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A NEW SYNTHETIC ROUTE TO FUNCTIONALLY SUBSTITUTED CYCLOPENTENONES

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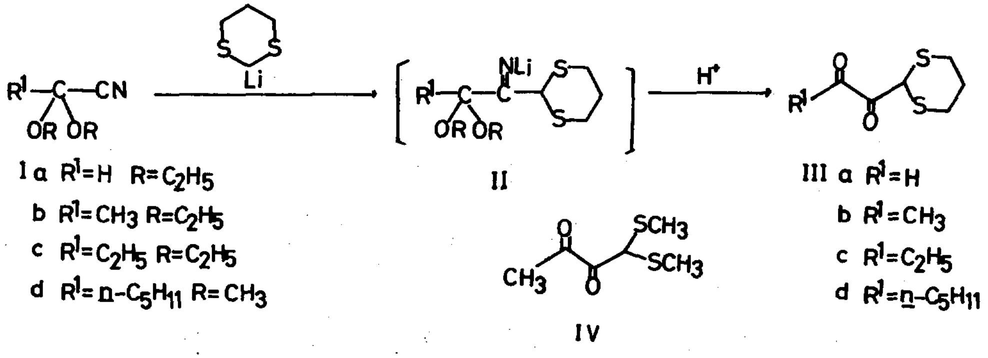
Efforts directed toward the synthesis of cyclopentenone derivative has continued unabated. Many reports of their syntheses were related to the development of γ-diketone synthesis$^{1)}$, and a few reports involved the combination of C-2 and C-3 fragments.$^{2)}$ Our interests have been directed toward effective methods for the synthesis of cyclopentenones with various substituents. We have now found a new synthetic route to functionally substituted cyclopentenones which involves an intra-molecular Wittig reaction by the treatment of the anion of α-diketone with vinyltriphenylphosphonium salts, which were documented as useful reagents by Schweizer$^{3)}$. In addition, a convenient preparation of α-oxoalkanoyl-1,3-dithianes has been generated from 2,2-dialkoxynitriles$^{4)}$ and 2-lithium-1,3-dithiane$^{5)}$.

2,2-Dialkoxynitriles were converted into α-oxoalkanoyl-1,3-dithiane by the reaction with 2-lithium-1,3-dithiane in an equimolar ratio followed by hydrolysis as shown in SCHEME I. For example, to a solution of 2-lithium-1,3-dithiane

