One-pot synthesis of the derivatives of 2-cyclopent-2-en-1-one by $SOCl_2$/EtOH

Zhiguo Hu* and Zhibing Dong

College of Chemistry and Environmental Science, Henan Normal University, Xinxiang, 453007, Henan, P. R. China

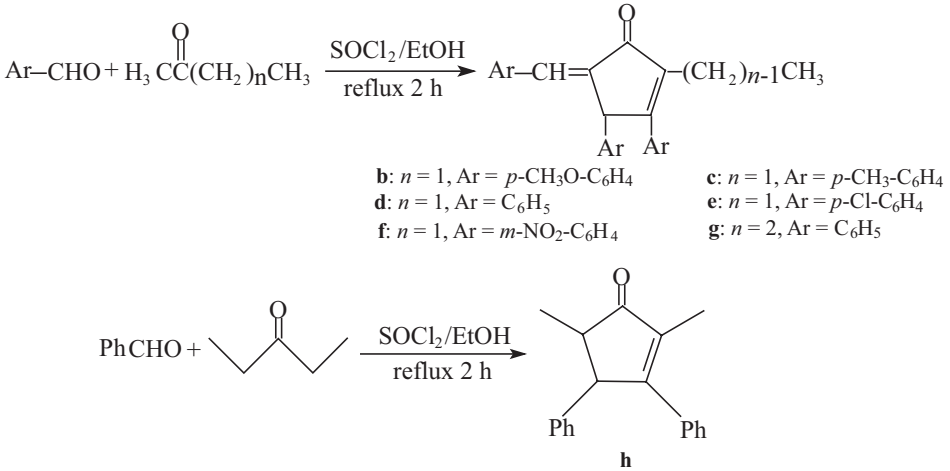
A simple and efficient method for the synthesis of derivatives of cyclopent-2-en-1-one is presented. Aromatic aldehydes reacted with aliphatic ketones in the presence of thionyl chloride in anhydrous ethanol to give seven derivatives of 2-cyclopenten-1-one in one step with reasonable yields. The structures of the products were established.

Keywords: derivatives of 2-cyclopent-2-en-1-one, $SOCl_2$/EtOH

Crossed aldol–condensation reactions are important synthetic reactions for carbon–carbon bond formation.[1] As classical methods, they were performed in the presence of strong acids or bases and many successful examples including transition metal enolates as well as main group metal enolates have been reported in the recent literature.[2] However, traditional acid- or base-catalysed reactions suffer from reverse reactions, and a metal chloride was reported to promote the self-condensation of ketones rather than the crossed aldol-condensation.[3] These methods generally resulted in mono- or di-substituted α,β-unsaturated carbonyl compounds. It is well known that the base-catalysed reaction of butanone with benzaldehyde gave preferential reactions at C_1 of the ketone, while the acid-catalysed reaction occurred preferentially at C_3 of the ketone. Kenichi and Atsuchi[4] reported the synthesis of a regioselective compound condensed from C_1 of the ketone in the presence of Co^{2+}–VP–MMA (in a sealed tube, in vacuum). Chuit and Corriu[5] synthesised similar regioselective compounds by using tetraalkoxysilane in the presence of fluoride ions. On the contrary, Nasser and Kasemi[6] used $RuCl_3$ as the catalyst to synthesise the other α,β-unsaturated carbonyl compound regioselectively condensed from C_1. Francis and Andrew[7] once synthesised methylanhydracetonebenzil through the condensation of benzil and acetone under the influence of potassium hydroxide, and benzylidenemethylanhydracetonebenzil was obtained when methylanhydracetonebenzil reacted with benzaldehyde under the influence of alcoholic potassium in the cold. By the reaction of zirconium chloride catalysts (120–130°C, 12 h), Yuki and Hashimoto[8] synthesised 2,3,4,5-tetrasubstituted cyclopent-2-en-1-ones with low yield from the corresponding ketones and aldehydes. Huang and coworkers[9] synthesised some derivatives of 2-cyclopenten-1-one in the presence of $TiCl_4$-2THF using Schlenk techniques. Based on the synthesis of 1,3,5-triarylbenzene,[10] asymmetric 1,3,5-triaryl-benzene,[11] chalcones,[12] α,α'-bis(substituted benzylidene) ketones,[13] symmetric trisannelated benzenes[14] and unsymmetric trisannelated benzenes[15] catalysed by $SOCl_2$/EtOH, we have developed this simple one-pot method for the crossed condensation of aromatic aldehydes with aliphatic ketones. Surprisingly, a series of new derivatives of cyclopent-2-en-1-one were obtained in one step with reasonable yields (Scheme 1).

