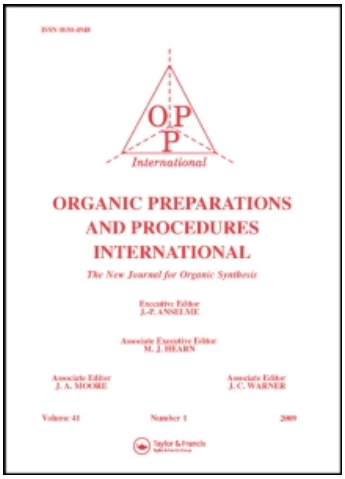

Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

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To cite this Article Venugopal, M. and Perumal, P. T.(1991) 'SYNTHESIS OF SUBSTITUTED 3-CHLORO-5-ARYLPENTA-2,4-DIEN-1-ALS AND OF 3-CHLORO-5-(5-FORMYLARYL)PENTA-2,4-DIEN-1-ALS BY THE VILSMEIER REACTION', Organic Preparations and Procedures International, 23: 6, 749 — 752
To link to this Article: DOI: 10.1080/00304949109458250
URL: http://dx.doi.org/10.1080/00304949109458250

ORGANIC PREPARATIONS AND PROCEDURES INT., 23 (6), 749-766 (1991)

OPPI BRIEFS

SYNTHESIS OF SUBSTITUTED 3-CHLORO-5-ARYLPENTA-2,4-DIEN-1-ALS AND OF 3-CHLORO-5-(5-FORMYLARYL)PENTA-2,4-DIEN-1-ALS BY THE VILSMEIER REACTION

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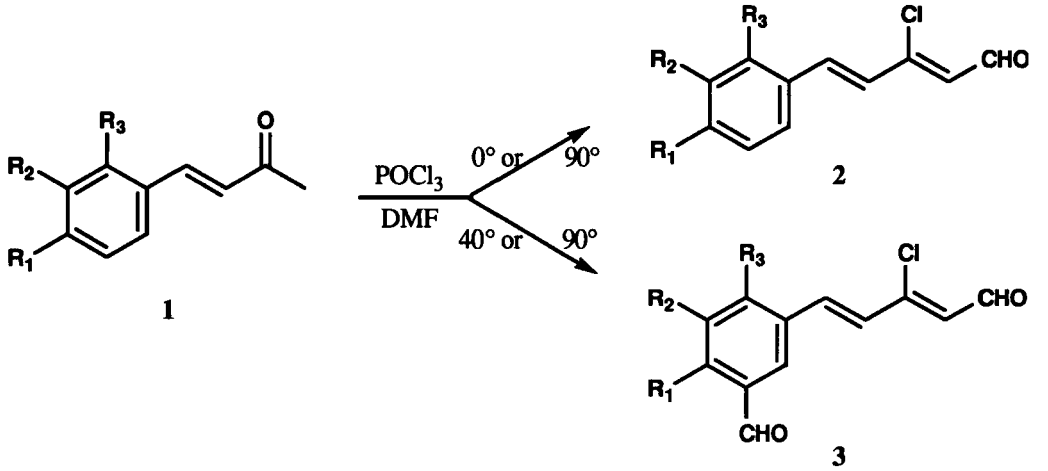
The Vilsmeier formylation[1] sometimes results in acylhalo addition[2] and ring annulation.[3,4] It has also been used for different synthetic reactions.[5] Earlier studies of Vilsmeier reaction on benzalacetone may also lead to monochloroformylation on the side-chain at 0°. The aim of the present investigation was to determine the role of temperature on the chloroformylation reaction.[6]



a) R_1, R_2 and R_3 = H b) R_1 and R_2 = H, R_3 = OMe, Me or Cl
c) R_1 and R_3 = H, R_2 = OMe d) R_2 and R_3 = H, R_1 = OMe, Me or Cl

In contrast to the monoformylation[7] of benzalacetone at 0°, diformylation occurred at 90°. Further increase in temperature leads to degradation products. The reaction with the monosubstituted benzalacetones indicates that the substituents play a vital role in determining whether formylation of aromatic ring occur or not. *ortho*-Substituted benzalacetones undergo diformylation at low temperature (40°), whereas *meta* and *para* substituted benzalacetones give the diformylated products at elevated temperature (90°). This may be attributed to steric and electronic effects.[8] Electrophilic attack of the Vilsmeier reagent on *ortho*-substituted compounds are sterically as well as electronically favored at the *para*-position to the substituent. In *meta*-substituted compounds,

electrophilic attack at the *meta*-position is controlled by steric factors more than by electronic effect, whereas in the *para*-substituted benzalacetones only monoformylation occurs due to the steric effect at both the *ortho* positions to the substituent. In addition, monoformylation can be also attributed to the bulky nature of the electrophile which cannot attack at the *ortho* position because of the steric effect even though it is electronically favored. The results are summarized in Table 1.

