

Research Article Schmidt Reaction of E-3-Benzylidenechromanones and E-3-Benzylidenethiochromanones

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On treatment with NaN₃/c. H_2SO_4 -HOAc or NaN₃/TFA, *E*-3-benzylidenechromanones are mostly converted to *E*- β -aminobenzylidenechromanones while *E*-3-benzylidenethiochromanones are converted to 3-benzylthiochromones. A structurally new type of product has been isolated for the reaction of *E*-3-benzylidene-4'-methoxychromanone with NaN₃/TFA. Mechanistic paths have been suggested for formation of the products.

1. Introduction

The Schmidt reaction [1] is an organic reaction involving alkyl/aryl migration over the carbon-nitrogen bond in an azide with expulsion of nitrogen. A key reagent introducing this azide group is hydrazoic acid, and the reaction product(s) depends on the nature of the substrate. Moreover, there are important variants of this reaction, developed mainly by Aubé et al. [2, 3], which include rearrangements through interactions of carbocations and alkyl azides or carbonyl compounds and alkyl azides, either intermolecularly or intramolecularly. Schmidt reaction of chromanones and their analogues has been studied by a number of groups [4–13]. Schmidt reaction of *E*-3-benzylideneflavanones (1) (Figure 1), done by us, produced some novel results [14-16]. In continuation of that work, we undertook the study of Schmidt reaction of E-3-benzylidenechromanones (2) and E-3-benzylidenethiochromanones (3). As in the case of 1, the reaction was performed under the two reaction conditions for these substrates also. The results obtained in this study are presented herein.

2. Results and Discussion

When the *E*-3-benzylidenechromanones $2\mathbf{a}-\mathbf{h}$ and the *E*-3-benzylidenethiochromanones $3\mathbf{a}-\mathbf{c}$ were treated with

NaN₃/c. H₂SO₄-HOAc at room temperature, none of them underwent significant change even after 24 h. On heating the reaction mixture at 60°C, the starting materials gradually changed to products, and the reactions were complete within 12 h (subsequently this temperature was found to be the optimum temperature for the reaction). Chromatography of the resulting crude materials obtained after work-up gave pure crystalline products in moderate yield from the reactions of **2a**-**f** and **3a**-**b**. From the reactions of **2g**-**h** and **3c**, any pure product could not be isolated. Characterization of the products from their spectral data showed that **2a**-**f** gave *E*- β -amino-3-benzylidene-4-chromanones (**4a**-**f**) whereas **3ab** gave *E*-3-benzoylthiochromones (**5a-b**) (Scheme 1, Table 1).

The products obtained from 2a-f were assigned *E*-configuration, as both the protons of their NH₂ group appeared at the same field in their ¹H NMR spectra. If the configuration was *Z*, these two N–H protons would have appeared at two different positions due to intramolecular hydrogen bonding of only one of them with >C=O [15, 16].

When the *E*-3-benzylidenechromanones **2a-b** and **2g** were treated with NaN₃ (1:1.5 mole ratio) in TFA and the mixture was kept for 4 days at room temperature, the first two substrates gave E- β -amino-3-benzylidenechromanones (**4a-b**) while the last one gave another type of product (**6**). Under the same reaction condition, *E*-3-benzylidenethiochromanone (**3a**), however,



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TABLE 1: Results of Schmidt reaction of E-3-benzylidenechromanones (2) and E-3-benzylidenethiochromanones (4) with NaN_3/c . H₂SO₄-HOAc.

Entry	Substrate	Product	Yield (%)
1	2a	4a	32
2	2b	4b	34
3	2c	4c	33
4	2d	4 d	31
5	2e	4e	38
6	2f	4f	33
7	2g	—	—
8	2h	—	—
9	3a	5a	30
10	3b	5b	32
11	3c	_	

TABLE 2: Results of Schmidt reaction of E-3-benzylidenechromanones (2) and E-3-benzylidenethiochromanone (3a) with NaN₃/ TFA.

Entry	Substrate	Product	Yield (%)
1	2a	4a	30
2	2b	4b	32
3	2g	6	29
4	3a	5a	34
4	3a	5a	34

gave 3-benzoylthiochromone (5a) (Table 2). Configuration of the product 6 could not be settled so far.

Suggested mechanisms for formation of 4 and 6 are given in Schemes 3 and 4, respectively. For formation of 5, the first step will be similar to the first step shown in Scheme 3. The resulting intermediate 7 (Figure 2) then follows a different path promoted by sulphur leading to 5. At this stage, no suggestion is being made about the nature of the path.

