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SHORT COMMUNICATIONS

# Opening of the A Ring in Taraxast-20(30)-en-3-one Oxime in the Beckmann Reaction

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Cytotoxic, antibacterial, and fungicidal activity of aza terpenoids [1–5] stimulated synthesis of nitrogen-containing taraxastanes on the basis of 3β-hydroxy-20(30)-taraxast-20(30)-ene (**I**) which was isolated by us from the Scotch thistle *Onopordum acanthium* L. according to the procedure described in [6]. As key stage we selected Beckmann rearrangement of cyclic ketone oximes to lactams with ring expansion. For this purpose we synthesized 3-oxo derivative **II** by oxidation of alcohol **I** with pyridinium chlorochromate (PCC) in methylene chloride at 25°C (3 h). The formation of taraxast-20(30)-en-3-one (**II**) was confirmed by the presence of a signal at $\delta_C$ 217.0 ppm ($C^3$=O) in the $^{13}C$ NMR spectrum.

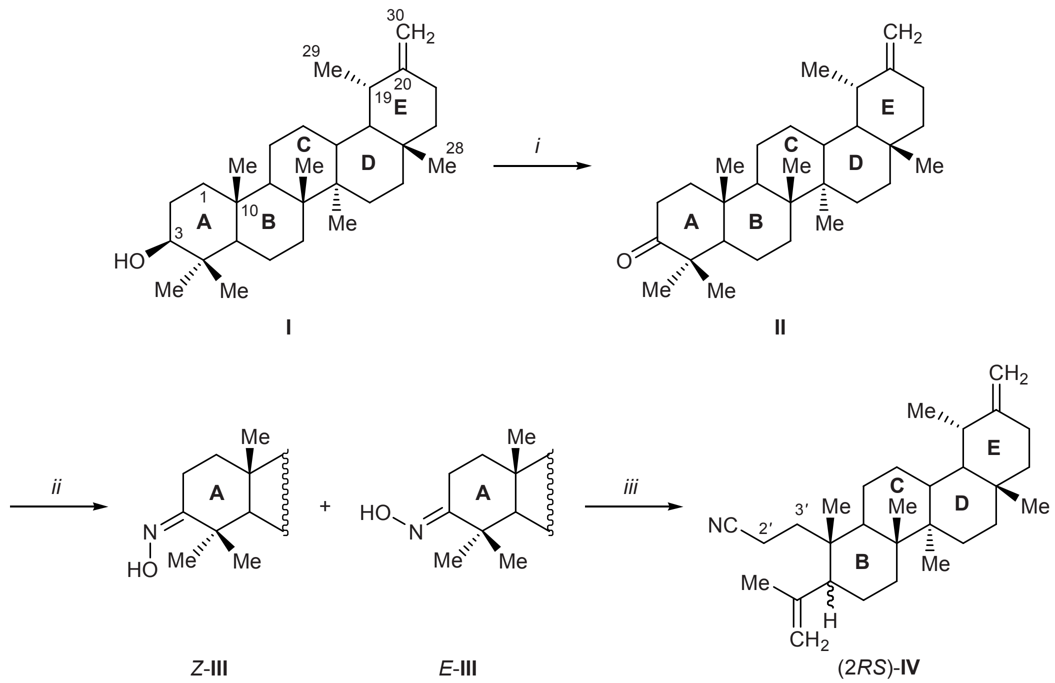
Neither taraxastane oximes nor their derivatives were reported previously. We succeeded in synthesizing taraxast-20(30)-en-3-one oxime (**III**) in the presence of *Tseokar*-100 zeolite. The reaction of taraxast-20(30)-en-3-one (**II**) with hydroxylamine hydrochloride in pyridine gave a mixture of isomeric *E*- and *Z*-oximes **III** at a ratio of 2:1, which was determined from the intensities of the $C^3$ signals ($\delta_C$ 167.0 and 166.9 ppm for the *E* and *Z* isomers, respectively) in the $^{13}C$ NMR spectra recorded with a long pulse delay (10 s) to ensure more complete relaxation [7].

