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NEW ROUTES TO THE SYNTHESIS OF *cis*-JASMONE FROM THE KETENE DERIVATIVES

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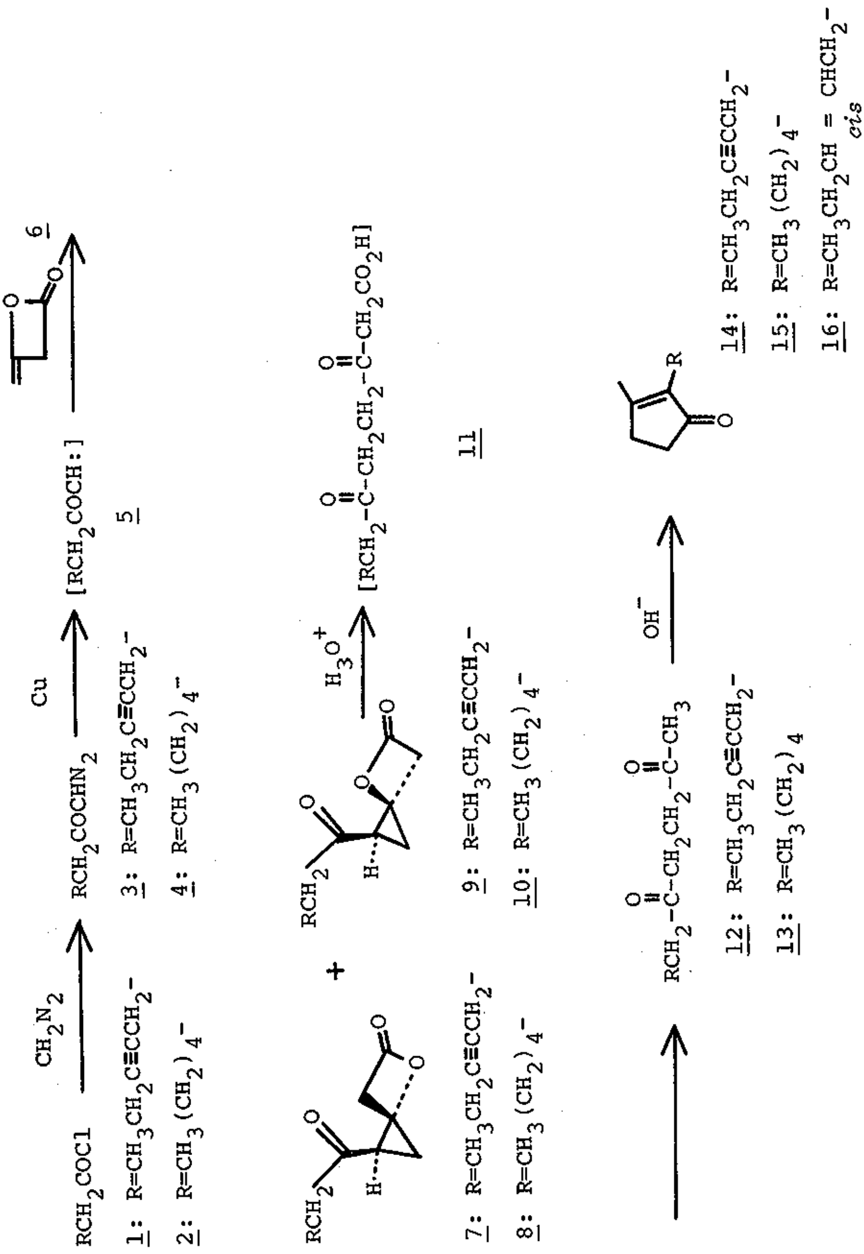
3-Undecyne-7,10-dione(12) and 2-methyl-5-(3-hexynyl)-furan(24), which are key intermediates for the synthesis of *cis*-jasmone(16), have been synthesized from ketene dimer(6) or the ketene dichlorides, (21) and (22), respectively.

cis-Jasmone(16), a fragrant constituent of the *Jasminum* genus, is one of the most popular synthetic objects for the organic chemists because of its economic values and its appropriate nature for testing new synthetic methodologies[1]. We report here two new approaches which allow relatively simple synthesis of *cis*-jasmone(16) from the heterocyclic ketone derivatives.