It is noteworthy that disposition of the NH_2 group in 4 is opposite to that of an analogous product from 1 [15, 16], though they are formed under similar reaction conditions. The absence of a 2-aryl group in 2 is possibly responsible for this difference. Regarding the formation of **6** in one case only, it may be mentioned that the conjugation of OMe with C=O in the intermediate 4g possibly makes it more reactive to undergo the reaction shown in Scheme 4.

3. Conclusions

We report here transformation of E-3-benzylidenechromanones (2) and E-3-benzylidenethiochromanones (3) to products of the types 4-6 by Schmidt reaction under two experimental conditions, which follow interesting mechanistic paths.

4. Experimental Section

Melting points were recorded on a Köfler block. IR spectra were recorded on a Perkin Elmer FT-IR spectrophotometer (Spectrum BX II) in KBr pellets. ¹H and ¹³C NMR spectra were recorded in CDCl₃ on a Bruker AV-300 (300 MHz) spectrometer. Analytical samples were routinely dried in vacuo at room temperature. Microanalytical data were recorded on two Perkin-Elmer 2400 Series II C, H, and N analyzers. Mass spectra were measured in the following ways: ESIMS(+) (Waters Micromass Q-Tof micro) and FAB-MS (Jeol the M Station JMS.700). Column chromatography was performed with silica gel (100-200 mesh), and TLC with silica gel G made of SRL Pvt. Ltd. Petroleum ether had the boiling range 60–80°C.

4.1. General Procedure for the Reaction of E-3-Benzylidenechromanones (2) and E-3-Benzylidenethiochromanones (3) under Schmidt Reaction Conditions

Condition I. An appropriate E-3-benzylidenechromanone (2)/E-3-benzylidenethiochromanone (3) (1 mmol) was dissolved in c. H₂SO₄-HOAc mixture (1:5, 6 mL) and to the solution sodium azide (1.5 mmol) was added in three portions at 5-minutes interval with stirring. The solution was heated at 60°C and the stirring was continued for 12 h and then diluted with water (150 mL). The resulting mixture was extracted with chloroform $(2 \times 25 \text{ mL})$ and the extract was dried over anhydrous sodium sulphate. The concentrate of the chloroform extract was chromatographed over silica gel using petroleum ether-ethyl acetate mixtures of increasing polarity as eluents to get pure products.

Condition II. An appropriate E-3-benzylidenechromanone (2)/E-3-benzylidenethiochromanone (3) (1 mmol) was dissolved in TFA (3 mL) at 5°C and to the cold solution sodium azide (1.5 mmol) was added in three portions at 5-minute intervals. The resulting mixture was kept at room temperature for 4 days and then diluted with water (150 mL). The resulting mixture was extracted with ether $(3 \times 35 \text{ mL})$ and the extract was dried over anhydrous sodium sulphate. The concentrate of the ether extract was chromatographed over silica gel using petroleum ether-ethyl acetate mixtures of increasing polarity as eluents to get pure products.

The products of the above reactions were characterized from their analytical and spectral data as given below.

Compound 4a. Colorless crystals (chloroform-petroleum ether), mp 190–192°C. IR (KBr): v (cm⁻¹) 3425 and 3300 (NH₂ str.), 2920, 1640 (C=O), 1600, 1575, 1570, 1515, 1485, 1440,



SCHEME 1: Schmidt reaction of *E*-3-benzylidenechromanones (2) and *E*-3-benzylidenethiochromanones (3).



Scheme 2: Product from Schmidt reaction (NaN₃/TFA) of 2g.



SCHEME 3: Suggested mechanism for formation of 4.

1404, 1360, 1310, 1210, 1105, 1042, 1010, 940, 845, 750, 710, and 700 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): $\delta_{\rm H}$ = 4.40 (2H, br. s, exchangeable with D₂O, NH₂), 4.78 (2H, s, >CH₂), 7.60 (1H, d, *J* = 8.1 Hz. H-8), 7.16 (1H, dt, *J* = 8.1 Hz and 0.9 Hz. H-6),

7.23–7.45 (6H, m, Ar-H), 8.16 (1H, dd, J = 8.1 and 1.5 Hz, H-5). Anal. Calcd. for $C_{16}H_{13}NO_2$: C, 76.48; H, 5.21; N, 5.57%. Found: C, 76.57; H, 5.15; N, 5.60%.