Beckmann rearrangement underlies a convenient method for the preparation of various N-substituted amides, in particular from ketone oximes derived from steroids having a carbonyl group in the **A** ring; for example, some aza steroids were obtained in such a way [8]. Beckmann rearrangement of oximes is commonly catalyzed by $PCl_5$ in diethyl ether, concentrated sulfuric acid, thionyl chloride, *p*-toluenesulfonyl chloride, and polyphosphoric acid. Isomeric taraxastane oximes *E*-**III** and *Z*-**III** failed to undergo Beckmann rearrangement in the presence of *p*-toluenesulfonyl chloride, whereas the reaction in the presence of thionyl chloride in anhydrous dioxane was accompanied by cleavage of the **A** ring with formation of nitrile **IV**. Syntheses of nitriles from oximes containing electron-withdrawing groups (OH, $NH_2$) in the α-position via *trans*-elimination of water (abnormal Beckmann rearrangement) have been reported [9]; nitriles were also formed together with lactams from triterpene **A**-oximes having methyl groups in the α-position [10].

Nitrile **IV** was obtained as a 1:2 mixture of (2*R*)- and (2*S*)-stereoisomers whose ratio was determined from the intentsities of the $C^{13}$ ($\delta_C$ 147.0, 113.9 ppm) and $C^{14}$ signals ($\delta_C$ 146.8 and 114.0 ppm) in the $^{13}C$ NMR spectrum. The spectrum also contained a signal at $\delta_C$ 120.3 ppm, which is typical of cyano group. In the $^1H$ NMR spectrum of **IV** we observed a multiplet at δ 2.1–2.4 ppm due to strongly coupled methylene protons on $C^{2'}$ in both stereoisomers ($2'-H_{ax}/2'-H_{eq}/3'-H_{ax}/3'-H_{eq}$ system).

Thus the transformation of ketone oxime **III** under the Beckmann rearrangement conditions involves transannular elimination of water from spatially close $C^{23}H_3$, $C^{24}H_3$, and (*E*/*Z*)-$C^3$=N–OH groups, leading to opening of the **A** ring and formation of unsaturated bonds (double C=C and triple C≡N).

**Taraxast-20(30)-en-3-one (II).** A solution of 0.25 g (0.6 mmol) of compound **I** in 25 ml of methylene chloride was quickly added under stirring to a suspension of 0.41 g (1.8 mmol) of pyridinium chlorochromate in 25 ml of methylene chloride. The mixture was stirred until the initial compound disappeared (TLC, EtOAc–$C_6H_{14}$, 1:10), diluted with 15 ml of chloro-




*i*: PCC, $CH_2Cl_2$, 3 h; *ii*: $NH_2OH \cdot HCl$, pyridine, 115°C, 2.5 h; *iii*: $SOCl_2$, dioxane, 15 min.

form, and filtered through a layer of silica gel. The solvent was distilled off, and the residue was subjected to chromatography on silica gel using hexane–ethyl acetate (15:1) as eluent. Yield 0.21 g (87%), colorless crystals, mp 128–130°C, $[\alpha]_D^{20}$ = +78.8° (*c* = 1.02, $CHCl_3$), $R_f$ 0.72 ($C_6H_{14}$–EtOAc, 5:1). IR spectrum (KBr), ν, $cm^{-1}$: 2910, 1720, 1715. $^1H$ NMR spectrum, δ, ppm: 1.04 s (6H, 23-H, 24-H), 0.85 s (3H, 25-H), 0.92 s (3H, 26-H), 0.91 s (3H, 27-H), 0.93 s (3H, 28-H), 0.99 d (3H, 29-H), 0.94–2.01 m (20H, $CH_2$), 4.48 s and 4.21 s (2H, 30-H). $^{13}C$ NMR spectrum, $\delta_C$, ppm: 39.56 ($C^1$), 33.93 ($C^2$), 217.04 ($C^3$), 39.01 ($C^4$), 55.06 ($C^5$), 19.01 ($C^6$), 33.79 ($C^7$), 40.85 ($C^8$), 49.65 ($C^9$), 36.83 ($C^{10}$), 20.99 ($C^{11}$), 26.11 ($C^{12}$), 38.78 ($C^{13}$), 42.05 ($C^{14}$), 27.29 ($C^{15}$), 38.11 ($C^{16}$), 34.59 ($C^{17}$), 48.79 ($C^{18}$), 38.63 ($C^{19}$), 154.04 ($C^{20}$), 25.94 ($C^{21}$), 38.61 ($C^{22}$), 25.26 ($C^{23}$), 23.50 ($C^{24}$), 15.52 ($C^{25}$), 15.85 ($C^{26}$), 14.48 ($C^{27}$), 16.53 ($C^{28}$), 26.01 ($C^{29}$), 107.25 ($C^{30}$). Found, %: C 85.28; H 12.15. $C_{30}H_{48}O$. Calculated, %: C 84.84; H 11.39.

