Indirect olefination of *o*-aminobenzaldehyde

Dibakar C. Deka* and Maumita Paul

Department of Chemistry, Gauhati University, Guwahati 781 014, Assam, India

Indirect olefination of *o*-aminobenzaldehyde, an unstable aldehyde which can not be successfully subjected to direct olefination, has been achieved with 100% *E*-selectivity. Wittig olefination of *o*-nitrobenzaldehyde and the reduction of nitro group under neutral condition are the key steps involved.

Keywords: indirect olefination, *o*-aminobenzaldehyde, reduction of nitro group, neutral condition

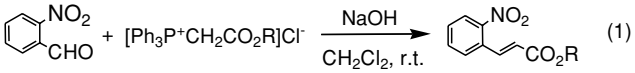
o-Aminobenzaldehyde is a potential intermediate in many organic syntheses[1-2] but its short shelf-life due to self-condensation during its preparation have rendered it unsuitable for synthetic chemists or trade.[3] For the same reasons direct olefination of *o*-aminobenzaldehyde has not been reported in spite of its great potentiality as a useful synthetic tool in many organic syntheses. In our effort to prepare alkyl *o*-aminocinnamates needed for our on going research by Wittig olefination of *o*-aminobenzaldehyde, we found ourselves handicapped because of the non-availability of *o*-aminobenzaldehyde or our inability to prepare enough *o*-aminobenzaldehyde.[4-7] This short coming has been finally overcome by developing an indirect methodology in which olefination of *o*-aminobenzaldehyde has been achieved in just two steps, and we are reporting here the results.

Unlike *o*-aminobenzaldehyde *o*-nitrobenzaldehyde is quite stable, has long shelf-life and can easily be prepared in the laboratory [8] or procured from commercial houses. Olefination of *o*-nitrobenzaldehyde followed by the reduction of the nitro group under neutral condition results in high yield of the olefination product of *o*-aminobenzaldehyde. Synthesis of several such olefination products of *o*-aminobenzaldehyde have been achieved with satisfactory results.

All the five *o*-nitrocinnamates shown in Table 1 have been prepared following Wittig methodology.[8] The phosphonium salts required for this purpose were prepared by standard procedures.[8] All the phosphonium salts are crystalline white solids characterised by sharp melting points. The *E/Z* ratio of the olefins reported in Table 1 has been estimated from the integration of the olefinic proton signals in ^{1}H NMR. *E* and *Z*-isomers have been identified based on the fact that olefinic protons in the *E*-isomers have higher coupling constant (here it is around 16 Hz in all the olefins) as compared to that in *Z*-isomers (about 12 Hz in almost all the olefins reported here). While the olefins in entries 1 and 2 (Table 1) are reported in literature[8] other three (entries 3 to 5) are unpublished. Melting points of the two reported olefins have been compared with those in literature (see Experimental).

Reduction of the nitro groups in alkyl *o*-nitrocinnamates was attempted by methods developed by Kakati and Deka,[7] and Lyons and Smith.[9] In the former case, although reduction apparently took place, isolation of the reduced product was difficult. In case of the later virtually no reaction took place. When this later methodology was modified by adding THF, the reduction was found to proceed smoothly, albeit slow, giving high yields of alkyl *o*-aminocinnamates with 100% *E*-selectivity (Table 2). Both the olefinic double bond and the ester functionality remained intact. Five different compounds were attempted, and in all of them the nitro group has been reduced selectively with no harm to both the olefinic and ester functionality. That the product is 100% *E*-olefin is obvious from the ^3J-values (about 16 Hz) of the olefinic proton signals. The olefinic proton signals corresponding to the minor *Z*-isomer observed with *o*-nitro cinnamates are completely absent after reduction. The minor *Z*-isomer present in the *o*-nitrocinnamates was left unreduced and rejected during chromatography. It is observed that reduction of nitro to amino group does not affect the coupling interaction of the olefinic protons as evident from the comparison of the coupling constants of the olefinic protons in nitro compounds with those of the corresponding values in amino compounds. All amino products show blue fluorescence in diethyl ether. Both the methyl and ethyl *o*-aminocinnamate (entries 1 and 2, Table 2) are reported earlier[8] but the other three (entries 3 to 5) could not be traced.

