TABLE I[a]

ARYLSULFONYL-1-METHYL-S-ISOTHIOSEMICARBAZIDES

$XSONHNHC(=NH)SCH_3$

I

X	Mp, °C	Yield, %	Formula	Calcd, % C	Calcd, % H	Found, % C	Found, % H
C_6H_5	124–125 dec	95	$C_8H_{11}N_3O_2S_2$	39.18	4.49	39.49	4.63
p-$CH_3OC_6H_4$	141–142 dec	91	$C_9H_{13}N_3O_3S_2$	39.31	4.72	39.36	4.70
p-$C_2H_5OC_6H_4$	157–158 dec	99	$C_{10}H_{15}N_3O_3S_2$	41.52	5.19	41.48	5.40
p-n-$C_3H_7OC_6H_4$	151–152 dec	93	$C_{11}H_{17}N_3O_3S_2$	43.59	5.61	43.50	5.32
p-n-$C_4H_9OC_6H_4$	132–133 dec	70	$C_{12}H_{19}N_3O_3S_2$	45.42	5.99	45.72	6.01
$C_6H_5CH_2$	142	62	$C_9H_{13}N_3O_2S_2$	41.69	5.01	41.79	4.8

[a] Melting points were taken in open capillary tubes. The yields reported are those after one recrystallization. Elemental analyses were made by Dr. J. Calderón, of Instituto "Alonso Barba" of Madrid, Spain.

mental conditions of Lora-Tamayo, *et al.*, were also tried, those of Hoggarth gave much better results. The formulas and experimental data for the compounds prepared are presented in Table I.

Experimental Section

The arysulfonylthiosemicarbazide (5 mmoles) was suspended in 5 ml of 1 *N* NaOH. Several minutes of vigorous stirring produced a clear yellow solution. To this was added 0.78 g (5.6 mmoles) of methyl iodide in 1 ml of 95% ethanol. Precipitation of the white, crystalline product was complete in 15–20 min. Samples for analysis were recrystallized from ethanol–water.

A New Naphthylacetamide Derivative

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Received October 5, 1965

Our interest in antiinflammatory drugs derived from naphthalene, of which thus far α-isopropyl-α-(2-dimethylaminoethyl)-1-naphthylacetamide (**I**)[1] has been the best representative, has led us to synthesize the 4-isobutyl derivative in analogy with 4-isobutylphenylacetic acid (ibufenac), a product known to exert a marked analgesic and antiinflammatory action.[2] The new compound, α-isopropyl-α-(2-dimethylaminoethyl)-4-isobutyl-1-naphthylacetamide, possesses an analgesic action distinctly superior to that of I.

Experimental Section[3]

The 1-isobutylnaphthalene required was obtained by a new general method for preparing 1-alkylnaphthalenes, which will be described in a later paper.

1-Chloromethyl-4-isobutylnaphthalene.—A mixture of trioxymethylene (8.5 g, 0.283 mole), glacial acetic acid (110 g), and anhydrous HCl (11.7 g, 0.321 mole) was gently heated until the trioxymethylene dissolved, and then 1-isobutylnaphthalene (40 g, 0.217 mole) was added and the flask carefully was closed and heated for 20 hr at 65–70°. After cooling, the mixture was poured into water, the separated oil was extracted with benzene, and the resulting solution was washed with water and Na_2CO_3 and then dried (Na_2SO_4). The benzene was removed *in vacuo* and the product was distilled, bp 135–137° (0.3 mm), giving a colorless oil (35.2 g, 69.8% yield).

Anal. Calcd for $C_{15}H_{17}Cl$: C, 77.40; H, 7.36; Cl, 15.23. Found: C, 77.24; H, 7.28; Cl, 14.95.

4-Isobutyl-1-naphthylacetonitrile.—A mixture of 1-chloromethyl-4-isobutylnaphthalene (46.5 g, 0.2 mole), KCN (17.8 g, 0.274 mole), ethanol (77 ml), and water (30 ml) was refluxed for 1 hr. The alcohol was distilled, the residue was extracted with ether, and the solution was washed with water and then dried (Na_2SO_4). After distilling the solvent, the residue was purified by distilling at 145–147° (0.4 mm), and the oily product then was treated with petroleum ether (bp 40–70°) to give colorless crystals (18.3 g, 41% yield). On recrystallization from petroleum ether, the compound melted at 78–79° (cor).

