Some β,β-Dialkyl–Substituted Aliphatic Acids and Their Derivatives

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DURING the course of other work, some unreported β,β-dialkyl–substituted acids and their derivatives (Table I, II, and III) were prepared.

The acids were obtained in high yields by the hydrolysis of the corresponding β,β,β-trialkylpropionitriles (*3*) with sulfuric acid in a manner similar to that of Sarel and Newman (*4*). Attempts to hydrolyze 3-ethyl-3-heptylundecanenitrile with potassium hydroxide in methyl, ethyl, and butyl Cellosolves gave only small amounts of the corresponding amide. However, it was possible to realize a 46% conversion of the nitrile to the amide by potassium hydroxide in butyl carbitol. Attempted hydrolysis of the nitrile in 100% phosphoric acid (*1*) failed.

Although trialkylacetic acids containing up to ten carbon atoms have been resolved (*2*), attempts to prepare alkaloid salts of 3-ethyl-3-heptylundecanoic acid with brucine, strychnine, and quinine afforded negative results. A salt of this acid was obtained with *d*-α-phenethylamine, but no solvent was found from which it could be recrystallized. The addition of water to an alcohol solution of the salt led to the regeneration of the starting components.

The substituted amides recorded in Table III were prepared by treating the crude acid chlorides, obtained from the corresponding substituted acids and thionyl chloride with an excess of amine. The esters in Table III resulted from the reactions of the crude acid chlorides with the appropriate alcohols in the presence of pyridine.

All melting points reported are uncorrected.

EXPERIMENTAL

3-Ethyl-3-heptylundecanamide. A modification of the method of Sarel and Newman (*4*) was employed. A mixture of 45.2 g. (0.14 mole) of 3-ethyl-3-heptylundecanenitrile (*3*) and 113 ml. of 96% sulfuric acid was heated for 4 hours at 80-90° and for 2 hours at 95-100°. It was allowed to cool and was poured onto 500 g. of crushed ice. The oil layer was taken up in ether, and the solution was washed with two portions of 5% sodium hydroxide solution and water, and dried over anhydrous magnesium sulfate. After removing the ether, the residue was distilled to give 29.8 g. (66%) of amide; b.p. 200–204°/1 mm., m.p. −1° to +1°; n_D^{25} 1.4672. Analysis, calculated for $C_{20}H_{41}NO$: C, 77.10; H, 13.27. Found: C, 76.71; H, 13.31.

3-Ethyl-3-heptylundecanoic Acid. A mixture of 42 grams (0.134 mole) of 3-ethyl-3-heptylundecanamide and 200 g. of 75% sulfuric acid was heated and stirred at 80–85° while 37.5 grams (0.54 mole) of sodium nitrite was added during 1 hour. The reaction mixture was cooled, diluted with 150 ml. of water and the oil layer was taken up in ether. The water layer was extracted with several portions of ether and the combined ether solutions were washed with water and dried over anhydrous magnesium sulfate. The ether was removed and the residue was distilled to afford 33.4 grams (74%) of acid; b.p. 181–187°/1 mm., n_D^{25} 1.4561. Analysis, calculated for $C_{20}H_{40}O_2$: C, 76.86; H, 12.90; Neut. Equiv. 312. Found: C, 76.86; H, 13.15; Neut. Equiv. 317.

Attempted Preparation of Salts of Alkaloids and 3-Ethyl-3-heptylundecanoic Acid. A solution of 10 grams (0.03 mole) of 3-ethyl-3-heptylundecanoic acid, 12.6 grams (0.03 mole) of brucine and 200 ml. of absolute alcohol was refluxed for 2 hours and allowed to stand in a refrigerator for 50 hours. No precipitate resulted, and removal of the alcohol and addition of ether to the residue gave brucine. A number of other concentrations of acid and brucine in alcohol, acetone and ethyl acetate were tried, but salt formation