Firstly, an excess of ketene dimer(6) was treated with the known diazoketone[2](3), prepared from 4-heptynoyl chloride[3](1), at 90° in the presence of copper powder to give a 14 % yield of the "<u>trans</u>" β-spirolactone(7)[4](oil; ν_{max}^{neat} 1825, 1710 cm^{-1}; δ^{CDCl_3} 1.08(3H, t, J=7.0Hz), 3.62(2H, ABq, J=17.0Hz)) and a 6.5 % yield of the "cis" β-spirolactone(9)(oil; ν_{max}^{neat} 1830, 1710 cm^{-1}; δ^{CDCl_3} 1.08(3H, t, J=7.0Hz), 3.65(2H,s)) after a purification by silica gel chromatography. Feasibility of intermolecular insertion of α-ketocarbenes into the carbon-carbon double bond of ketene dimer(6) was originaly discovered by Kato and Katagiri[5] using diazoacetophenone and ethyl diazoacetate as α-ketocarbene precursors and the stereochemical assignment of the products, (7) and (9), depended on their conclusions. Stereochemistry of the isomeric β-spirolactones, (7) and (9), however, was not important from the synthetic point of view, since both of the isomers, as well as an epimeric mixture were cleanly transformed into known 3-undecyne-7,10-dione[6](12)(oil; ν_{max}^{neat} 1710 cm^{-1}; δ^{CDCl_3} 1.09(3H, t, J=7.0Hz), 2.18(3H, s), 2.25-2.80(10H, m)) in 60-70 % yield by refluxing with 10 % hydrochloric acid. Stirring for 18 hr with 5 % aqueous sodium hydroxide at room temperature converted <u>12</u> into the known 2,3-dehydrojasmone[6](14)(oil, 2,4-dinitrophenylhydrozone, mp 163-164°(lit.[6] mp. 166°); ν_{max}^{neat} 1695, 1640 cm^{-1}; δ^{CDCl_3} 1.09(3H, t, J=7.0Hz), 1.20(3H, s)) in 80 % yield which has been transformed into *cis*-jasmone(16) in an excellent yield after *cis*-hydrogenation over the Lindlar catalyst[2,6].

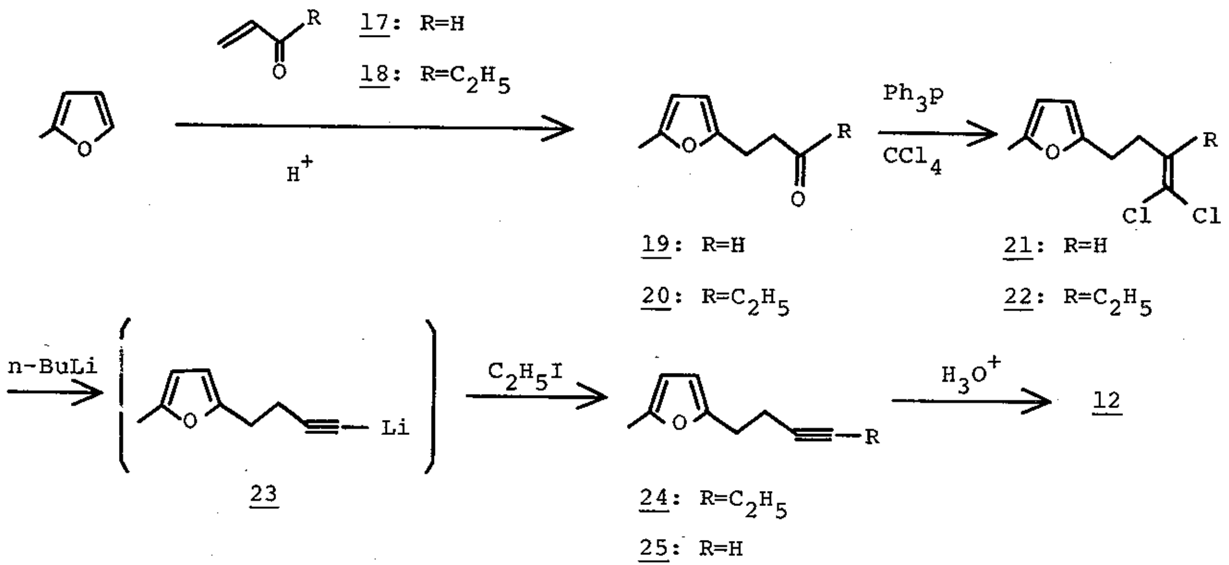
Scheme 1


RCH_2COCl
CH_2N_2
RCH_2COCHN_2
Cu
$[RCH_2COCH:]$
5
6
1: $R=CH_3CH_2C≡CCH_2-$
2: $R=CH_3(CH_2)_4-$
3: $R=CH_3CH_2C≡CCH_2-$
4: $R=CH_3(CH_2)_4-$
RCH_2
H
+
H_3O^+
$[RCH_2-C(=O)-CH_2CH_2CH_2-C(=O)-CH_2CO_2H]$
11
7: $R=CH_3CH_2C≡CCH_2-$
8: $R=CH_3(CH_2)_4-$
9: $R=CH_3CH_2C≡CCH_2-$
10: $R=CH_3(CH_2)_4-$
$RCH_2-C(=O)-CH_2CH_2CH_2-C(=O)-CH_3$
OH^-
R
O
12: $R=CH_3CH_2C≡CCH_2-$
13: $R=CH_3(CH_2)_4$
14: $R=CH_3CH_2C≡CCH_2-$
15: $R=CH_3(CH_2)_4-$
16: $R=CH_3CH_2CH = CHCH_2-$ cis

