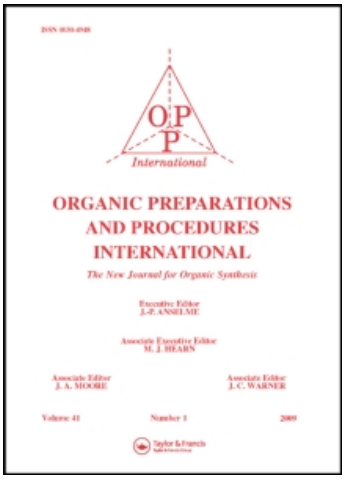

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BORON TRIFLUORIDE MEDIATED, ONE-POT SYNTHESIS OF 3-METHYL-1,2-DIHYDRONAPHTHALENES

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BORON TRIFLUORIDE MEDIATED, ONE-POT SYNTHESIS OF 3-METHYL-1,2-DIHYDRONAPHTHALENES

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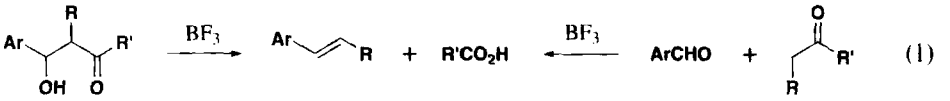
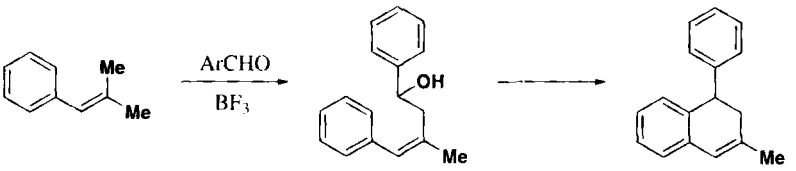
During the course of an investigation involving the stereoselective synthesis of 1,3-diols by reduction of β-hydroxyketones, a number of the prerequisite ketones were prepared *via* aldol condensations.[1] We discovered an unprecedented boron trifluoride initiated cleavage during this study when boron trifluoride was used as an aldol catalyst in non-ethereal solvents. The new cleavage reaction resulted in the formation of (*E*)-arylalkenes and carboxylic acids.[2,3] It was then found that this new boron trifluoride initiated Aldol-Grob reaction sequence could be carried out in a tandem fashion starting from aromatic aldehydes and ketones (*Eq. 1*).[4,5]



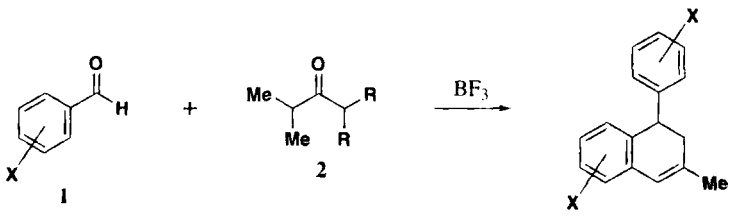
(1)

During the investigation of the new boron trifluoride catalyzed Aldol-Grob reaction, we discovered a novel reaction involving the addition of the starting aromatic aldehydes to the product styrenes in the presence of the acetic acid complex of boron trifluoride [6] followed by a Friedel-Crafts cycloalkylation (*Eq. 2*).[7-9]



(2)

Initially, the styrene starting materials were generated using the Aldol-Grob sequence. We now report the boron trifluoride mediated, one-pot synthesis of 3-methyl-1,2-dihydronaphthalenes using α,α-dimethyl ketones and aromatic aldehydes (*Eq. 3*). Our results are summarized below. The Friedel-Crafts alkylations represent important carbon-carbon bond forming sequences in organic chemistry.[10-13]



1a X = H
1b X = *p*-CH_3
1c X = *m*-Cl
1d X = *m*-Br
1e X = *p*-F
1a X = H

R = CH_3
R = CH_3
R = CH_3
R = CH_3
R = CH_3
R = H

3a X = H
3b X = *p*-CH_3
3c X = *m*-Cl
3d X = *m*-Br
3e X = *p*-F

(3)

At present, the reaction would appear to be limited to α,α-dimethyl ketones; all other ketones examined to date have simply resulted in dimerization and polymerization products. Reduction and aromatization reactions can also occur and generally lead to loss of product. Although a detailed mechanistic study has not been completed, the consistent formation of 1,2-dihydronaphthalene derivatives would point toward the intermediacy of a carbocation. The boron trifluoride mediated Aldol-Grob reaction sequence results in the formation of an arylalkenes (alkene isomerization induced by BF_3) which presumably react with excess aldehyde to generate the benzyl alcohol intermediate (*Eq. 2*).

The yields of the new boron trifluoride addition reaction are dependent on the stability of the starting alkene in the presence of the boron trifluoride acetic acid complex. Monosubstituted styrenes, for example, readily polymerize in a relatively short time under the reaction conditions. Other boron trifluoride complexes also induce the reaction but side-reactions are minimized when the acetic acid complex is utilized.

EXPERIMENTAL SECTION

All reactions were carried out in dry hexane in oven dried glassware under a nitrogen atmosphere. Air and moisture sensitive compounds were introduced by means of a syringe through a rubber septum. All reagents were used as received (Aldrich Chemical Co.). The products were purified by chro-

matography using 230-400 mesh ASTM 60 Å silica gel. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a 250 MHz Bruker AC 250 spectrometer and resonances are given in ppm (δ) relative to TMS. Elemental analyses were performed by Atlantic MicroLabs, Norcross, GA.