Table I. Substituted Nitriles

							Analysis			
							Calcd.		Found	
R_1	*R_2*	R_3	B.P./Mm.	n_D^{25}	Yield	Formula	C	H	C	H
Carbethoxyalkylidenenitriles, $R_1R_2C=C(CO_2C_2H_5)CN$										
CH_3	C_7H_{15}		148–151°/1	1.4643	77	$C_{14}H_{23}NO_2$	70.85	9.77	71.00	9.89
C_3H_7	C_5H_{11}		135–137.5°/1	1.4670	90	$C_{14}H_{23}NO_2$	70.85	9.77	71.11	9.88
C_4H_9	C_4H_5•		170.5–171.8°/16	1.4660	72	$C_{14}H_{23}NO_2$	70.85	9.77	70.75	10.16
2-Carbethoxy-3,3-dialkylnitriles, $R_1R_2R_3CCH(CO_2C_2H_5)CN$										
C_2H_5	C_2H_5	C_2H_5	143–146°/15	1.4493	86	$C_{12}H_{21}NO_2$	68.21	10.02	68.13	9.95
CH_3	C_2H_5	C_7H_{15}	149–152°/0.5	1.4471	72	$C_{16}H_{29}NO_2$	71.86	10.93	71.73	10.81
C_3H_7	C_3H_7	C_4H_9	133–135.5°/1	1.4498	69	$C_{16}H_{29}NO_2$	71.86	10.93	71.57	10.94
C_3H_7	C_4H_9	C_5H_{11}	130–131°/0.25	1.4507	73	$C_{18}H_{33}NO_2$	73.17	11.26	73.33	11.14
C_4H_9	C_4H_9	C_4H_9	150–151°/1	1.4524	79	$C_{18}H_{33}NO_2$	73.17	11.26	73.18	11.24
C_3H_7	C_4H_9	C_6H_{13}	161–164°/1	1.4523	57	$C_{19}H_{35}NO_2$	73.73	11.40	74.09	11.20
3,3-Dialkylnitriles, $R_1R_2R_3CCH_2CN$										
C_2H_5	C_2H_5	C_2H_5	92–94°/15	1.4353	53	$C_9H_{17}N$	77.63	12.31	77.83	12.04
CH_3	C_2H_5	C_7H_{15}	115–116°/0.5	1.4398	77	$C_{13}H_{25}N$	79.93	12.90	79.90	12.69
C_2H_5	C_4H_9	C_4H_9	137–140°/1.5	1.4452	78	$C_{15}H_{29}N$	80.64	13.09	80.94	13.13
C_3H_7	C_4H_9	C_5H_{11}	122–124°/0.5	1.4452	84	$C_{15}H_{29}N$	80.64	13.09	80.70	12.95
C_3H_7	C_4H_9	C_6H_{13}	127–130°/1	1.4470	84	$C_{16}H_{31}N$	80.94	13.16	81.24	12.89

Table II. 3,3-Dialkyl Substituted Acids, $R_1R_2R_3CCH_2CO_2H$

								Analysis					
								Calcd.			Found		
R_1	R_2	R_3	B.P./Mm.	M.P.	n_D^{25}	Yield	Formula	C	H	N.E.	C	H	N.E.
C_2H_5	C_2H_5	C_2H_5	134.5-137°/18	41-42°[a]	...	71	$C_9H_{18}O_2$[b]	68.31	11.47	158.2	68.03	11.23	158.6
C_3H_7	C_3H_7	C_4H_9	147-148°/1	...	1.4488	87	$C_{13}H_{26}O_2$[c]	72.84	12.23	214.3	72.96	12.10	216.0
C_3H_7	C_4H_9	C_5H_{11}	155-157.5°/1	...	1.4502	94	$C_{15}H_{30}O_2$[d]	74.32	12.48	242.4	74.45	12.54	246.4
C_4H_9	C_4H_9	C_4H_9	150-153°/1	35-36°[a]	1.4511	98	$C_{15}H_{30}O_2$[e]	74.32	12.48	242.4	74.18	12.24	246.1

