(indicator, Phenolphthalein). Eqiv. Weight Calcd. : (2 COOH) 309, 308. Found : 313. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 1753 (ester), 1701 (=CO of -COOH).

Isolation and Determination of Sapogenin from (II)——Crude saponin was obtained from 700 g. of (II), from which above-mentioned sapogenin and its diacetate were prepared by the same way as in the case of (III). This sapogenin was identified with (V).

The authors are indebted to Prof. S. Shibata of this Faculty for his valuable suggestions. Their thanks are also due to Mr. Tomiyama, a cultivator in Nagano Prefecture, and to Tsumura Laboratory for supplying the material and to the members of Analysis Room of the Institute of Applied Microbiology of this University for elemental analyses, and of Infrared Analysis Room of this Faculty for spectral measurements.

Summary

Comparative studies were made on the chemical nature of the sapogenins obtained by hydrolysis of two kinds of the saponins isolated from the roots of *Polygala senega* var. *latifolia* et *P. tenuifolia*. As the results, it was confirmed that the sapogenin of the former is completely identical with that of the latter and it is possible consider that both the compounds are the same as one of those obtained by Tschesche and Gupta from a Polygalaceous plant, *Bredemeyera floribunda*.

(Received February 1, 1961)

UDC 547.852.7

Raymond N. Castle[*1] **and Masayuki Onda**[*2] : Cinnoline Chemistry. VIII. α-(ω-Dialkylaminoalkyl)-α-phenyl-4-cinnolineacetonitriles and Related Compounds.[1,2]

(*Department of Chemistry of the University of New Mexico*[*1])

The purpose of the present investigation was the synthesis of a variety of α-(ω-dialkylaminoalkyl)-α-phenyl-4-cinnolineacetonitriles and 4-[(1-phenyl-ω-dialkylamino)-alkyl]cinnotines for pharmacological screening.

The methods of Cutler, Surrey and Cloke[3] were used in the present work with some modification. Phenylacetonitrile (I) was alkylated with the ω-dialkylaminoalkyl halide (II) in dry benzene solution using sodium amide as the base to form the reactive carbanion. All of the (ω-dialkylaminoalkyl)phenylacetonitriles (III) that have not previously been reported in the literature are recorded in Table I. These were identified and analyzed as the picrates.

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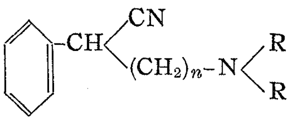
1) For paper VII in this series see R. N. Castle and M. Onda : J. Org. Chem, in press.

2) The authors are grateful to Dr. S. Yamada and Dr. K. Abe of Tanabe Seiyaku Company, Ltd., Tokyo, for the carbon, hydrogen and nitrogen analyses.

3) R. A. Cutler, A. R. Surrey, J. B. Cloke : J. Am. Chem. Soc., **71**, 3375 (1949).

The α-(ω-dialkylaminoalkyl)-α-phenyl-4-cinnolineacetonitriles (V) were prepared by allowing 4-chlorocinnoline[4] (IV) to react with (III) in dry benzene solution using sodium amide to promote the reaction. The compounds of type (V) and their properties are listed in Table II.

Table I.



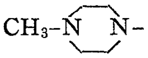
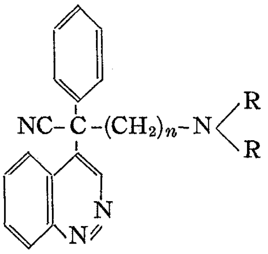
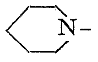
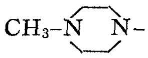
n	R>N- (R, R)	b.p. (°C)	mm.	Yield (%)	m.p. of Picrate (°C)	Formula	Analyses (%) Calcd.			Analyses (%) Found			Description of Picrate and Solvent Used for Cyrstallization
							C	H	N	C	H	N	
2		145~148	0.15	79	161~163	$C_{21}H_{23}O_7N_5$	55.13	5.07	15.31	54.96	5.31	15.35	Yellow needles (EtOH)
2		164~166	0.75	80	163~165	$C_{20}H_{21}O_8N_5$	52.28	4.61	15.24	51.91	5.25	15.19	Yellow plates (EtOH)
3	$\begin{matrix}CH_3\\CH_3\end{matrix}>N-$	152~127	0.05	62	109~110	$C_{19}H_{21}O_7N_5$	52.87	4.91	16.24	52.98	5.18	16.50	Yellow prisms (EtOH)
3	$\begin{matrix}C_2H_5\\C_2H_5\end{matrix}>N-$	151~154	0.2	70	105~107	$C_{21}H_{25}O_7N_5$	54.90	5.48		55.01	5.27		Yellow plates (EtOH)
3		160~162	0.2	63	224~226 (dec.)	$C_{28}H_{29}O_{14}N_9$	46.99	4.08	17.62	46.94	4.32	17.77	Yellow needles (Me_2CO)

