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SYNTHESIS OF 1,4-DIEN-3-ONES AND 2-CYCLOPENTENONES

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Abstract—Aluminium trichloride catalyzed reaction of trimethylvinylsilane with α,β-unsaturated acyl chlorides gives 1,4-dien-3-ones, from which 2-cyclopentenones may be prepared.

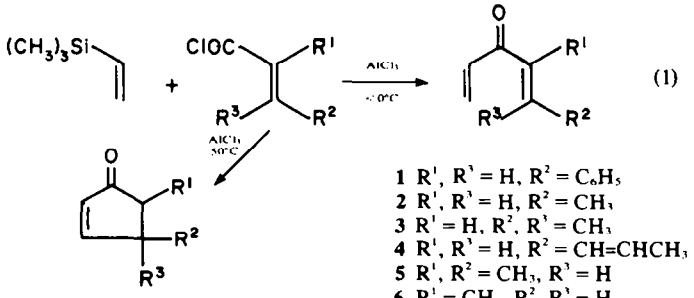
In conjunction with our studies of the chemistry of silyl nitronates and of a novel prostaglandin synthesis,[1-3] we wished to have accesss to a facile route to certain vinyl ketones, a class of compounds well known for their instability and capricious behaviour. The most obvious route is Friedel–Crafts acylation of ethylene by acyl chlorides in the presence of aluminium chloride.[4-9] Due to the accompanying polymerization and addition of hydrogen chloride across the vinyl function with formation of β-chloro ketones in this route, we turned to the more promising route *via* vinyltrimethylsilane (eqn 1).[10-13]

The outcome of this reaction is also very sensitive to the reaction conditions. Thus, mode of addition, catalyst, temperature, solvent, reaction time, and work-up influence the yield and product composition considerably. Aluminium chloride seems generally to be the most suitable catalyst and methylene chloride, chloroform and 1,2-dichloroethane are suitable solvents but in a few cases the use of 1,2-dichloroethene had a favourable effect on the yield. The yield of hexa-1,4-dien-3-one **2**, and octa,1,4,6-trien-3-one **4** was considerably enhanced by use of 1,2-dichloroethene as cosolvent in that the addition of hydrogen chloride across the vinylic bond was repressed. The addition of trimethylvinylsilane to the aluminium chloride/α,β-unsaturated acyl chloride complex is recommended. Prolonged reaction time favours the formation of the hydrogen chloride adduct and increased temperature the Nazarov cyclization to cyclopentenones.

We had an immediate interest in synthesizing **1**, **2** and **3** which are specifically designed for our prostaglandine synthesis.[2,3] **1** and **3** were obtained in *ca* 50–70% yield by carrying out the reaction at $-10°$ in methylene chloride and at room temperature in 1,2-dichloroethene, respectively. The preparation of **2** required that the reaction procedure was followed precisely in order to minimize the Nazarov product **8** and the formation of the hydrogen chloride adduct **17**. *Ca* 40% yield of **2** was obtained (distilled product). The crude dienones can be used directly for the subsequent synthesis of 2-isoxazolines, e.g. **19** and **20**. The cyclopentenones and the hydrogen chloride adducts of type **17** do not interfere with the 1,3-dipolar addition.[1-3]

The dienone synthesis was extended to a few other α,β-unsaturated acid chlorides. **4** was obtained in 66% yield from sorboyl chloride. Metacryl chloride gave only a polymeric product and **6**, **12** and **16** could not be detected in the reaction mixture. 2,3-Dimethylacryloyl chloride gave rise to a mixture of **11**, **15**, and the silyl derivative **18** (major) which surprisingly survives the Friedel–Crafts conditions. The expected product **5** was not detected.

By running the acylation at higher temperature, *ca* 50°, and for a longer time the reaction proceeded further and the corresponding cyclopentenones **7**, **8** and **10** were selectively obtained in good yields. **7**, **8** and **11** were rearranged to **13**, **14** and **15** respectively in refluxing benzene or toluene in the presence of basic aluminium



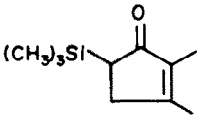
(1)

1 $R^1, R^3 = H, R^2 = C_6H_5$
2 $R^1, R^3 = H, R^2 = CH_3$
3 $R^1 = H, R^2, R^3 = CH_3$
4 $R^1, R^3 = H, R^2 = CH{=}CHCH_3$
5 $R^1, R^2 = CH_3, R^3 = H$
6 $R^1 = CH_3, R^2, R^3 = H$