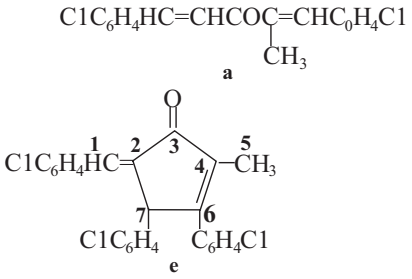
Results and discussion

A white crystalline compound was obtained when *p*-chlorobenzaldehyde was condensed with butanone in the $SOCl_2$/EtOH system, and it was expected to be compound **a** (Scheme 2) at first. But after checking its mass spectrum (*m/z*: 439, M^+), we found that 3 mol of *p*-chlorobenzaldehyde condensed with 1 mol of butanone. The band at 1677 cm^{-1} in the IR spectrum indicated a carbonyl in the structure, 1611 cm^{-1}, 1641 cm^{-1} indicated a carbon–carbon double bond and 841 cm^{-1}, 819 cm^{-1} suggested the existence of a *p*-substituted aromatic ring. ^1H NMR ($CDCl_3$, ppm): 1.98(s, 3H, CH_3), 5.06(s, 1H, CH), 6.90–7.34(m, 12H, Ar–H), 7.53(s, 1H, =CH); ^{13}C NMR ($CDCl_3$, ppm): 10.5, 51.4, 129.3, 129.4, 129.4, 129.8, 130.0, 131.9, 132.5, 133.1, 133.4, 133.5, 135.8, 136.1, 137.6, 137.9, 138.9, 164.8, 197.5. This showed the compound had an unsaturated 5-membered ring which suggested **e** (Scheme 2) as the structure. The structure could also be



Scheme 1 The synthesis of derivatives of cyclopent-2-en-1-one.

* Correspondent. E-mail: zhiguohu@yahoo.com



Scheme 2

confirmed by an HMQC spectrum (shown in Table 1, see Scheme 2 **e** at the same time). Taking benzaldehyde as the example of aromatic aldehydes (four substituted benzaldehydes) to react with aliphatic ketones, and taking butanone as the example of ketones (butanone, 2-pentanone, 3-pentanone) to react with aromatic aldehydes, we obtained a series of compounds (**b**, **c**, **d**, **f**, **g**, **h**) which had similar structures to compound **e**.

During the course of the crossed-condesation reaction, self-condensation of ketones was also observed as a side reaction. In order to prevent this, thionyl chloride and the ketone were dropped into the mixture of aldehyde and anhydrous ethanol. High temperature increased the yield of the products. The yield of the product **d** was only 65% when the reaction was carried out at room temperature but the yield was 83% when the reaction was refluxed. There was almost no product when the system was cooled below 0°C (ice-salt cold bath). The optimal reaction time was 2 hours and the optimal ratio of $SOCl_2$ to ketone was 2 : 1. Furthermore, we found that the alcohol was indispensable in the catalyst system as well as serving as reaction solvent. Other solvents such as toluene and pyridine were also used, but only alcohols catalysed this aldol reaction. There was no significant variation of yields between using anhydrous CH_3OH and anhydrous C_2H_5OH.