Compound **4b.** Pale yellow crystals (chloroform-petroleum ether), mp 202-203°C. IR (KBr): ν (cm⁻¹) 3435 and 3305 (NH₂ str.), 3120, 2910, 1635 (C=O), 1575, 1572, 1490, 1442, 1414, 1360, 1215, 1110, 1052, 1015, 945, 940, 850, 745, and 710, 662 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): $\delta_{\rm H} = 4.46$ (2H, br, s, exchangeable with D₂O, NH₂), 4.76 (2H, s, >CH₂), 7.06 (1H, dd, J = 8.1 Hz and 0.9 Hz, H-6), 7.14–7.21 (3H, m, H-8, H-2' and H-6'), 7.38–7.44 (3H, m, H-7, H-3' and H-5'), 8.15 (1H, dd, J = 7.8 and 1.5 Hz, H-5). Anal. Calcd. for C₁₆H₁₂ClNO₂: C, 67.26; H, 4.23; N, 4.90%. Found: C, 67.32: H, 4.21; N 4.93%.

Compound **4c**. Colorless crystalline solid (chloroformpetroleum ether), mp 102–104°C. IR (KBr): ν (cm⁻¹) 3356 and 3196 (NH₂ str.), 3020, 2810, 1640 (C=O), 1517, 1433, 1361, 1217, 1123, 1015, 1005, 831, 696, 602 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): $\delta_{\rm H} = 2.33$ (3H, s, –CH₃), 4.40 (2H, br, s, exchangeable with D₂O, NH₂), 4.76 (2H, s, >CH₂), 6.95 (1H, d, *J* = 8.1 Hz, H-8), 7.19–7.45 (5H, m, Ar-H). 7.94 (1H, br. s, H-5). ¹³C NMR (75 MHz, CDCl₃): $\delta_{\rm c} = 20.7$ (–CH₃), 72.8, 117.3, 119.45, 127.3, 129.1, 129.4, 130.7, 132.2, 133.1, 133.7, 136.7, 154.2, 156.8, 184.8 (C=O). Anal. Calcd. for C₁₇H₁₅NO₂: C, 76.96; H, 5.70; N, 5.28%. Found: C, 76.98; H, 5.67; N, 5.26%.

Compound **4d**. Colorless crystalline solid (chloroformpetroleum ether), mp 145-146°C. IR (KBr): ν (cm⁻¹) 3376 and 3209 (NH₂ str.), 2358, 1639 (C=O), 1517, 1434, 1359, 1218, 1122, 1055, 1015, 822, 743, 666, 558 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): 2.33 (3H, s, -CH₃), 2.36 (3H, s, -CH₃) 4.32 (2H, br. s, exchangeable with D₂O, NH₂), 4.75 (2H, s, >CH₂), 6.95 (1H, d, *J* = 7.5 Hz, H-8), 7.12–7.26 (5H, m, Ar-H), 7.94 (1H, br. s, H-5). ¹³C NMR (75 MHz, CDCl₃): $\delta c = 20.6$ (-CH₃),



SCHEME 4: Suggested mechanism for formation of 6.



Figure 2

21.2 (-CH₃), 72.7, 117.0, 118.3, 119.4, 126.2, 129.4, 129.7, 129.8, 130.5, 132.1, 133.0, 133.6, 133.6, 135.8, 136.8, 154.3, 156.7, 184.8 (C=O). Anal. Calcd. for $C_{18}H_{17}NO_2$: C, 77.40; H, 6.13; N, 5.01%. Found: C, 77.44; H, 6.05; N, 5.10%, MS FAB, [MH⁺] *m/z*: 280.

Compound **4e**. Colorless crystalline solid (chloroformpetroleum ether), mp 134–136°C. IR (KBr): 3365 and 3201 (NH₂ str.), 2361, 1643 (C=O), 1518, 1435, 1358, 1264, 1216, 1123, 1059, 824, 750, 604 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): $\delta_{\rm H} = 2.34$ (3H, s, -CH₃), 4.30 (2H, br. s, exchangeable with D₂O, NH₂), 4.76 (2H, s, >CH₂), 6.96 (1H, d, J = 8.1 Hz, H-8), 7.20 (3H, br. d, J = 8.4 Hz, H-7, H-3' and 5'), 7.41 (2H, d, J = 8.4 Hz, H-2' and 6'), 7.93 (1H, br. s, H-5). ¹³C NMR spectrum (75 MHz, CDCl₃): $\delta c = 20.1$ (CH₃), 72.2, 115.5, 118.9, 127.6, 128.6, 128.8, 131.5, 131.7, 131.9, 132.7, 133.3, 134.5, 153.7, 156.2, 184.0 (C=O). Anal. Calcd. for C₁₇H₁₄ClNO₂: C, 68.12; H, 4.71; N, 4.67%. Found: C, 68.22; H, 4.70; N, 4.69%.