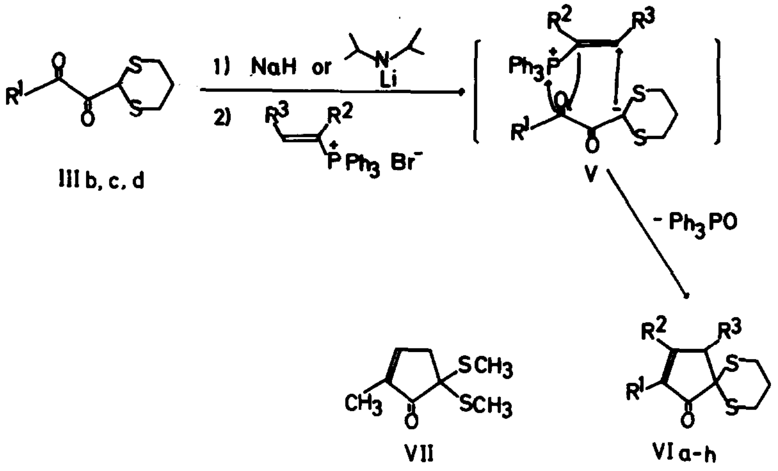


SCHEME I

prepared from 15.6 g (0.13 moles) of 1,3-dithiane and n-butyllithium in n-hexane (1 equiv.) in 312 ml of tetrahydrofuran (THF) was added 18.6 g of 2,2-diethoxypropionitrile Ib (1 equiv.) in 18 ml of THF at -78° under nitrogen. After 40 min at -78° the mixture was warmed to room temperature and stirred for 1 hr. After the usual work-up, the product was hydrolyzed with 300 ml of 4% aqueous hydrochloric acid at room temperature for 2 hr to give 16.8 g of 2-pyruvoyl-1,3-dithiane IIIb (bp 102-104°/0.2 mm; 68% yield) [IIIb: mp 51° (recrystallization from petroleum ether), ir ν (nujol); 1710 cm^{-1}, nmr (60 MHz, in $CDCl_3$, δ ppm); 1.75-3.50 (6H, m), 2.42 (3H, s, methyl), 5.05 (1H, s, methyne).]. Under similar conditions, 2-α-oxobutyryl-1,3-dithiane IIIc (bp 100-103°/0.2 mm) was produced in 78.5% yield from 2,2-diethoxybutyronitrile Ic and 2-α-oxo-n-heptanoyl-1,3-dithiane IIId (mp 33°) was formed in 52% yield from 2,2-dimethoxy-n-heptanonitrile Id[6). However, 2-glyoxyloyl-1,3-dithiane IIIa (enol form) was obtained in poor yield. Extension of the reaction of Ib with lithium formaldehyde dimethyl mercaptal proceeded similarly to give 1,1-dimethyldithio-2,3-butanedione IV in 49% yield. These α-diketones were adopted as starting materials in the synthetic route for 5,5-dithiocyclopentanones according to SCHEME II.

Reaction of vinyltriphenylphosphonium salts with the enolate anion of IIIb-d, IV, which was prepared using sodium hydride or lithium diisopropylamide, gave cyclopentenone derivatives VIa-h, VII via an intra-molecular Wittig reaction. The product yields are summarized in TABLE 1. Cyclopentenones VIa-f, VII were produced in a moderate yield from vinyl- and isopropenyltriphenylphosphonium bromide, but Vg, h was formed in poor yields from propenyltriphenylphosphonium bromide. Several attempts using IIIa were unsuccessful.

The following experimental procedure illustrates the reaction of lithium 2-pyruvoyl-1,3-dithiane with vinyltriphenylphosphonium bromide as a representative example: To a solution 1.9 g (10 mmoles) of 2-pyruvoyl-1,3-dithiane in 25 ml of THF was added 1 molar equivalent of lithium diisopropylamide in THF at -10~-5° under nitrogen. After stirring for 30 min 3.7 g (1 equiv.) of vinyltriphenylphosphonium bromide in 30 ml of dimethyl sulfoxide (DMSO) was added at -10~0° and stirred at room temperature overnight. After the usual work-up,



SCHEME II

TABLE 1. Yield of 5,5-Dithiocyclopent-2-en-1-one Derivatives

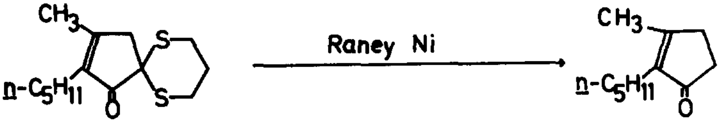
compound no.	R_1	R_2	R_3	yield (%)
VIa	CH_3	H	H	$55^{b)}$
VIb	C_2H_5	H	H	$63^{b)}$
VIc	CH_3	CH_3	H	$52^{b)}$, $21^{a)}$
VId	C_2H_5	CH_3	H	$35^{a)}$
VIe	$\underline{n}$-C_5H_{11}	H	H	$31^{b)}$
VIf	$\underline{n}$-C_5H_{11}	CH_3	H	$51^{b)}$
VIg	CH_3	H	CH_3	$7^{b)}$
VIh	C_2H_5	H	CH_3	$9^{b)}$
VII	CH_3	H	H	$33^{b)}$

a) Sodium hydride was used.

b) Lithium diisopropylamide was used.

the product was purified by silica gel dry–column chromatography (benzene-n-hexane 4 : 1) to give 1.1 g of 2-methyl-5,5-[propanediyl-(1,3)-dithio]cyclopent-2-en-1-one VIa [bp 102-105°/0.06 mm; ir ν(nujol); 1705, 1645 cm^{-1}; nmr (100 MHz, in CCl_4, δppm); 1.79 (3H, m, CH_3), ca. 1.7-2.3 (2H, m), 2.43 (2H, d of m, J=14.5 Hz), 2.53 (2H, m), 3.86 (2H, d of d of d, J=14.5, 12.5, 2.7 Hz), 6.90 (1H, m, olefinic)].

These dithiocyclopentenone derivatives should find wide application. Indeed, one application toward the synthesis of dihydrojasmone was attempted. Desulfurization of VIf with Raney nickel (W-2) in refluxing in benzene for 4 hr gave dihydrojasmone VIII1) in 70% yield.



VIf VIII

Acknowledgement

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