7 $R^1, R^3 = H, R^2 = C_6H_5$
8 $R^1, R^3 = H, R^2 = CH_3$
9 $R^1 = H, R^2, R^3 = CH_3$
10 $R^1, R^3 = CH{=}CHCH_3$
11 $R^1, R^2 = CH_3, R^3 = H$
12 $R^1 = CH_3, R^2, R^3 = H$

13 $R^1 = H$, $R^2 = C_6H_5$
14 $R^1 = H$, $R^2 = CH_3$
15 R^1, $R^2 = CH_3$
16 $R^1 = CH_3$, $R^2 = H$

17



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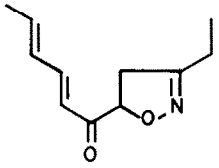

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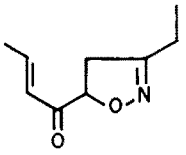

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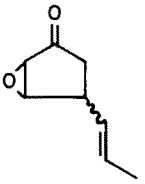

21

oxide. **10** gave the epoxide **21** on treatment with basic hydrogen peroxide.

EXPERIMENTAL

1-Phenyl-1,4-pentadien-3-one, 1. To cinnamoyl chloride (0.83 g, 5 mmol) and aluminium chloride (0.70 g, 5.2 mmol) in methylene chloride (7 ml) was added trimethylvinylsilane (0.50 g, 5 mmol) in methylene chloride (3 ml) at −10° with stirring. After 5 min the mixture is poured into ice–water (20 ml) containing ammonium chloride (2.5 g). The aqueous layer was extracted with CH_2Cl_2 (10 ml) and the combined organic phases were washed once with water and twice with saturated aqueous sodium bicarbonate, dried and evaporated (crude yield 0.66 g). It gave 430 mg of pure **1**, 55%, by prep TLC (SiO_2, CH_2Cl_2). ^1H NMR ($CDCl_3$): δ 5.80 (1H, dd, J 1.2 and 10.4 Hz), 6.32 (1H, dd, J 1.2 and 17.3 Hz), 6.64 (1H, dd, J 10.4 and 17.3 Hz), 6.94 (1H, d, J 16 Hz), 7.2–7.65 (5H, m), 7.60 (1H, d, J 16 Hz). The compound has been prepared earlier;[14] b.p. 100–101°/1 mmHg.

1,4-Hexadien-3-one, 2. Crotonoyl chloride (6.2 g, 0.060 mol) and aluminium chloride (8.4 g, 0.063 mol) were dissolved in 1,2-dichloroethene (80 ml) and methylene chloride (45 ml) in a three-necked flask equipped with thermometer, stirrer, and a separation funnel. The mixture was cooled to −15–−20° and a precooled solution of trimethylvinylsilane (6.0 g, 0.060 mol) in 1,2-dichloroethene (20 ml) was added during a few min, then stirred for 18 min keeping the temperature constant, then poured into ice–water (160 ml) containing ammonium chloride (20 g). The phases were separated and the aqueous phase was extracted once with methylene chloride (20 ml). The combined organic phases were washed once with water and twice with saturated aqueous sodium bicarbonate, dried and evaporated. The crude 1,4-hexadien-3-one **1** (4.4 g, 77%) contained small amounts of **17** (^1H NMR ($CDCl_3$) triplets at δ 3.00 and 3.78) and traces of **8**. **1** distills at 39–41°/12 mmHg (lit[6], b.p. 57°/16 mmHg), 2.25 g, 39% with some polymerization. ^1H NMR ($CDCl_3$): δ 1.93 (3H, dd, J 1.2 and 6.7 Hz), 5.78 (1H, dd, J 1.1 and 10.6 Hz), 6.25 (1H, dd, J = 1.1 and 17.5 Hz), 6.36 (1H, dq, J = 1.1 and 15.5 Hz), 6.57 (1H, dd, J 10.6 and 17.5 Hz), 6.93 (1H, dq, J 6.7 and 15.5 Hz).

