are summarized in the following Table.

Ready accessibility of the starting materials, high regioselectivity of the fragmentation, good overall yields (29-51%) of the practically "one-pot" transformation, make 2a and 3a very useful synthetic equivalents of cyclohex-2-enone and cyclopent-2-enone C(2) carbanions respectively.

Table:

Substrate	Electrophile	Products[a]	Yield[b]	Ref
2	MeI		46	6
2	CH_2=CH-CH_2Br		43	7
2	$PhCH_2Cl$		50	6
2	$MeSCH_2Cl$		29	8
2	CH≡C-CH_2Br		51	9
2	$BrCH_2C(OEt)=CHCO_2Et$		42	10
3	MeI		45	11
3	$BrCH_2CO_2Et$		39	12
3	CH_2=CH-CH_2Br		41	13

[a] All known compounds were characterized by comparison with literature data. All new compounds were fully characterized by full spectral and analytical data.

[b] Yields refer to isolated products after bulb-to-bulb distillation.

References and Notes.

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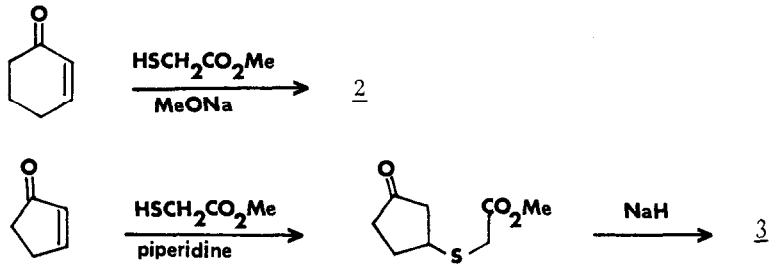
2. Some solutions have been advanced in literature. A.B. Smith III, S.J. Branca N.N. Pilla and M.A. Guaciaro, J. Org. Chem., 1982, 47, 1855 and references therein quoted.

* These compounds were prepared in satisfactory overall yield (64 and 45% respectively) via a Michael-Dieckmann sequence involving a base-catalyzed reaction between cyclohex-2-enone or cyclopent-2-enone and methyl mercapto-acetate, the first following a reported one-step procedure[3], the second (mp 75-77°C) by sodium hydride-induced intramolecular cyclization of the initial adduct as outlined below:



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8. IR (neat) 1670 cm^{-1}; ^{1}HNMR ($CDCl_3$): δ 2.05 (s, 3H), 2-2.2 (m, 2H), 2.3-2.6 (m, 4H), 3.3 (m, 2H), 6.9 (m, 1H).

9. IR (neat) 3260, 1670 cm^{-1}; ^{1}HNMR ($CDCl_3$): δ 1.9-2.1 (m, 2H), 2.1 (m, 1H), 2.3-2.6 (m, 4H), 3.2 (m, 2H), 7.2 (m, 1H).

10. IR (neat) 1750, 1720, 1670, 1620 cm^{-1}; ^{1}HNMR ($CDCl_3$): δ 1.2 (t, J=7Hz, 3H), 1.25 (t, J=7Hz, 3H); 1.9-2.1 (m, 2H), 2.2-2.55 (m, 4H), 3.7 (m, 2H), 3.8 (q, J=7Hz, 2H), 4.1 (q, J=7Hz, 2H), 5.1 (s, 1H), 6.7 (m, 1H).

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