**Taraxast-20(30)-en-3-one oxime (III, a 1:2 mixture of *Z* and *E* isomers).** Compound **II**, 0.28 g (0.65 mmol), was dissolved in 40 ml of anhydrous pyridine, 0.323 g (4.68 mmol) of hydroxylamine hydrochloride was added, the mixture was heated to the boiling point, 2 g of calcined *Tseokar*-100 was added, and the mixture was heated for 2.5 h under reflux with stirring until the initial compound disappeared (TLC, EtOAc–$C_6H_{14}$, 1:10). The mixture was cooled, diluted with 100 ml of 5% hydrochloric acid, and extracted with chloroform (3×20 ml). The extract was washed with a solution of sodium hydrogen carbonate and dried over calcium chloride, the solvent was distilled off, and the residue was subjected to chromatography on silica gel using hexane–ethyl acetate (15:1) as eluent. Yield 0.25 g (89%), $R_f$ 0.41 ($C_6H_{14}$–EtOAc, 5:1). IR spectrum (KBr), ν, $cm^{-1}$: 3300–3150, 1670, 1470, 1380. $^1H$ NMR spectrum, δ, ppm: 1.15 s (6H, 23-H, 24-H), 0.804 s (3H, 25-H), 0.90 s (3H, 28-H), 0.926 s (3H, 27-H), 0.94 s (3H, 28-H), 0.98 d (3H, 29-H), 0.96–1.96 m (20H, $CH_2$), 4.63 s and 4.49 s (2H, 30-H), 9.13 m (1H, NOH). $^{13}C$ NMR spectrum, $\delta_C$, ppm: 27.32 ($C^1$, *E*), 26.91 ($C^1$, *Z*), 22.88 ($C^2$, *E*), 23.29 ($C^2$, *Z*), 166.89 ($C^3$, *E*), 167.00 ($C^3$, *Z*), 40.34 ($C^4$, *E*), 39.65 ($C^4$, *Z*), 55.57 ($C^5$, *E*), 55.79 ($C^5$, *Z*), 19.49 ($C^6$, *E*), 21.37 ($C^6$, *Z*), 33.76 ($C^7$), 41.78 ($C^8$), 50.08 ($C^9$), 40.92 ($C^{10}$), 21.60 ($C^{11}$), 25.87 ($C^{12}$), 39.34 ($C^{13}$), 42.16 ($C^{14}$, *E*), 42.05 ($C^{14}$, *Z*), 27.32 ($C^{15}$), 37.17 ($C^{16}$), 34.51 ($C^{17}$), 46.75 ($C^{18}$), 36.99 ($C^{19}$), 154.52 ($C^{20}$), 25.47 ($C^{21}$), 39.21 ($C^{22}$), 25.61 ($C^{23}$, *E*), 25.52 ($C^{23}$, *Z*), 21.74 ($C^{24}$, *E*), 22.68 ($C^{24}$, *Z*), 17.17 ($C^{25}$), 15.94 ($C^{26}$), 14.64 ($C^{27}$), 19.49 ($C^{28}$), 25.87 ($C^{29}$), 107.16 ($C^{30}$). Found, %: C 82.11; H 11.35; N 3.90. $C_{30}H_{49}NO$. Calculated, %: C 81.94; H 11.23; N 3.19.