The present study leads to the conclusion that electrophilic attack of the Vilsmeier reagent on the benzene ring is subjected to steric as well as electronic effects.

EXPERIMENTAL SECTION

The NMR was recorded on a Bruker 90 Mz instrument. The IR was recorded on a Nicolet FT-IR instrument. Mps were determined on a hot stage instrument and are uncorrected. Mass spectra were recorded on a Shimadzu Quadrupole GC-MS. Elemental analyses were carried out using a Heraeus-CHIN-RAPID Analyzer.

TABLE 1. Reaction Products of Substituted Benzalacetones[a]

Substrate	Temp (°C)	Product	mp (°C)	Yield (%)
Benzalacetone	0	3-Chloro-5-phenylpenta-2,4-dien-1-al	67	65
	90	3-chloro-5-(3-formylphenyl)penta-2,4-dien-1-al	115	60
o-Methoxybenzal-acetone	40	3-Chloro-5-(5-formyl-2-methoxyphenyl)penta-2,4-dien-1-al	80	65
o-Methylbenzal-acetone	40	3-Chloro-5-(5-formyl-2-methylphenyl)penta-2,4-dien-1-al	71	69
o-Chlorobenzal-acetone	40	3-Chloro-5-(5-formyl-2-chlorophenyl)penta-2,4-dien-1-al	75	68
m-Methoxybenzal-acetone	90	3-Chloro-5-(5-formyl-3-methoxyphenyl)penta-2,4-dien-1-al	115	65
p-Methoxybenzal-acetone	90	3-Chloro-5-(4-methoxyphenyl)penta-2,4-dien-1-al	80	62
p-Methylbenzal-acetone	90	3-Chloro-5-(4-methylphenyl)penta-2,4-dien-1-al	72	65
p-Chlorobenzal-acetone	90	3-Chloro-5-(4-chlorophenyl)penta-2,4-dien-1-al	75	65

a) The products were identified by ^{1}H and ^{13}C NMR, IR, and mass spectra.

Typical Procedure. Preparation of 3-Chloro-5-(3-formylphenyl)penta-2,4-dien-1-al.- Benzalacetone 1.46 g (10 mmol) was dissolved in 8 ml of DMF, cooled to 0° and 5 ml of $POCl_3$ was added dropwise over 30 minutes and the mixture was stirred for 2 hrs at room temperature. The temperature was raised to 900 and the mixture was stirred for 3 hrs and then poured into a mixture of crushed ice (200 g) containing sodium acetate (4 g). The product was extracted with chloroform (3 x 25 ml) and dried over anhydrous sodium sulfate. After removal of the solvent, the crude product was chromatographed through a short column of silica gel (60-120 mesh) using 3:7 ratio of chloroform and petroleum ether as an eluent to give 1.32 g (60%) of 3-chloro-5-(3-formylphenyl)penta-2-4-dien-1-al as a yellow solid, mp. 115°. ^1H NMR: δ 7.43 (m, 3H), 7.6 (m, 2H), 7.8 (d, 1H), 8.6 (d, 1H), 10.01 (s, 1H), 10.45 (s, 1H) ^{13}C NMR: 122.9, 124.99, 126.49, 127.95, 129.22, 130.1, 131.63, 134.81, 139.75, 147.93, 189.28, 191.2; IR: 1701 cm^{-1}, 1680 cm^{-1}; MS (EI):M/Z (%) 220 (M^+, 50), 221 (M^{+1}, 12), 222 (M^{+2}, 18), 192 (15), 195 (85), 157 (80), 139 (40), 128 (base, 100), 102 (3), 77 (70).
Anal. Calcd. for $C_{12}H_9ClO_2$: C, 65.32; H, 4.11. Found: C, 65.28; H, 4.16

3-Chloro-5-phenylpenta-2,4-dien-1-al: yellow solid, mp. 67°, lit.[7a] mp 67°. ^1H NMR: δ 6 7.5 (m, 6H), 7.8 (d, 1H), 8.65 (d, 1H), 10.05 (s, 1H); ^{13}C NMR: δ 124.95, 126.47, 127.59, 128.68, 129.6, 134.73, 138.7, 147.48, 188.48; IR: 1672 cm^{-1}.
Anal. Calcd for $C_{11}H_9ClO$: C, 68.58; H, 4.71. Found: C, 68.61; H, 4.18