Preparation of 3-Methyl-1-phenyl-1,2-dihydronaphthalene (3a). Representative Procedure.- To a dry, 25 mL round-bottomed flask were added 2,4-dimethyl-3-pentanone (0.114 g, 1 mmol), benzaldehyde (0.223 g, 2.2 mmol), hexane (5 mL) and BF_3•$2CH_3COOH$ (1 mmol). The reaction mixture was stirred at reflux for 3 hrs and then quenched with water (5 mL). The product was extracted into ether (3 x 10 mL), and purified by silica gel chromatography (hexane as eluent) to afford 0.133 g (60%) of 3-methyl-1-phenyl-1,2-dihydronaphthalene as a pale yellow oil, bp: 190-191°. (**3a**): ^1H NMR ($CDCl_3$/TMS): δ 6.75 - 7.45 (m, 9 H), 6.26 (s, 1 H), 4.06 - 4.12 (t, 1 H, J = 8.71 Hz), 2.49-2.52 (d, 2 H, J = 8.6 Hz), 1.64 (s, 3 H); ^{13}C NMR ($CDCl_3$): δ 144.6, 136.6, 136.5, 134.9, 128.3, 127.4, 126.6, 126.4, 126.3, 126.2, 125.3, 122.8, 44.3, 37.3, 23.3.

A 49% yield of **3a** was obtained when 2-methyl-3-pentanone was used.

Anal. Calcd for $C_{17}H_{16}$: C, 92.72; H, 7.28. Found: C, 92.43; H, 7.53

3,7-Dimethyl-1-(4-methylphenyl)-1,2-dihydronaphthalene (3b), 58% yield, pale yellow oil, bp 203-204°; ^1H NMR ($CDCl_3$/TMS): δ 6.90-7.07 (m, 6 H), 6.62 (s, 1 H), 6.22 (s, 1 H), 3.96 - 4.04 (t, 1 H, J = 8.52 Hz), 2.45 - 2.46 (d, 2 H, J = 8.09 Hz), 2.28 (s, 3 H), 2.15 (s, 3 H), 1.82 (s, 3 H); ^{13}C NMR ($CDCl_3$): δ 141.8, 136.6, 135.7, 135.6, 135.3, 132.3, 129.0, 128.2, 128.1, 127.1, 125.2, 122.7, 44.1, 37.6, 23.3, 21.2, 20.9.

Anal. Calcd for $C_{19}H_{20}$: C, 91.88, H, 8.12. Found: C, 91.74; H, 8.23

6-Chloro-1-(3-chlorophenyl)-3-methyl-1,2-dihydronaphthalene (3c), 56% yield, yellow solid, mp 36-37 °; ^1H NMR ($CDCl_3$/TMS): δ 6.70 - 7.46 (m, 7 H), 6.19 (s, 1 H), 3.99 - 4.06 (t, 1 H, J = 8.23 Hz), 2.49 - 2.52 (d, 2 H, J = 7.55 Hz), 1.86 (s, 3 H); ^{13}C NMR ($CDCl_3$): δ 146.3, 138.7, 136.5, 134.8, 134.3, 132.6, 129.9, 129.4, 128.6, 128.2, 127.8, 126.4, 125.3, 122.1, 43.5, 37.2, 23.4.

Anal. Calcd for $C_{17}H_{14}Cl_2$: C, 70.60, H, 4.88. Found: C, 70.54, H. 4.95

6-Bromo-1-(3-bromophenyl)-3-methyl-1,2-dihydronaphthalene (3d), 54% yield, yellow solid, mp 32-33 °C; ^1H NMR ($CDCl_3$/TMS): δ 6.67 - 7.46 (m, 7 H), 6.18 (s, 1 H), 3.98 - 4.05 (t,1 H, J = 8.43 Hz), 2.49 - 2.52 (d, 2 H, J = 7.48 Hz) 1.85 (s, 3 H); ^{13}C NMR ($CDCl_3$): δ 146.4, 138.1, 136.9, 134.4, 131.2, 130.7, 130.1, 129.7, 129.0, 128.5, 126.8, 125.2, 122.0, 120.7, 43.6, 37.1, 23.4.

Anal. Calcd for $C_{17}H_{14}Br_2$: C, 54.00, H, 3.73. Found: C, 53.91, H, 3.79

7-Fluoro-1-(4-fluorophenyl)-3-methyl-1,2-dihydronaphthalene (3e), 50% yield, yellow solid, mp 39-40°; ^1H NMR ($CDCl_3$/TMS): δ 6.45 - 7.47 (m, 7 H), 6.24 (s, 1 H), 4.03 - 4.10 (t, 1 H, J = 8.83 Hz) 2.45 - 2.49 (d, 2 H, J = 8.65 Hz), 1.86 (s, 3 H); ^{13}C NMR ($CDCl_3$): δ 164.3, 163.6, 160.4, 159.5, 139.5, 138.8, 138.7, 135.7, 133.3, 131.1, 129.7, 129.6, 127.9, 127.8, 127.3, 126.6, 126.5, 121.9, 115.8, 115.5, 115.4, 115.1, 114.4, 113.4, 113.1, 43.9, 37.1, 23.3.

Anal. Calcd for $C_{17}H_{14}F_2$: C, 79.67, H, 5.51; Found: C, 79.56, H, 5.60

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