5-Methyl-1,4-hexadien-3-one, 3. Trimethylvinylsilane (8 g, 0.08 mol) in 1,2-dichloroethene (40 ml) is added with stirring to 3,3-dimethylacryloyl chloride (8.5 g, 0.072 mol) and aluminium chloride (10.2 g, 0.077 mol) in 1,2-dichloroethene (120 ml) at room temperature. After 30 min the soln was poured into ice–water (350 ml) containing ammonium chloride (42 g). The aqueous phase is extracted with methylene chloride (20 ml) and the combined organic phases were washed once with water, twice with a saturated aqueous sodium bicarbonate solution, dried over sodium sulfate, evaporated, and distilled giving **3**, 5.1 g, b.p. 44–48°/10 mmHg (lit[10] 30°/0.8 mmHg). ^1H NMR ($CDCl_3$): δ 1.91 (3H, d, J 1.2 Hz), 2.15 (3H, d, J 1.2 Hz), 5.68 (1H, dd, J 1.1 and 10.8 Hz), 6.17 (1H, dd, J 1.1 and 17.6 Hz), 6.36 (1H, dd, J 10.8 and 17.6 Hz).

1,4,6-Octatrien-3-one, 4. Trimethylvinylsilane (6 g, 0.06 mol) in 1,2-dichloroethene (15 ml) was added slowly with stirring to sorboyl chloride (7.8 g, 0.060 mol) and aluminium chloride (8.8 g 0.066 mol) in 1,2-dichloroethene (70 ml) then stirred for 3 min at −5–0°, poured into ice–water (160 g) and ammonium chloride (21 g) and worked up as for **3** (yield 4.8 g, 66%, sufficiently pure for further reactions). Distillation *in vacuo* gave 1.1 g of **4** (15%), b.p. 42–44°/0.22 mmHg leaving a large quantity of a polymerized product in the distillation flask. ^1H NMR ($CDCl_3$): δ 1.86 (3H, dd, J 0.9 and 4.8 Hz), 5.72 (1H, dd, J 1.2 and 10.6 Hz), 5.9–7.5 (6H, m).

4-Phenyl-2-cyclopentenone 7. Trimethylvinylsilane (0.60 g, 6 mmol) in carbon tetrachloride (5 ml) was added to cinnamoyl chloride (0.83 g, 5 mmol) and aluminium chloride (0.7 g, 5.2 mmol) in carbon tetrachloride at *ca* 50°. The mixture is gently refluxed for 30 min, cooled, and hydrolyzed in ice–water (20 ml) containing ammonium chloride (2.5 g). Usual workup gives **7** (0.36 g, 46%) purified by preparative TLC (SiO_2, $CHCl_3$, 1% CH_3OH). ^1H NMR ($CDCl_3$): δ 2.29 (1H, dd, J 2.8 and 18.3 Hz), 2.87 (1H, dd, J 6.6 and 18.3 Hz), 4.0–4.3 (1H, m), 6.28 (1H, dd, J 2 and 6 Hz), 7.0–7.4 (5H, m), 7.63 (1H, dd, J 2 and 6 Hz).

4-Methyl-2-cyclopentenone **8**, was prepared as for **7** from crotonoyl chloride in 63% yield, b.p. 47–49°/12 mmHg (lit[15] 62–63°/25 mmHg). ^1H NMR ($CDCl_3$): δ 1.20 (3H, d, J 7 Hz), 1.91 (1H, dd, J 1.6 and 18.2 Hz), 2.56 (1H, dd, J 6.0 and 18.2 Hz), 2.85–3.29 (1H, m), 6.15 (1H, dd, J 2 and 5.6 Hz), 7.53 (1H, dd, J2 and 5.6 Hz).

4-Propenyl-2-cyclopentenone **10**, was obtained in *ca* 80% yield (crude) by refluxing a mixture of trimethylvinylsilane (2.0 g, 0.02 mol), sorboyl chloride (2.6 g, 0.02 mol) and aluminium chloride (2.7 g, 0.02 mol) in 1,2-dichloroethane for 1 h. The crude product was sufficiently pure for further reactions. It decomposed on distillation, b.p. 58–60°/15 mmHg, yield 18%. ^1H NMR ($CDCl_3$): δ 1.68 (3H, d, J 4.8 Hz), 2.25 (1H, dd, J 18.2 and 2.3 Hz), 2.65 (1H, dd, J 18.2 and 6.0 Hz), 3.4–3.8 (1H, m), 5.1–5.8

(2H, m), 6.13 (1H, dd, *J* 5.6 and 1.8 Hz), 7.53 (1H, dd, *J* 5.6 and 1.8 Hz).