3-Chloro-5-(5-formyl-2-methoxyphenyl)penta-2,4-dien-1-al: yellow solid, mp. 80°, lit.[7a] mp. 80°. ^1H NMR: δ 3.86 (s, 3H), 6.95 (d, 2H), 7.65 (d, 2H), 7.81 (d, 1H), 8.52 (d, 1H) 10.1 (s, 1H), 10.47 (s, 1H): ^{13}C NMR: δ 55.6, 114.86, 120.66, 128, 129.5, 131.5, 148, 162.9, 189.1, 191.3; IR: 1675 cm^{-1}, 1703 cm^{-1}.
Anal. Calcd. for $C_{13}H_{11}ClO_3$: C, 62.29; H, 4.42. Found: C, 63.33; H, 4.40

3-Chloro-5-(5-formyl-2-methoxyphenyl)penta-2,4-dien-1-al: brown solid, mp. 71°. ^1H NMR: δ 2.48 (s, 3H), 7.3 (m, 3H), 7.7 (m, 1H), 8.3 (d, 1H), 8.5 (d, 1H), 10.01 (s, 1H), 10.47 (s, 1H) ^{13}C NMR: δ 21.7, 123.51, 126.71, 127.6, 131.09, 131.39, 133.52, 138.79, 145.3, 189.16, 191.12; SR: 1702 cm^{-1}, 1678 $cm1^{-1}$.
Anal. Calcd. for $C_{13}H_{11}ClO_2$: C, 66.53; H, 4.72. Found: C, 66.41; H, 4.69

3-Chloro-5-(5-formyl-2-chlorophenyl)penta-2,4-dien-1-al: brown solid, mp. 75°. ^1H NMR: δ 7.34 (m, 4H), 8.11 (d, 1H), 8.45 (d, 1H), 10.06 (s, 1H), 10.44 (s, 1H) ^{13}C NMR: δ 125.2, 127.06, 127.3, 128.31, 130.26, 131.98, 135.2, 142.76, 189.1, 190.87; IR: 1705 cm^{-1}, 1680 cm^{-1}.
Anal. Calcd. for $C_{12}H_8Cl_2O_2$: C, 56.50; H, 3.16. Found: C, 56.62; H, 3.16

3-Chloro-5-(5-formyl-3-methoxyphenyl)penta-2,4-dien-1-al: yellow solid, mp. 115°. ^1H NMR: δ 3.85 (s, 3H) 7.27 (m, 4H), 7.81 (d, 1H), 8.52 (d, 1H), 10.02 (s, 1H) 10.48 (s, 1H) ^{13}C NMR: δ 55.25, 113.91, 117.58, 121.91, 122.97, 130.62, 147.62, 160.01, 189.1, 191; IR: 1702 cm^{-1}, 1675 cm^{-1}.

Anal. Calcd. for $C_{13}H_{11}ClO_3$: C, 62.29; H, 4.42. Found: C, 62.30; H, 4.39

3-Chloro-5-(4-methoxyphenyl)penta-2,4-dien-1-al: yellow solid, mp. 80°, lit[7a] mp. 80°. ^1H NMR: δ 3.84 (s,3H), 6.2 (d, 1H), 6.8 (d, 1H), 7.37 (m, 5H) 10.19 (s, 1H) IR: 1667 cm^{-1}.
Anal. Calcd. for $C_{12}H_{11}ClO_2$: C, 64.73: H, 4.98. Found: C, 64.78; H, 4.30

3-Chloro-5-(4-methoxyphenyl) penta-2,4-dien-1-al: yellow solid, mp. 72°. ^1H NMR: δ 2.36 (s, 3H), 7.4 (m, 7H), 10.02 (s, 1H) ^{13}C NMR: δ 21.8, 125.2, 126.1, 127, 128.2, 129, 133.3, 137.2, 146.4, 189.1; SR: 1669 cm^{-1}.
Anal. Calcd. for $C_{12}H_{11}ClO$: C, 69.74; H, 5.37. Found: C, 69.81; H, 5.36

3-Chloro-5-(4-chlorophenyl)penta-2 ,4-dien-1-al: brown solid, mp. 75°. ^1H NMR: 7.5 (m, 7H), 10.3 (s, 1H) IR: 1670 cm^{-1}.
Anal. Calcd. for $C_{11}H_8Cl_2O$: C, 1 58.18: H, 3.55. Found: C, 58.23; H, 3.53

Acknowledgement.- The authors are thankful to CSIR, New Delhi and UGC New Delhi for financial support.

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