Novel Syntheses of 3-Methylene- and 3,6-Dimethylene-tetrahydropyran-2-one and 3,5-Dimethylenetetrahydrofuran-2-one Derivatives

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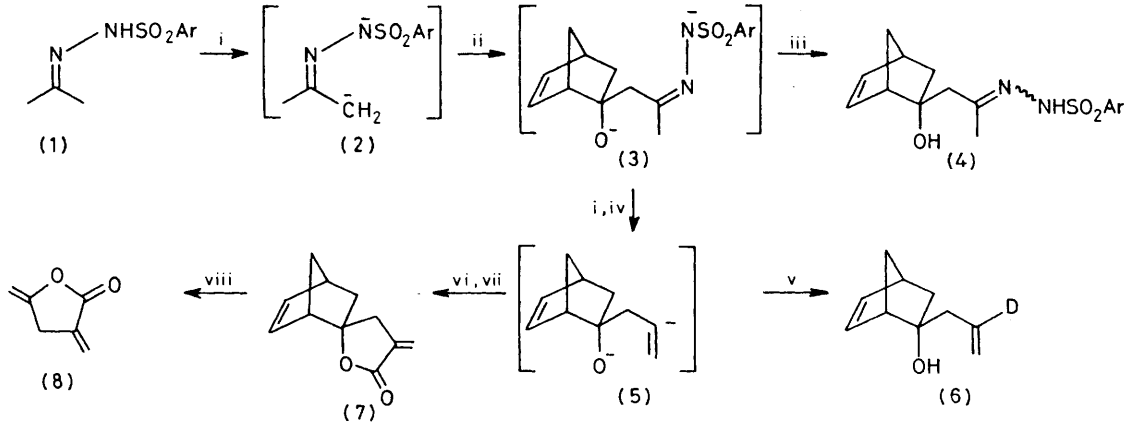
Summary By modification of the Shapiro reaction, the title compounds were prepared by short convenient syntheses.

RECENTLY, we have described the application of the Shapiro reaction to the synthesis of 3-methylenetetrahydrofuran-2-ones.[1] Derivatives of the 3,5-dimethylenetetrahydrofuran-2-one unit (**8**) occur naturally in the obtsusilactones and mahubenolides.[2] Herein we describe a convenient two-step synthesis of (**8**) and syntheses of the related 3-methylene-(**23c**), 3,6-dimethylene-(**21**), and 3-ethylidene-6-methylene-(**24**) tetrahydropyran-2-one derivatives.

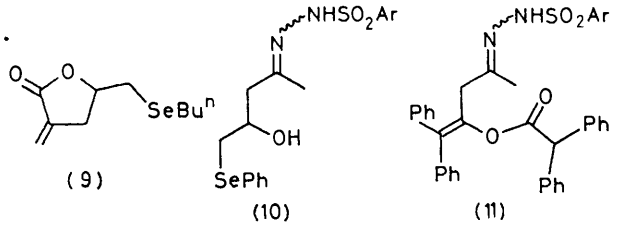
The lactone (**8**) should be available from acetone 2,4,6-tri-isopropylphenylsulphonylhydrazone (**1**) and a keten equivalent. Thus, reaction of the dianion (**2**), obtained from (**1**), with bicyclo[2.2.1]hept-2-en-5-one, n-butyl-lithium, carbon dioxide, and acetic acid in sequence gave the lactone (**7**) [61% from (**1**)]† (Scheme 1). The product was stereochemically homogeneous (^{1}H and ^{13}C n.m.r. and t.l.c. analy-



SCHEME 1. Reactions i—vi were carried out in 1,2-dimethoxyethane (DME). Ar = 2,4,6-Pr$^i_3$C$_6$H$_2$. i, Bu^{n}Li, −78 °C; ii, bicyclo-[2.2.1]hept-2-en-5-one, −65 °C; iii, HOAc, −65 °C; iv, −3 °C; v, D_2O; vi, CO_2, −78 °C; vii, HOAc, CH_2Cl_2, 20 °C; viii, 550 °C, 10^{-4} mmHg.

† All new compounds were fully characterised by microanalyses and spectral data.

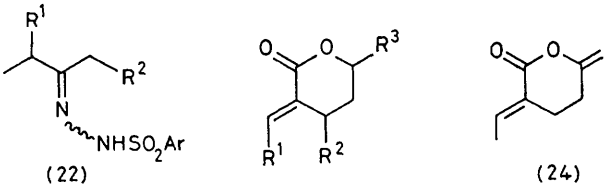
sis) and plausibly resulted from *exo* carbanion attack.[3] The intermediacy of the dianions (**3**) and (**5**) followed from, respectively, trapping with acetic acid and D_2O to give the hydrazone (**4**) [56% from (**1**)] as a *syn–anti* mixture, and the olefin (**6**) [70% from (**1**), 91% D incorporation]. The lactone (**7**) on flash vacuum pyrolysis at 550 °C and 10^{-4} mmHg gave 3,5-dimethylenetetrahydrofuran-2-one (**8**) (83%) *via* a retro Diels–Alder[4] reaction.



(9) (10) (11)

Alternative keten equivalents were examined. Reaction of the hydrazone (**1**) with phenylselenylacetaldehyde (available *via* 2-bromo-1,1-diethoxyethane and 1,1-diethoxy-2-phenylselenylethane) as in Scheme 1, gave only the lactone (**9**) (2%) formed *via* the hydrazone (**10**) (59%) and benzoic acid (17%). The dianion (**2**) and diphenylketen gave the diacylated product (**11**) (25%).