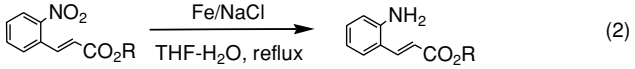
Table 1 Wittig olefination of *o*-nitrobenzaldehyde



(1)

Entry	*R*	Yield/%	*E/Z*
1	Me	80	89/11
2	Et	91	91/9
3	*n*-Pr	74	91/9
4	*iso*-Pr	93	92/8
5	*n*-Bu	82	92/8

Table 2 Reduction of nitro olefins to corresponding amino olefins



(2)

Entry	*R*	Yield/%	*E/Z*	Time/h
1	Me	77	100/0	72
2	Et	72	100/0	80
3	*n*-Pr	75	100/0	90
4	*iso*-Pr	60	100/0	120
5	*n*-Bu	65	100/0	130

Experimental

Alkyl cinnamates (Table 1) were prepared following procedures available in literature.[10] All ^{1}H and ^{13}C NMR spectra were recorded at 400 MHz using $CDCl_3$ as the solvent and TMS as the internal reference. IR spectra were scanned either as a liquid film on a KBr plate or as a KBr pellet. Elemental analyses for the unreported compounds were done with a Perkin Elmer Intruments Series II CHNS/O Analyzer 2400. Melting points were determined under atmospheric pressure and uncorrected.

Reduction of the nitro compounds into corresponding amines

To a stirred solution of the nitro compound (1 eq) in 10:1 THF: H_2O (25 ml), iron powder (0.4 eq) and NaCl (0.1 eq) was added and the resulting mixture was refluxed for several hours. The progress of the reaction was monitored on TLC, and time to time iron powder in small amount was added to accelerate the reduction process. When enough progress in the reaction mixture was observed, the reaction mixture was brought to r.t. and partitioned between diethyl ether and

* Correspondent. Email: dcdeka@rediffmail.com

water. The ether phase was separated, washed with brine and dried over anhydrous Na_2SO_4. The product amine was isolated from the crude by column chromatography on silica gel (60–120 mesh) using 1:10 ethyl acetate and petroleum ether as the eluent.

Spectral data

Methyl o-nitrocinnamate: *E/Z* = 89/11, m.p. 71 °C (lit. 73)[8]. ^{1}H NMR: δ 3.56 (s, OMe, *Z*-isomer), 3.79 (s, OMe, *E*-isomer), 6.05 (d, *J* = 11.6 Hz, olefinic H, *Z*-isomer), 6.34 (d, *J* = 15.8 Hz, olefinic H, *E*-isomer), 7.5–7.6 (complex m, aromatic protons), 8.02 (d, *J* = 8.8 Hz, one of the aromatic protons), 8.08 (d, *J* = 15.8 Hz, olefinic H, *E*-isomer), 8.1 (d, *J* = 11.6 Hz, olefinic H, *Z*-isomer). ^{13}C NMR: δ 52.35, 123.01, 125.08, 129.30, 130.53, 130.66, 133.74, 140.29, 148.42, 166.30 IR: cm^{-1} 2965, 1715, 1644, 1521, 1352, 1203, 870, 758.

Ethyl o-nitrocinnamate: E/Z = 91/9, m.p. 40 °C (lit. 44)[8]. ^{1}H NMR: δ 1.06 (t, *J* = 7.0 Hz, CH_3, *Z*-isomer), 1.31 (t, *J* = 7.1 Hz, CH_3, *E*-isomer), 3.98 (q, *J* = 7.0 Hz, CH_2, *Z*-isomer), 4.25 (q, *J* = 7.1 Hz, CH_2, *E*-isomer), 6.07 (d, *J* = 12.0 Hz, olefinic H, *Z*-isomer), 6.33 (d, *J* = 15.8 Hz, olefinic H, *E*-isomer), 7.4–7.7 (complex m, aromatic protons), 8.0 (d, *J* = 8 Hz, one of the aromatic proton), 8.07 (d, *J* = 15.8 Hz, olefinic H, *E*-isomer), 8.09 (d, *J* = 12.0 Hz, olefinic H, *Z*-isomer). ^{13}C NMR: δ 14.66, 61.19, 123.40, 125.00, 129.25, 130.49, 130.59, 133.73, 139.90, 148.37, 165.82 IR:cm^{-1} 2991, 1721, 1655, 1532, 1352, 1183, 758.

n-Propyl o-nitrocinnamate: E/Z =89/11, liquid. ^{1}H NMR: δ 0.85 (t, CH_3, *Z*-isomer), 0.97 (t, *J* = 7.6 Hz, CH_3, *E*-isomer), 1.20 (m, CH_2, *Z*-isomer), 1.44 (m, CH_2, *E*-isomer), 3.97 (t, OCH_2, *Z*-isomer), 4.23 (t, *J* = 6.8 Hz, OCH_2, *E*-isomer), 6.1 (d, *J* = 11.6 Hz, olefinic H, *Z*-isomer), 6.37 (d, *J* = 16 Hz, olefinic H, *E*-isomer), 7.5–7.7 (complex m, 3 aromatic protons), 8.03 (d, *J* = 8 Hz, one of the aromatic protons), 8.11 (d, *J* = 16 Hz, olefinic proton, *E*-isomer). ^{13}C NMR: δ 14.06, 24.59, 63.12, 123.48, 125.05, 129.28, 130.44, 130.73, 133.69, 139.94, 148.40, 165.93 IR: cm^{-1} 2961, 1716, 1639, 1572, 1526, 1346, 1282, 1180, 975, 863, 757, 737. Calculated for $C_{12}H_{13}NO_4$ (in %): C 61.27, H 5.57, N 5.95 Found: C 60.86, H 5.79, N 5.55.