Anal. Calcd for $C_{16}H_{17}N$: C, 86.05; H, 7.67; N, 6.27. Found: C, 85.48; H, 7.73; N, 6.18.

α-(2-Dimethylaminoethyl)-4-isobutyl-1-naphthylacetonitrile.—This procedure follows the method previously described.[4] 4-Isobutyl-1-naphthylacetonitrile (26.8 g, 0.12 mole) was alkylated with 2-(*N*,*N*-dimethylamino)-1-chloroethane (13.55 g, 0.126 mole), refluxing for 5 hr in benzene (400 ml) in the presence of sodamide (4.9 g, 0.126 mole). The product obtained was distilled at 170–173° (0.4 mm) to give a colorless oil (22.9 g, 65% yield).

Anal. Calcd for $C_{20}H_{26}N_2$: C, 81.58; H, 8.90; N, 9.52. Found: C, 81.04; H, 9.01; N, 9.30.

α-Isopropyl-α-(2-dimethylaminoethyl)-4-isobutyl-1-naphthylacetonitrile.—Alkylation of the above nitrile (22.9 g, 0.078 mole) with 2-bromopropane (12.4 g, 0.101 mole) was performed by refluxing for 18 hr in benzene (500 ml) and in the presence of sodamide (3.94 g, 0.101 mole). The distilled product, bp 174–176° (0.6 mm), was a colorless oil (17.6 g, 67.1% yield).

Anal. Calcd for $C_{23}H_{32}N_2$: C, 82.09; H, 9.59; N, 8.33. Found: C, 81.16; H, 9.40; N, 8.17.

α-Isopropyl-α-(2-dimethylaminoethyl)-4-isobutyl-1-naphthylacetamide.—The hydrolysis was performed according to the general method recently reported.[1b] α-Isopropyl-α-(2-dimethylaminoethyl)-4-isobutyl-1-naphthylacetonitrile (33.6 g, 0.1 mole) was refluxed for 120 hr with a 1:1:1 mixture (131 ml) of concentrated H_2SO_4, glacial acetic acid, and water. The crude product was distilled at 188–191° (0.25 mm) to give a viscous oil (12.05 g, 34% yield).

Anal. Calcd for $C_{23}H_{34}N_2O$: C, 77.92; H, 9.67; N, 7.90. Found: C, 78.52; H, 9.59; N, 7.73.

(1) α-Isopropyl-α-(2-dimethylaminoethyl)-1-naphthylacetamide, naphthypramide. (a) S. Casadio, G. Pala, E. Marazzi-Uberti, and G. Coppi, *Experientia*, **20**, 457 (1964); (b) S. Casadio, G. Pala, T. Bruzzese, E. Crescenzi, E. Marazzi-Uberti, and G. Coppi, *J. Med. Chem.*, **8**, 594 (1965); (c) G. Pala, S. Casadio, T. Bruzzese, E. Crescenzi, and E. Marazzi-Uberti, *ibid.*, **8**, 698 (1965).

(2) S. S. Adams, E. E. Cliffe, B. Lessel, and J. S. Nicholson, *Nature*, **200**, 271 (1963).

(3) The boiling points are uncorrected.

(4) S. Casadio, G. Pala, E. Crescenzi, T. Bruzzese, E. Marazzi-Uberti, and G. Coppi, *J. Med. Chem.*, **8**, 589 (1965).

Derivatives of 2-Azabicyclo[2.2.2]octane. II[1,2]

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Received October 15, 1965

Amides of formula **I**, related to the respiratory stimulant, diethylnicotinamide, were prepared. Reduction of these compounds gave a series of compounds represented by formulas II–V.

(1) Part I of this series: F. J. Villani and C. A. Ellis, *J. Med. Chem.*, **9**, 185 (1966).

(2) Isoquinuclidine, the cotamon name of this ring system, is used throughout this manuscript.