Compound **4f.** Colorless crystalline solid (chloroformpetroleum ether), mp 160–162°C. IR (KBr): $\nu_{max} = 3367$ and 3206 (NH₂ str.), 1641 (C=O), 1504, 1435, 1358, 1251, 1216, 1116, 1006, 823, 722, 653 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): $\delta_{\rm H} = 2.36$ (3H, s, -CH₃), 4.43 (2H, br. s, exchangeable with D₂O, NH₂), 4.76 (2H, s, >CH₂), 6.92–7.37 (6H, m, Ar-H), 8.12 (1H, br. s, H-5), Anal. Calcd. for C₁₇H₁₄ClNO₂: C, 68.12; H, 4.71; N, 4.67%. Found: C, 68.21; H, 4.65; N, 4.73%.

Compound **5a**. Pale brown crystalline solid (chloroformpetroleum ether), mp 142-143°C. IR (KBr): $\nu_{max} = 1653$ (C=O), 1616 (C=O), 1587, 1560, 1525, 1433, 1357, 1309, 1269, 1255, 1224, 1178, 883, 798, 748, 711, 669 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): $\delta_{\rm H} = 7.45$ (1H, t, J = 7.8 Hz, H-6), 7.56– 7.69 (5H, m, Ar-H), 7.85 (2H, br. d, J = 7.5 Hz, H-2' and H-6'), 8.27 (1H, s, H-2), 8.56 (1H, br. d, J = 8.1 Hz, H-5). Anal. Calcd. for $C_{16}H_{10}O_2S$: Calcd.: C, 72.16; H, 3.78%. Found: C, 72.20; H, 3.86% MS FAB, $[MH^+] m/z$: 267.

Compound **5b.** Brownish crystalline solid (chloroformpetroleum ether), mp 118-119°C, IR (KBr): $\nu_{max} = 1645$ (C=O), 1622 (C=O), 1585, 1568, 1519, 1438, 1339, 1363, 1265, 1087, 999, 887, 810, 795, 752 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): $\delta_{\rm H} = 7.42$ (2H, d, J = 8.4 Hz, H-3' and H-5'), 7.59– 7.70 (3H, m, Ar-H), 7.76 (2H, d, J = 8.7 Hz, H-2' and H-6'), 8.32 (1H, s, H-2), 8.55 (1H, br. d, J = 7.8 Hz, H-5). Anal. Calcd. for C₁₆H₁₁ClO₂S: Calcd.: C, 63.47; H, 3.66%. Found: C, 63.43; H, 3.75%.

Compound 6. Very light yellow crystalline solid (chloroformpetroleum ether), mp 188–190°C. IR (KBr): $v_{max} = 3115$ (N-H), 2931, 1684 (C=O), 1633 (-CONH-), 1550, 1507, 1464, 1327, 1310, 1212, 1174, 1110, 937, 769, 756 cm⁻¹. ¹H NMR (300 MHz, $CDCl_3$): $\delta_H = 2.96-3.02$ (1H, m, H-3), 3.80 and 3.83 (each 3H, s, 2 x OMe), 4.25 (1H, dd, J = 12 Hz and 4.7 Hz, H_a-2), 4.49 (1H, dd, J = 12 Hz and 3.5 Hz, H_b-2), 5.36 (1H, dd, J =7.9 Hz and 6.9 Hz, >CH-NH-Ar), 6.88-6.93 (4H, m, protons ortho to OMe in two $-C_6H_4$ -OMe-*p* moieties), 7.01 (1H, br. d, J = 8.4 Hz, H-8), 7.02 (1H, br. t, J = 8.6 Hz, H-6), 7.10 (1H, br. d, J = 7.2 Hz, N–H), 7.40 (2H, d, J = 8.7 Hz, protons meta to OMe in a >CH-C₆H₄-OMe-p moiety), 7.51 (1H, dt, J = 9and 1.8 Hz, H-7), 7.71 (2H, d, J = 8.7 Hz, protons meta to OMe in a $-CO-C_6H_4$ -OMe-*p* moiety), 7.87 (1H, dd, J = 7.8 and 1.5 Hz, H-5). Anal. Calcd. for C₂₅H₂₃NO₅: C, 71.93; H, 5.55; N, 3.36%. Found: C, 72.19; H, 5.83; N, 3.59%. MS (ES⁺) Calcd. for C₂₅H₂₃NO₅ (M+Na)⁺: Calcd. 440.15; found 439.98.

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