Table II.



n	R>N- (R, R)	b.p. (°C)	mm.	Yield (%)	Solvent	Formula	Analyses (%) Calcd.		Analyses (%) Found		Description
							C	H	C	H	
2	$\begin{matrix}CH_3\\CH_3\end{matrix}>N-$	198~201	0.015	87	Benzene	$C_{20}H_{20}N_4$	75.91	6.37	75.82	6.49	Red syrup
2	$\begin{matrix}C_2H_5\\C_2H_5\end{matrix}>N-$	200~204	0.005	87	〃	$C_{26}H_{30}O_4N_4$ (acidic succinate)	67.51	6.53	67.78	6.46	Red syrup (free base) Acidic succinate : m.p. 147~148° Yellow granules from *n*-propanol
2		m.p. 171~172°		79	Toluene	$C_{23}H_{24}N_4$	77.49	6.78	77.55	6.66	Yellow granules (EtOH)
2		235~238	0.02	74	〃	$C_{22}H_{22}ON_4$	73.71	6.20	73.80	6.21	Red syrup
3	$\begin{matrix}CH_3\\CH_3\end{matrix}>N-$	216~220	0.025	73	〃	$C_{21}H_{22}N_4$	76.33	6.71	76.49	6.90	〃
3	$\begin{matrix}C_2H_5\\C_2H_5\end{matrix}>N-$	216~219	0.025	85	〃	$C_{23}H_{26}N_4$	77.05	7.31	77.26	7.42	〃
3		248~252	0.025	70	〃	$C_{24}H_{27}N_5$	74.77	7.06	74.66	7.13	〃

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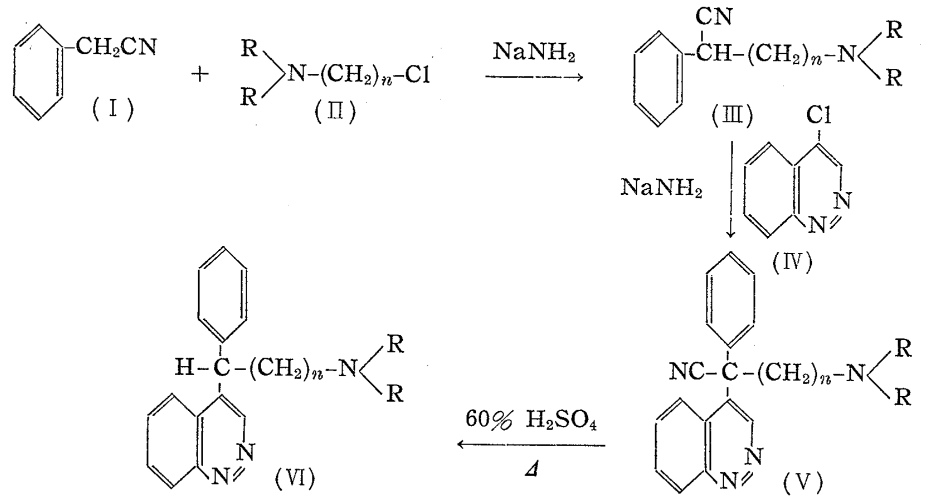
4) R.N. Castle, M. Onda : J. Org. Chem., **26**, 2374 (1961).

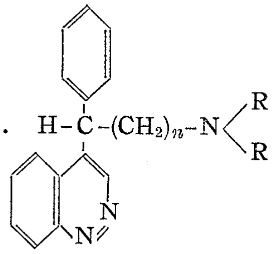


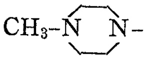
The 4-[(1-phenyl-ω-dialkylamino)alkyl]cinnolines (VI) were prepared by hydrolysis and decarboxylation of the nitriles of type (V) in sulfuric acid solution. The compounds of type (VI) and their properties are listed in Table III.

The type (V) nitriles all had a weak but definite absorption peak in the 4.5 μ region of the infrared spectrum. The infrared spectra of the type (VI) compounds revealed the absence of an absorption peak in the 4.5 μ region. The cinnoline ring absorption peak in the 6.3~6.4 μ region was present in all the compounds listed in Tables II and III.