[a] Recrystallized from acetonitrile. [b] Obtained by heating 3,3-diethylvaleronitrile at 150° with potassium hydroxide and ethylene glycol for 30 hours. [c] Nitrile (1 mole) heated with 96% H_2SO_4 (16 moles) at 80-90° for 8 hours followed by treatment with sodium nitrite (4 moles) at 80-90°. [d] Nitrile (1 mole) heated with 75% H_2SO_4 (7 moles) at 80-90° for 8 hours, then 120-125° for 3 hours; followed by sodium nitrite (6 moles) at 80-90°. [e] Nitrile (1 mole) heated with 96% H_2SO_4 (12 moles) at 80-90° for 8 hours, and the amide was isolated but not purified. The crude amide was suspended in 12 moles of 75% H_2SO_4 and treated with sodium nitrite (4 moles) at 80-90°.

Table III. Derivatives of 3,3-Dialkyl Substituted Acids

Amides, $R_1R_2R_3CCH_2CONHR_4$

								Analysis			
								Calcd.		Found	
R_1	R_2	R_3	R_4	B.P./Mm.	M.P.	n_D^{25}	Formula	C	H	C	H
C_4H_9	H	H	C_4H_9	149-151°/1	22-23°	1.4483	$C_{12}H_{25}NO$	72.30	12.64	72.25	12.72
C_7H_{15}	CH_3	C_2H_5	H	164-167°/1	...	1.4644	$C_{13}H_{27}NO$	73.18	12.76	72.92	12.95
C_5H_{11}	C_4H_9	C_3H_7	H	...	65.5-66°[a]	...	$C_{15}H_{31}NO$	74.63	12.94	74.92	12.95
C_4H_9	C_4H_9	C_4H_9	H	...	112.5-112.9°[b]	...	$C_{15}H_{31}NO$	74.63	12.94	74.86	13.04
C_4H_9	C_3H_7	C_3H_7	i-C_4H_9	...	43-43.5°[c]	...	$C_{17}H_{35}NO$	75.77	13.09	76.06	13.08
C_4H_9	C_3H_7	C_3H_7	s-C_4H_9	...	58-59°[c]	...	$C_{17}H_{35}NO$	75.77	13.09	75.82	13.33
C_4H_9	C_3H_7	C_3H_7	t-C_4H_9	...	86.5-87.0°[c]	...	$C_{17}H_{35}NO$	75.77	13.09	75.93	12.99
C_5H_{11}	C_4H_9	C_3H_7	C_4H_9	160-161°/1	...	1.4630	$C_{19}H_{39}NO$	76.70	13.21	76.55	12.88
Esters, $R_1R_2R_3CCH_2CO_2R_4$											
C_5H_{11}	C_4H_9	C_3H_7	CH_3	100-100.3°/1	...	1.4402	$C_{16}H_{32}O_2$	74.94	12.58	74.90	12.30
C_2H_5	C_2H_5	C_2H_5	CH_3	85-86°/20	...	1.4300	$C_{10}H_{20}O_2$	69.72	11.70	69.75	11.63
C_2H_5	C_2H_5	C_2H_5	$(CH_3)_3CCH_2$	125.9-126.4°/18	...	1.4331	$C_{14}H_{28}O_2$	73.63	12.36	73.65	12.13

[a] Recrystallized from aqueous ethanol. [b] Recrystallized from 95% ethanol. [c] Recrystallized from ethyl acetate.

did not take place. Negative results were obtained also with the acid and strychnine in chloroform and quinine in alcohol.

A solution of 3 grams (0.01 mole) of 3-ethyl-3-heptylundecanoic acid and 1.2 grams (0.01 mole) of d-α-phenethylamine in 10 ml. of anhydrous ether was allowed to stand at room temperature for 24 hours. Upon removal of the ether, a white salt was obtained; m.p. 49-50°. It was soluble in all of the common solvents. It dissolved slowly in nitromethane and acetonitrile, but was insoluble in water and ethyl cyanoacetate. When water was added to an alcoholic solution of the salt, an oil formed which could not be induced to crystallize.

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