Isopropyl o-nitrocinnamate: E/Z = 92/8, liquid. ^{1}H NMR: δ 1.05 (d, *J* = 6.4 Hz, $2CH_3$, *Z*-isomer), 1.35 (d, *J* = 6.4 Hz, $2CH_3$, *E*-isomer), 4.35 (m, *J* = 6.4 Hz, CH, *Z*-isomer), 5.14 (m, *J* = 6.4 Hz, *E*-isomer), 6.06 (d, *J* = 12 Hz, olefinic H, *Z*-isomer), 6.33 (d, *J* =15.6 Hz, olefinic H, *E*-isomer), 7.5–7.65 (complex m of 3 aromatic protons), 8.01 (d, *J* = 8 Hz, one of the aromatic protons), 8.07 (d, *J*= 16 Hz, olefinic H, *E*-isomer), 8.15 (d, *J* = 12 Hz, olefinic H, *Z*-isomer). ^{13}C NMR: δ 22.28, 68.67, 123.98, 125.01, 129.26, 130.38, 130.73, 133.66, 139.63, 148.40, 165.37 IR: cm^{-1} 2979, 1707, 1635, 1570, 1522, 1342, 1198, 1104, 983, 914, 862, 792, 755. Calculated for $C_{12}H_{13}NO_4$ (in %): C 61.27, H 5.57, N 5.95 Found: C 61.66, H 5.88, N 5.84.

n-Butyl o-nitrocinnamate (liquid): E/Z = 92/8, liquid. ^{1}H NMR: δ 0.97 (t, *J* = 7.2 Hz, CH_3), 1.44 (m, CH_2), 1.65 (m, CH_2), 3.97 (t, *J* = 6.8 Hz, OCH_2, *Z*-isomer), 4.24 (t, *J* = 7.2 Hz, OCH_2, *E*-isomer), 6.11 (d, *J* = 11.6 Hz, olefinic H, *Z*-isomer), 6.37 (d, *J* = 15.6 Hz, olefinic H, *E*-isomer), 7.5–7.7 (complex m, 3 aromatic protons), 8.04 (d, *J* = 8.4 Hz, one of the aromatic protons), 8.11 (d, *J* = 15.6 Hz, olefinic H, *E*-isomer), 8.17 (d, *J* = 11.6 Hz, olefinic H, *Z*-isomer). ^{13}C NMR: δ 13.71, 19.14, 30.61, 64.69, 123.07, 124.61, 128.83, 129.95, 130.34, 133.20, 139.49, 147.97, 165.48 IR :cm^{-1} 2960, 1717, 1640, 1572, 1527, 1347, 1291, 1181, 976, 863, 787, 757. Calculated for $C_{13}H_{15}NO_4$ (in %): C 62.64, H 6.07, N 5.62 Found: C 62.35, H 5.82, N 5.42.

Methyl (E)-o-aminocinnamate: M.p. 63 °C (lit. 65)[8]. ^{1}H NMR: 3.82 (s, 3H, OMe,), 3.96 (bs, 2H, NH_2), 6.35 (d, *J* =15.6 Hz, 1H, olefinic H), 6.69 (d, *J* = 8 Hz, 1H, aromatic), 6.76 (t, *J* = 8 Hz, 1H, aromatic), 7.17 (t, *J* = 7.5 Hz, 1H, aromatic), 7.37 (d, *J* = 7.7 Hz, 1H, aromatic), 7.82 (d, *J* = 15.8 Hz, 1H, olefinic). ^{13}C NMR: δ 52.03, 116.95, 117.84, 119.13, 120.03, 128.26, 131.51, 140.49, 145.76, 167.82 IR: cm^{-1} 3421, 3350, 2966, 1711, 1629, 1470, 1440, 1332, 1178, 984, 861, 769.