Compound (V), ($R=C_2H_5$: $n=2$) was tested as an inhibitor of cholesterol biosynthesis and found to be inactive. Screening data on the other compounds are not available.

TABLE III.



n	R>N- (R, R)	b.p. (°C)	mm.	Yield (%)	Formula	Analyses (%) Calcd. C	Calcd. H	Found C	Found H	Description
2	CH_3>N- CH_3	176~179	0.015	92	$C_{19}H_{21}N_3$	78.31	7.26	78.44	7.01	Red syrup
2	C_2H_5>N- C_2H_5	178~181	0.015	70	$C_{21}H_{25}N_3$	78.95	7.89	79.21	7.87	Orange syrup
2		210~212	0.02	80	$C_{22}H_{25}N_3$	79.75	7.54	80.18	6.82	Red syrup
2		222~226	0.015	67	$C_{21}H_{23}O_3N$	75.64	6.95	76.08	7.10	〃
3	CH_3>N- CH_3	190~194	0.02	85	$C_{20}H_{23}N_3$	78.65	7.59	78.29	7.38	〃
3	C_2H_5>N- C_2H_5	200~204	0.025	89	$C_{22}H_{27}N_3$	79.23	8.16	79.06	8.07	〃
3		216~220	0.015	50	$C_{23}H_{28}N_4$	76.62	7.82	76.94	7.92	〃

Experimental[*3]

Preparation of the (ω-Dialkylaminoalkyl)phenylacetonitriles——This procedure is illustrated with the preparation of 2-phenyl-4-piperidinobutyronitrile. To a solution of 14.5 g. of phenylacetonitrile in 40 ml. of dry benzene was added 5.0 g. of $NaNH_2$ and the suspension stirred in an ice bath for 15 min. A solution of 19.9 g. of 1-(2-chloroethyl)piperidine in 20 ml. of dry benzene was added to the nitrile suspension over a period of 10 min. with stirring and cooling. This was followed by refluxing and stirring for 1 hr. After the reaction mixture was cooled, diluted with Et_2O, washed with water and dried, there was obtained 22.4 g. (79%) of a colorless liquid boiling at 145~148° at 0.15 mm. Hg. This compound gave a picrate, yellow needles, m.p. 161~163°, after recrystallization from EtOH. This compound is listed in Table I.

The Preparation of α-(ω-Dialkylaminoalkyl)-α-phenyl-4-cinnolineacetonitriles——This procedure is illustrated with the preparation of α-(2-dimethylaminoethyl)-α-phenyl-4-cinnolineacetonitrile.

To a stirred solution of 5.8 g. of 2-phenyl-4-dimethylaminobutyronitrile in 58 ml. of dry benzene was added 1.4 g. of $NaNH_2$ and the suspension refluxed for 1.5 hr. A solution of 4.6 g. of 4-chlorocinnoline[4)] in 20 ml. of dry benzene was added over a period of 10 min. with cooling, and then the mixture was refluxed for 3 hr. The reaction mixture was diluted with Et_2O, washed with water and dried. There was obtained 7.8 g. (87%) of a red syrup, b.p. 198~201°, at 0.015 mm. Hg. This compound is listed in Table II.

Preparation of the 4-[(1-Phenyl-ω-dialkylamino)alkyl]cinnoline——A solution of 1.0 g. of α-(2-dimethylaminoethyl)-α-phenyl-4-cinnolineacetonitrile in 1.5 ml. of conc. H_2SO_4 and 1.5 ml. of water was refluxed for 16 hr. The acid reaction mixture was poured into ice-NaOH solution and extracted with Et_2O. The ether extract was washed with water and dried. There was obtained 0.83 g. (92%) of a red syrup boiling at 176~179° at 0.015 mm. Hg. This compound is listed in Table III.

The authors are grateful to Smith, Kline and French Laboratories for a research grant which made this work possible and to Dr. James W. Wilson for his interest in this work.

Summary

Five new (ω-dialkylaminoalkyl)phenylacetonitriles were prepared and these and other similar nitriles were condensed with 4-chlorocinnoline in the presence of sodium amide to produce seven new α-(ω-dialkylaminoalkyl)-α-phenyl-4-cinnolineacetonitriles. All of these condensed nitriles were hydrolyzed and decarboxylated to seven new 4-[(1-phenyl-ω-dialkylamino)alkyl]cinnolines. These latter two classess of compounds were prepared for pharmacological screening.

(Received September 25, 1961)

[*3] All melting points are uncorrected. The infrared spectra were determined on a Perkin-Elmer Infracord.