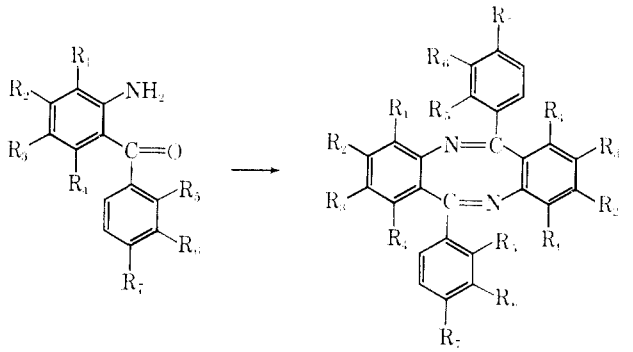
TABLE I



Starting material[a] Structure	g	Solvent (ml)	Catalyst (ml)	Reaction time, hr	Yield %	Mp, °C	Formula	Product Calcd, % C	Calcd, % H	Found, % C	Found, % H	λ_{max}, mμ[b]	ε × 10⁻³
R₁–R₇ = H	19.7	C_6H_5Cl (250)	MCl_3 (7.5 g)	8	71	191–193	$C_{26}H_{15}N_3$[c]					255	35
R₃ = Cl[d]	20	Xylene (86)	BF_3–Et_2O (1.3)	6[e]	88	217–219	$C_{26}H_{13}Cl_2N_3$[f]	73.08	3.77	73.37	3.86	260	38
R₃ = F[g]	0.5	C_6H_5Cl (15)	BF_3–Et_2O (0.05)	17	65	189–191	$C_{26}H_{13}F_2N_3$	79.17	4.09	79.17	3.69	258	34
R₃ = Br[h]	6.9	C_6H_5Cl (25)	BF_3–Et_2O (0.4)	16	23	231–234	$C_{26}H_{13}Br_2N_3$	60.48	3.12	60.48	2.98	260	43
R₃ = CF_3[i]	13.3	C_6H_5 (150)	$TiCl_4$ (2.2)	2	23	204–207	$C_{28}H_{13}F_6N_3$	67.90	3.26	68.07	3.23	260	39
R₃ = OCH_3[j]	3.9	C_6H_5Cl (80)	BF_3–Et_2O (0.2)	6	55	204–206	$C_{28}H_{23}N_3O_3$	80.36	5.30	80.56	5.72	255	38
R₃ = R₅ = Cl[k]	13.3	C_6H_5Cl (50)	$TiCl_4$ (2.7)	16	60	213–215	$C_{26}H_{11}Cl_5N_3$	62.93	2.84	63.21	2.85	*l*	
R₃ = Br, R₅ = F[i]	5.9	C_6H_5Cl (20)	BF_3–Et_2O (0.5)	16	63	232–234	$C_{26}H_{11}Br_2F_2N_3$	56.55	2.56	56.42	2.74	250	40
R₃ = Cl, R₅ = CH_3[j]	2.4	C_6H_5Cl (10)	$TiCl_4$ (0.4)	16	60	187–189	$C_{28}H_{18}Cl_2N_3$	73.85	4.43	73.94	4.72	259	29
R₃ = Cl, R₅ = OCH_3[j]	1.0	C_6H_5Cl (15)	BF_3–Et_2O (0.1)	16	13	258–260	$C_{28}H_{18}Cl_2N_3O_2$	69.00	4.14	68.85	4.19	*m*	
R₃ = R₆ = Cl[n]	13.3	C_6H_5Cl (50)	BF_3–Et_2O (0.7)	16	64	191–194	$C_{26}H_{11}Cl_5N_3$	62.93	2.84	62.97	3.02	255	40
R₃ = Cl, R₇ = F[i]	2.7	C_6H_5Cl (15)	BF_3–Et_2O (0.25)	16	76	252–254	$C_{26}H_{14}Cl_2F_2N_3$	67.40	3.05	67.19	2.82	261	37
R₃ = NO_2[o]	24.2	C_6H_5Cl (100)	$TiCl_4$ (5.8)	16	87	293–296	$C_{26}H_{16}N_5O_4$	69.64	3.60	69.93	3.82	291[p]	28
R₆ = Cl[q]	5.8	C_6H_5Cl (25)	BF_3–Et_2O[r] (1.5), $TiCl_4$ (1.3)	16	52	184–185	$C_{26}H_{16}Cl_2N_2$	73.08	3.77	73.25	4.00	255	37
R₂ = Cl[j]	46.4	C_6H_5Cl (200)	BF_3–Et_2O (2.6)	16	84	255–256	$C_{26}H_{16}Cl_2N_2$	73.08	3.77	73.10	3.53	255	39
R₄ = Cl[j]	11.6	C_6H_5Cl (50)	BF_3–Et_2O (0.65)	16	52	241–245	$C_{26}H_{16}Cl_2N_2$	73.08	3.77	73.38	3.99	259	38
R₁ = R₃ = Br[s]	18.0	C_6H_5Cl (50)	BF_3–Et_2O[r] (3.2), $TiCl_4$ (2.6)	16	63	273–274	$C_{26}H_{14}Br_2N_2$	46.33	2.09	46.39	2.17	262	43
R₂ = R₃ = Cl[k]	8.0	C_6H_5Cl (30)	BF_3–Et_2O (0.4)	16	84	350–352	$C_{26}H_{12}Cl_4N_2$	62.93	2.84	63.05	3.09	260	40