The lactone (**21**) should be available *via* the iodolactonisation of 2-methylenehex-5-enoic acid (**19**). The allylation of dianion (**2**) provided an easy route to acid (**19**) *via* (**12**) and (**16**) (Scheme 2). Clearly the regioselectivity of reaction [(**15**) *vs.* (**18**) and (**13**) *vs.* (**19**)] was controlled by the exclusive formation[5] of the *syn*-dilithio species (**14**) and (**17**), and by the predominance of *anti* stereochemistry when the hydrazones were isolated and allowed to equilibrate in solution at room temperature. The anions (**14**) and (**17**) did not equilibrate under the reaction conditions. The acid (**19**) was not fully characterised but was iodolactonised giving (**20**) [50% overall yield from (**16**)]. Subsequent reaction with DBU gave the novel 3,6-dimethylenetetrahydropyran-2-one (**21**) (64%). As in Scheme 2 butanone 2,4,6-tri-isopropylphenylsulphonylhydrazone was allylated giving the hydrazones (**22a**) (major) and (**22b**) (minor) (75% yield) which then gave the lactones (**23a**) (39%) and (**23b**)



(22)

a; R^1 = H, R^2 = $CH_2CH{=}CH_2$

b; R^1 = $CH_2CH{=}CH_2$, R^2 = H

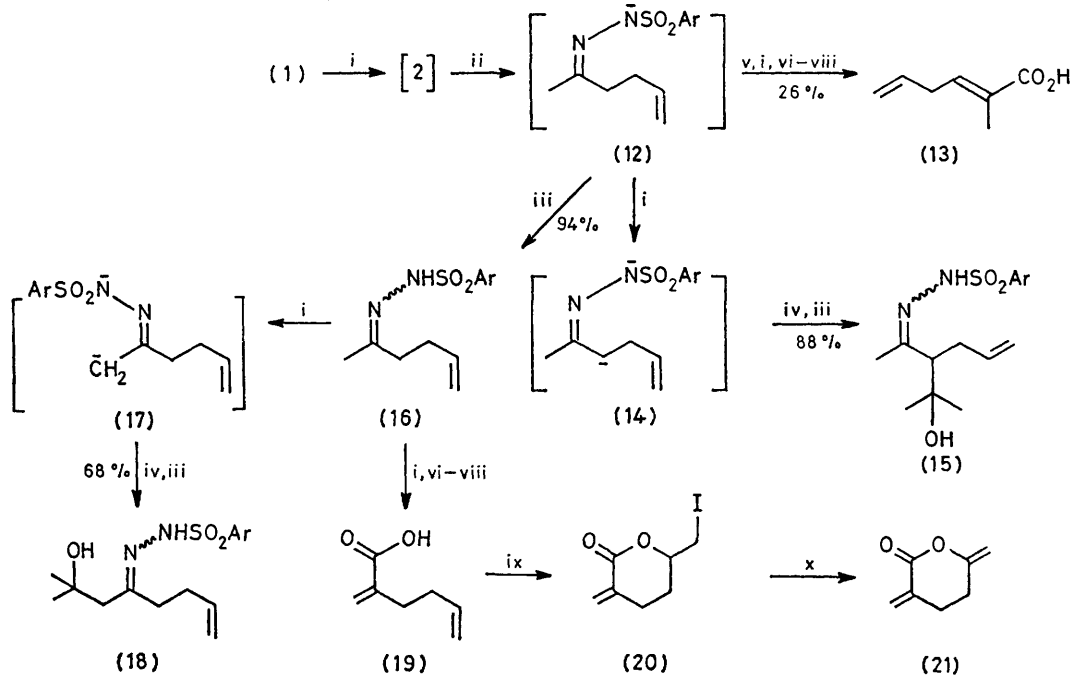
(23)

a; R^1 = Me, R^2 = H, R^3 = CH_2I

b; R^1 = H, R^2 = Me, R^3 = CH_2I

c; R^1 = R^2 = H, R^3 = n-C_8H_{17}

(24)



Scheme 2. All reactions, except ix and x, were carried out in DME. i, Bu^nLi, −78 °C; ii, $CH_2{=}CHCH_2Br$, −60 °C; iii, HOAc, −78 to −50 °C; iv, Me_2CO, −78 °C; v, $Me_2NCH_2CH_2NMe_2$, −78 °C; vi, −3 °C; vii, CO_2, −78 °C; viii, CF_3CO_2H; ix, CH_2Cl_2, H_2O, $NaHCO_3$, KI_3, 20 °C; x, PhH, 1,5-diazabicyclo[5.4.0]undec-5-ene (DBU), 74 °C.

The hydrazones (**15**), (**16**), and (**18**) were of *syn*-stereochemistry on initial isolation but isomerised at room temperature. At equilibrium the hydrazone (**16**) was *ca.* 15:85 *syn*:*anti*. In the sequences (**16**)—(**18**) and (**16**)—(**21**) the *syn* isomer gave rise to minor side products.

(6%). Dehydrohalogenation of (**23a**) gave the dialkylidene lactone (**24**) (71%). Reaction of 5-hydroxytridecan-2-one with 2,4,6-tri-isopropylphenylsulphonylhydrazine, n-butyllithium (−78 to −3 °C), carbon dioxide (−78 °C), and trifluoroacetic acid in sequence gave the lactone (**23c**) (23%).

Clearly, application of the Shapiro reaction provides the most convenient syntheses of the lactones (**8**), (**21**), (**23a—c**), and (**24**) and analogues.

We thank the S.R.C. for support.

(*Received*, 16*th August* 1979; *Com.* 880.)

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