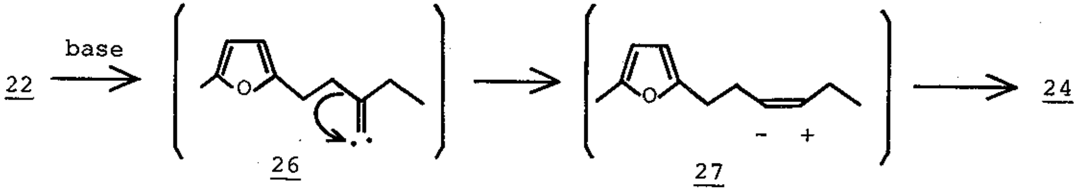
Similarly, the insertion of the saturated α-ketocarbene(5) generated from the known α-diazoketone precursor[7](4) into ketene dimer(6) afforded a 29 % yield of the "trans" β-spirolactone(8) (mp. 64-65°; ν_{max}^{Nujol} 1825, 1720 cm^{-1}; δ^{CDCl_3} 0.89(3H, t, J=4.5Hz), 3.3-3.9(2H, ABq, J=16.5 Hz)) and an 11 % yield of the "cis" β-spirolactone(10)(mp. 83-85°; ν_{max}^{Nujol} 1825, 1720 cm^{-1}; δ^{CDCl_3} 0.88 (3H, t, J=4.5 Hz), 3.70(2H, s)). Both of the spirolactones, (8) and (10), as well as an epimeric mixture were converted into dihydrojasmone(15)(oil, 2,4-dinitrophenylhydrazone, mp. 120-122° (lit.[8] mp. 122-123°); ν_{max}^{neat} 1700, 1650 cm^{-1}; δ^{CDCl_3} 0. 88(3H, t, J=4.5 Hz), 1.15-1.70(8H, m), 2.05(3H, s), 2.3-2.6(4H, m)) *via* undecane-7,10-dione(13)(oil; ν_{max}^{neat} 1710 cm^{-1}; δ^{CDCl_3} 0.88(3H, t, J=4.5Hz), 1.1-1.8(8H, m), 2.19(3H, s), 2.45(2H, t, J=7.0 Hz), 2.79(4H, s)) by treating with 10 % hydrochloric acid followed by 5 % aqueous sodium hydroxide.

Secondly, the known furylpropionaldehyde[9](19) prepared from 2-methylfuran and acrolein was heated with 2 molar equiv of triphenylphosphine in carbon tetrachloride[10] to give a 49 % yield of the unstable ketene dichloride derivative(21)(oil, ν_{max}^{neat} 1615 cm^{-1}; δ^{CCl_4} 2.22(3H, s), 2.35-2.96(4H, m), 5.64(1H, t, J=5.5Hz), 5.75(2H, m)) which upon treating with 3 molar equiv of *n*-butyllithium in a mixture of tetrahydrofuran and hexamethylphosphramide(HMPA) at -78°[11], followed by ethyl iodide at 0° was converted into 2-methyl-5-(3-hexynyl)furan(24)(bp. 96-115° (25mmHg)(Kugelrohr); δ^{CCl_4} 1.08(3H, t, J=7.0Hz), 2.22(3H, s), 2.0-3.0(6H, m), 5.85(2H, m)) in 13 % yield. Since the compound (24) has been converted into the 1,4-diketone(12) through acid

Scheme 2



Scheme 3



catalyzed hydrolysis[6], this conversion consisted a new route to the synthesis of *cis*-jasmone(16). When HMPA was not present in the reaction medium, incomplete alkylation occurred to form only a 3 % yield of the desired product(24) accompanied with a 15 % of the *endo*-acetylene derivative(25)(bp 73-96°(25mmHg)(Kugelrohr); ν_{max}^{neat} 3280; δ^{CCl_4} 1.85(1H, t, J=2.0Hz), 2.22(3H, s), 2.33-3.0(4H, m), 5.85(2H, m)).

In order to avoid the alkylation stage, various base treatments were applied to the ketene dichloride derivative(22) expecting to form a reactive carbenoid intermediate(26) which would subsequently rearrange into the acetylene derivative(24). By following the above procedure, 2-methylfuran was converted into the unstable ketene dichloride(22)(oil; ν_{max}^{neat} 1615 cm^{-1}; δ^{CCl_4} 1.02(3H, t, J=7.5Hz), 2.21(3H, s), 2.25(2H, q, J=7.5Hz), 2.48-2.75(4H, m), 5.75(2H, m)) *via* 2-methyl-5-(3-oxopentyl)furan (20)(oil; ν_{max}^{neat} 1708 cm^{-1}; δ^{CCl_4} 1.01(3H, t, J=7.5Hz), 2.20(3H, s), 2.36(2H, q, J=7.5Hz), 2.65-2.95(4H, m), 5.75(2H, m)) and the former(22), when treated with 4 molar equiv of sodium in boiling *p*-cymene[12], was transformed into the desired acetylene derivative (24) in 19 % yield.

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