4,5-*Dimethyl-2-cyclopentenone*, **11**, 2,3-*dimethyl-2-cyclopentenone*[16] **15**, *and* 2,3-*dimethyl-5-trimethylsilyl-2-cyclopentenone* **18**. Trimethylvinylsilane (4.0 g, 0.04 mol) in 1,2-dichloroethene (10 ml) is added slowly with stirring to tigloyl chloride (4.9 g, 0.04 mol) and aluminium chloride (5.6 g, 0.04 mol) in 1,2-dichloroethene (50 ml). The mixture is heated to 50° for 40 min. Usual workup gives a crude mixture of the isomeric cyclopentenones **11**, **15**, and **18**. **18** (major) was obtained al a colourless liquid, somewhat impure, b.p. 73–78° at 0.45 mmHg. ^{1}H NMR ($CDCl_3$): δ 0.0 (9H, s), 0.48 (1H, dd, *J* 7.6 and 9.4 Hz), 1.68 (3H, s), 1.8–2.9 (2H, m). MS: 182 (M^+), 73 ($Si(CH_3)_3^+$). IR (film), 1712 (s), 1666 (s).

3-*Phenyl-2-cyclopentenone*, **13**, was prepared by refluxing **7** (0.36 g) over basic alumina, Merck (1.8 g) in toluene (5 ml) for 3 h. The product **13** was purified by prep. TLC (SiO_2, $CHCl_3$, 1% MeOH). 0.29 g, 81%. ^{1}H NMR ($CDCl_3$): δ 2.5–3.0 (4H, m), 6.59 (1H, br.s), 7.3–7.8 (5H, m).

3-*Methyl-2-cyclopentenone* **14**, was prepared by refluxing **8** (2.2 g) over basic alumina, Merck 90, activity I (7 g) in benzene (20 ml) for 3 h, b.p. 66–67°/12 mmHg (lit[17] 74°/15 mmHg). ^{1}H NMR ($CDCl_3$): δ 2.13 (3H, br.s), 2.3–2.7 (4H, m), 5.88 (1H, q, *J* 1.6 Hz).

3-*Ethyl-5-sorboyl-2-isoxazoline* **18**. 1,4,6-Octatrien-3-one (1.1 g), the trimethylsilyl ester of *aci*-nitropropane,[18] and two drops of triethylamine in benzene were reacted for 20 h at room temperature and were then refluxed for 30 min with toluene-p-sulphonic acid (200 mg). The solution was washed with aqueous sodium bicarbonate, evaporated and chromatographed (SiO_2, $CHCl_3$). **18**, 1.4 g, 81%, was obtained as a colourless oil. ^{1}H NMR ($CDCl_3$): δ 1.17 (3H, t, *J* 7.5 Hz), 1.88 (3H, d, *J* 5.0 Hz), 2.38 (2H, q, *J* 7.5 Hz), 3.16 (1H, d, *J* 10.6 Hz), 3.19 (1H, d, *J* 7.5 Hz), 5.01 (1H, dd, *J* 7.4 and 10.6 Hz), 5.9–6.4 (3H, m), 7.1–7.7 (1H, m).

3-*Ethyl-5-crotonoyl-2-isoxazoline* **19**. 1,4-Hexadien-3-one (2.25 g), the trimethylsilyl ester of *aci*-nitropropane (3.8 g), and three drops of triethyl amine in benzene (10 ml) were left standing for 24 h at room temperature. Toluene-p-sulphonic acid (0.5 g) was added and the solution was refluxed for 30 min. Washing with aqueous sodium bicarbonate and evaporation of the solvent gave a practically pure product **19** in 60% yield. ^{1}H NMR ($CDCl_3$): δ 1.16 (3H, t, *J* 7.5 Hz), 1.93 (3H, dd, *J* 1.1 and 6.7 Hz), 2.39 (2H, q, *J* 7.5 Hz), 3.16 (1H, d, *J* 10.6 Hz), 3.19 (1H, d, *J* 7.5 Hz), 4.93 (1H, dd, *J* 7.5 and 10.6 Hz), 6.51 (1H, dq, *J* 1.1 and 15.5 Hz), 7.07 (1H, dq, *J* 6.7 and 15.5 Hz).

2,3-*Oxido-4-propenylcyclopentanone* **20**, was prepared from **10** in 80% yield as a mixture of stereoisomers by base-catalyzed epoxidation with hydrogen peroxide in aq EtOH for 15 min at room temperature, b.p. 60°/0.05 mmHg. ^{1}H NMR ($CDCl_3$): δ 1.70 (3H, d, *J* 5.2 Hz), 1.7–3.3 (3H, m), 3.31 (1H, d, *J* 2 Hz), 3.76 (1H, d, *J* 2 Hz), 5.1–5.9 (2H, m). IR (film): 1752 cm^{-1}. MS: M^+ 138.

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