We also found that the electronic nature of substrates had a marked effect on the reaction. The results of the condensation reactions are shown in Table 2. Strong electron-withdrawing groups on the aromatic rings led to increased yields (entries 4 and 5), while electron-donating groups decreased the yield (entries 1 and 2). And with the increase of the carbon chain of the aliphatic ketone, the yield of the products decreased (entries 6 and 7).

As for the mechanism, we believe that the condensation in our reaction is not catalysed by HCl. Robert *et al.*[16] once reported the synthesis of triarylbenzenes by HCl with low yield (26%) under the action of anhydrous HCl for 18 days and we reported the synthesis of triarylbenzenes in the presence of thionyl chloride in anhydrous ethanol with high yield 85% (only within 1 hour).[10] Moreover, Elmorsy *et al.*[17] reported the mechanism of the condensation of acetophenone by $SiCl_4$/EtOH which went through the silyl enol ether of the ketone. We believe therefore, that the reaction proceeds via the reaction of the enol sulfite ester of ketones and that the byproduct HCl may accelerate the reaction.

Table 2 The synthesis of derivatives of cyclopent-2-en-1-one

Entry	Product	M.p./°C	Yield/%
1	**b**	119–121	71
2	**c**	183–185	75
3	**d**	155–157	83
4	**e**	178–179	84
5	**f**	211–212	85
6	**g**	159–161	70
7	**h**	117–118	75

Conclusion

In conclusion, we have developed a simple and general method for the synthesis of the derivatives of cyclopent-2-en-1-one (**b, c, e, f, g** are new compounds) in one step. The advantages of this method are the cheap catalyst, short reaction times, reasonable yields and simple manipulation.

Experimental

Melting points were determined on the Kofler micro melting point apparatus without correction. IR spectra were recorded on a PTS-40 IR spectrophotometer in KBr. ^{1}H NMR (in $CDCl_3$) and ^{13}C NMR (in $CDCl_3$) spectra were measured using TMS as internal standard on a BRUKER 250 AC NMR spectrometer. The mass spectra were measured on an Agilent GC–MS spectrometer. The high-resolution mass spectra (ESI–HRMS) were determined on an Ion Spec (7.0 T) spectrometer.

Synthesis of compound (**d**): *a typical experimental procedure*
Thionyl chloride (8.8 ml, 0.12 mol) and butanone (5.4 ml, 0.06 mol) were dropped synchronously into a stirred mixture of the benzaldehyde (24.2 ml, 0.24 mol) and anhydrous ethanol (14.6 ml, 0.25 mol). The mixture was refluxed for 2 hours and then saturated aqueous Na_2CO_3 was added and the mixture was filtered. The solid was washed successively with ethanol, water, anhydrous ethanol and di ethyl ether.

Compound spectroscopic data (**b**): M.p. 119–121°C; ^{1}H NMR ($CDCl_3$, ppm): 2.02(s, 3H, CH_3), 3.64(s, 3H, OCH_3), 3.75(s, 3H, OCH_3), 3.79(s, 3H, OCH_3), 5.06(s, 1H, CH), 6.60–7.41(m, 12H, Ar–H), 7.50(s, 1H, =CH); IR (KBr, cm^{-1}): 2835, 1640, 1640, 1610, 1463, 1350, 1178, 1034, 831, 578, 563; HRMS(*m/z*): Calcd. For $C_{28}H_{27}O_4$ [M^+ + H]: 427.1915. Found: 427.1919.

(**c**): M.p. 183–185°C; ^{1}H NMR ($CDCl_3$, ppm): 2.01(s, 3H, CH_3), 2.15(s, 3H, CH_3), 2.28(s, 3H, CH_3), 2.31(s, 3H, CH_3), 5.15(s, 1H, CH), 6.86–7.36(m, 12H, Ar–H), 7.52(s, 1H, =CH); IR (KBr, cm^{-1}): 3033, 1680, 1641, 1604, 1345, 832; HRMS(*m/z*): Calcd. For $C_{28}H_{27}O$ [M^+ + H]: 379.2056. Found: 379.2062.