Ethyl (E)-o-aminocinnamate: M.p. 76 (lit. 78)[8]. ^{1}H NMR: δ 1.3 (t, *J* = 7 Hz, 3H, CH_3), 3.99 (bs, 2H, NH_2), 4.25 (q, *J* = 7 Hz, 2H, CH_2), 6.34 (d, *J* = 15.8 Hz, 1H, olefinic), 6.68 (d, *J* = 8 Hz, 1H, aromatic), 6.75 (t, *J* = 7.6 Hz, 1H, aromatic), 7.15 (t, *J* = 7.6 Hz, 1H, aromatic), 7.36 (d, *J* = 8 Hz, 1H, aromatic), 7.82 (d, *J* =15.8 Hz, 1H, olefinic). ^{13}C NMR: δ 14.82, 60.81, 116.96, 118.34, 119.14, 120.14, 128.27, 131.43, 140.24, 145.71, 167.42 IR: cm^{-1} 3474, 3373, 2980, 1706, 1619, 1313, 1189, 1034, 756.

Propyl (E)-o-aminocinnamate: M.p. 65–66 °C. ^{1}H NMR: δ 0.97 (t, *J* = 7.6 Hz, 3H, CH_3), 1.43 (m, 2H, CH_2), 3.75 (bs, 2H, NH_2), 4.21 (t, *J* = 6.8 Hz, 2H, OCH_2), 6.36 (d, *J* = 16 Hz, 1H, olefinic), 6.70 (d, *J* = 8 Hz, 1H, aromatic), 6.76 (t, *J* = 8 Hz, 1H, aromatic), 7.17 (t, *J* = 8 Hz, 1H, aromatic), 7.38 (d, *J* = 7.6 Hz, 1H, aromatic), 7.83 (d, *J* = 16 Hz, 1H, olefinic). ^{13}C NMR: δ 14.52, 24.95, 62.63, 117.50, 118.50, 119.74, 120.69, 128.24, 131.47, 140.19, 144.84, 167.60 IR: cm^{-1} 3464, 3377, 2960, 1702, 1622, 1491, 1460, 1306, 1261, 1178, 982, 751. Calculated for $C_{12}H_{15}NO_2$ (in %): C 70.22, H 7.37, N 6.82 Found: C 70.59, H 7.50, N 6.99.

Isopropyl (E)-o-aminocinnamate: M.p. 62 °C. ^{1}H NMR: δ 1.31 (d, *J* = 6.4 Hz, 6H, $2CH_3$), 3.98 (bs, 2H, NH_2), 5.13 (m, *J* = 6.4 Hz, 1H, CH), 6.33 (d, *J* = 16 Hz, 1H, olefinic), 6.70 (d, *J* = 8 Hz, 1H, aromatic), 6.76 (t, *J* = 7.8 Hz, 1H, aromatic), 7.16 (t, *J* = 8 Hz, 1H, aromatic), 7.77 (d, *J* = 8 Hz, 1H, aromatic), 7.80 (d, *J* = 15.6 Hz, 1H, olefinic). ^{13}C NMR: δ 22.41, 68.10, 116.91, 118.84, 119.08, 120.15, 128.26, 131.36, 140.00, 145.73, 166.97 IR :cm^{-1} 3409, 3348, 3240, 2977, 1701, 1622, 1461, 1350, 1305, 1187, 1101, 981, 860, 749. Calculated for $C_{12}H_{15}NO_2$ (in %): C 70.22, H 7.37, N 6.82 Found: C 70.02, H 7.57, N 6.89.

Butyl (E)-o-aminocinnamate: M.p. 69–71 °C. ^{1}H NMR: δ 0.96 (t, *J* = 7.6 Hz, 3H, CH_3), 1.43 (m, 2H, CH_2), 1.68 (m, 2H, CH_2), 3.97 (bs, 2H, NH_2), 4.20 (t, *J* = 6.8 Hz, 2H, OCH_2), 6.35 (d, *J* = 15.6 Hz, 1H, olefinic), 6.70 (d, *J* = 8.2 Hz, 1H, aromatic), 6.76 (t, *J* = 8 Hz, 1H, aromatic), 7.16 (t, *J* = 7.8 Hz, 1H, aromatic), 7.38 (d, *J* = 8 Hz, 1H, aromatic), 7.82 (d, *J* = 15.6 Hz, 1H, olefinic). ^{13}C NMR: δ 14.22, 19.65, 31.21, 64.74, 116.92, 118.37, 119.13, 120.12, 128.29, 131.41, 140.18, 145.67, 167.50 IR :cm^{-1} 3461, 3375, 2960, 1702, 1623, 1490, 1460, 1324, 1303, 1260, 1177, 982, 864, 756. Calculated for $C_{13}H_{17}NO_2$ (in %): C 71.21, H 7.81, N 6.39 Found: C 71.44, H 7.79, N 6.52.

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