**3-[(2*R*,*S*)-2-Isopropenyl-1,4a,4b,6a,10-pentamethyl-9-methylideneperhydrochrysen-1-yl]propanenitrile (IV, *R*:*S* = 2:1).** Isomeric oximes **III**, 0.2 g (0.44 mmol), were dissolved in 30 ml of anhydrous dioxane, 0.6 ml of freshly distilled thionyl chloride was added, and the mixture was stirred for 15 min at room temperature until the initial compound disappeared (TLC, EtOAc–$C_6H_{14}$, 1:10). The solvent was distilled off, the residue was treated with 10 ml of water and extracted with chloroform (3×20 ml), the extracts were combined, washed with water until neutral reaction, and dried over calcium chloride, the solvent was removed, and the residue was subjected to chromatography on silica gel using hexane–ethyl acetate (15:1) as eluent. Yield 0.168 g (84%), $R_f$ 0.66 ($C_6H_{14}$–EtOAc, 5:1). IR spectrum (KBr), ν, $cm^{-1}$: 2235, 1470, 1380. $^1H$ NMR spectrum, δ, ppm: 1.01 s (3H, 16-H), 1.03 s (3H, 17-H), 0.93 s (3H, 18-H), 0.95 s (3H, 19-H), 0.99 d (3H, 20-H), 0.92–2.05 m (16H, $CH_2$), 4.23 s and 4.77 s (2H, 21-H, *R*), 4.23 s and 4.87 s (2H, 21-H, *S*), 2.14–2.41 m (2H, 2-H), 4.65 s (2H, 14-H). $^{13}C$ NMR spectrum, $\delta_C$, ppm: 34.74 and 32.48 ($C^{3'}$), 14.06 and 14.76 ($C^{2'}$), 120.31 and 121.20 ($C^{1'}$), 146.87 and 147.01 ($C^{13}$), 39.36 and 38.78 ($C^2$), 21.54 and 23.80 ($C^3$), 33.27 ($C^4$), 40.46 ($C^{4a}$), 50.83 ($C^{12a}$), 46.75 ($C^1$), 21.54 ($C^{12}$), 26.91 ($C^{11}$), 39.59 ($C^{10b}$), 42.14 ($C^{4b}$), 27.97 ($C^5$), 37.10 ($C^6$), 34.51 ($C^{6a}$), 46.67 ($C^{10a}$), 40.81 ($C^{10}$), 154.51 ($C^9$), 25.63 ($C^8$), 36.19 ($C^7$), 22.66 and 22.75 ($C^{15}$), 114.07 and 113.94 ($C^{14}$), 17.70 ($C^{16}$), 16.16 ($C^{17}$), 14.61 ($C^{18}$), 19.89 ($C^{19}$), 24.27 ($C^{20}$), 107.40 ($C^{21}$). Found, %: C 85.67; H 11.31; N 3.02. $C_{30}H_{47}N$. Calculated, %: C 85.44; H 11.23; N 3.32.

The IR spectra were recorded on Specord 75IR spectrometer from samples dispersed in mineral oil. The $^1H$ and $^{13}C$ NMR spectra were measured on Jeol FX 90Q (89.55 and 22.50 MHz, respectively) and Bruker AMX-300 spectrometers (300.13 and 75.62 MHz, respectively) using $CDCl_3$ as solvent; the chemical shifts were determined relative to tetramethylsilane as internal reference. The optical rotation was measured on a Perkin–Elmer-141 polarimeter. The melting points were determined on a Boetius melting point apparatus. The progress of reactions was monitored by TLC on Silufol plates; spots were visualized by treatment with a solution of 4-methoxybenzaldehyde in ethanol. Column chromatography was performed on KSKG silica gel. Pyridinium chlorochromate was prepared according to the procedure described in [11].

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