(**d**): M.p. 155–157°C (m.p.[9] 150–152°C); ^{1}H NMR ($CDCl_3$, ppm): 2.04(s, 3H, CH_3), 5.19(s, 1H, CH), 7.02–7.45(m, 15H, Ar–H), 7.61(s, 1H, =CH); IR (KBr, cm^{-1}): 2919, 2850, 1679, 1641, 1611, 1447, 1343, 1130, 770, 703, 689; 563; HRMS(*m/z*): Calcd. For $C_{25}H_{21}O$ [M^+ + H]: 337.1587. Found: 337.1581.

(**e**): M.p. 178–179°C; ^{1}H NMR ($CDCl_3$, ppm): 1.98(s, 3H, CH_3), 5.06(s, 1H, CH), 6.90–7.34(m, 12H, Ar–H), 7.53(s, 1H, =CH); ^{13}C NMR ($CDCl_3$, ppm): 10.5, 51.4, 129.3, 129.4, 129.4, 129.8, 130.0, 131.9, 132.5, 133.1, 133.4, 133.5, 135.8, 136.1, 137.6, 137.9, 138.9, 164.8, 197.5; IR (KBr, cm^{-1}): 1677, 1641, 1611, 1491, 1341, 1091, 1011, 841, 819, 770, 515; HRMS(*m/z*): Calcd. For $C_{25}H_{16}{}^{35}Cl_3O$ [M^+–H]: 437.0272. Found: 437.0267(100%), 439.0237(96.53%).

(**f**): M.p. 211–212°C; ^{1}H NMR ($CDCl_3$, ppm): 2.14(s, 3H, CH_3), 5.47(s, 1H, CH), 7.28(s, 1H, =CH), 7.30–8.21(m, 12H, Ar–H); IR (KBr, cm^{-1}): 1696, 1622, 1535, 1351, 827, 810, 719; HRMS(*m/z*): Calcd. For $C_{25}H_{16}O_7N_3$ [M^+-H]: 470.0994. Found: 470.0990.

(**g**): M.p. 159–161°C; ^{1}H NMR ($CDCl_3$, ppm): 1.13(t, 3H, CH_3, J = 7.6 Hz), 2.24(m, 2H, CH_2), 5.09(s, 1H, CH), 6.70–7.41(m,

Table 1 NMR spectroscopic data of compound **e** ($CDCl_3$, δ in ppm)

Position of carbons	^{1}H NMR(δ, mult.)	^{13}C NMR (δ, mult.)	HMQC(^{1}H–^{13}C)
1	7.53 (s, 1H)	131.4 (s)	relative
2	No H	Between 129.3-138.9	not found
3	No H	197.5 (s)	not found
4	No H	Between 129.3-138.9	not found
5	1.98 (s, 3H)	10.5 (s)	relative
6	No H	164.8 (s)	not found
7	5.06 (s, 1H)	51.4 (s)	relative

15H, Ar–H), 7.58(s, 1H, =CH); IR (KBr, cm^{-1}): 3033, 2976, 1679, 1641, 1610, 1355, 1140, 752, 700; HRMS(*m/z*): Calcd. For $C_{26}H_{23}O$ $[M^+ + H]$: 351.1743. Found: 351.1750.

(**h**): M.p. 117–118°C (m.p[8]. 116–117°C); ^1H NMR ($CDCl_3$, ppm):1.35(d, 3H, J = 7.6 Hz, CH_3), 2.02(s, 3H, CH_3), 2.40(m, 1H, $CH–CH_3$), 3.97 (m, 1H, CH–Ph), 7.06–7.36 (m, 10H, Ar–H); IR (KBr, cm^{-1}): 3062, 2976, 2867, 1693, 1626, 1498, 1342, 755, 725, 699; Mass (*m/z*,%): 262(M^+, 100).

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