[a] R = H unless indicated otherwise. [b] All compounds with the exceptions indicated showed a shoulder or maximum at *ca.* 320 mμ (ε 5000–7000). [c] Known compound (see ref 2). [d] F. D. Chattaway, *J. Chem. Soc.*, **85**, 344 (1904). [e] Water was removed during the reaction with a Dean–Stark receiver. [f] Calcd: mol wt, 427. Found: mol wt, 445 (thermoosmosis). [g] J. F. J. Dippy and V. Moss, *J. Chem. Soc.*, 2205 (1952). [h] A. Angel, *ibid.*, **101**, 515 (1912). [i] G. Saucy and L. H. Sternbach, *Helv. Chim. Acta*, **45**, 2226 (1962). [j] L. H. Sternbach, R. I. Fryer, W. Metlesics, G. Sach, and A. Stempel, *J. Org. Chem.*, **27**, 3781 (1962). [k] L. H. Sternbach, E. Reeder, O. Keller, and W. Metlesics, *ibid.*, **26**, 4488 (1961). [l] λ 250 mμ (infl) (ε 27,000) and *ca.* 310 mμ (sh) (ε 5500). [m] λ 260 mμ (infl) (ε 21,000) and λ_{max} 307 mμ (ε 14,000). [n] This aminobenzophenone was prepared by Mr. L. A. Dolan according to method A; lit.[j] mp 107–109°. *Anal.* Calcd for $C_{13}H_9Cl_2NO$: C, 58.67; H, 3.41. Found: C, 58.97; H, 3.88. [o] K. Schofield and R. S. Theobald, *J. Chem. Soc.*, 1505 (1950). [p] Also 335 mμ (infl) (ε 19,000). [q] M. W. G. Coldham, J. W. Lewis, and S. G. P. Plant, *J. Chem. Soc.*, 4530 (1954). [r] Use of either of the two catalysts separately did not give satisfactory yields. [s] P. Ruggli and B. Hegedüs, *Helv. Chim. Acta*, **24**, 703 (1941).

The Preparation of 5-Substituted 5-(2-Naphthyl)hydantoins as Potential Anticonvulsants

RONALD D. GARRETT[1] AND HENRY R. HENZE

Department of Chemistry, The University of Texas, Austin, Texas

Received April 4, 1966

Previous research by Henze and Nunn,[2] on the synthesis of selected 5-substituted 5-(1-naphthyl)hydantoins as potentially efficacious anticonvulsant compounds[3] has suggested the preparation of a series of 5-substituted 5-(2-naphthyl)hydantoin analogs.

Experimental Section

2-Naphthyl Ketone Precursors.—Each ketone was prepared by the interaction of 2-naphthoyl chloride with the appropriate organocadmium reagent. Table I lists previously unreported 2-naphthyl ketones.

5-Substituted 5-(2-Naphthyl)hydantoin Synthesis.—A modified Bücherer–Bergs reaction was utilized for the preparation of each hydantoin. In a 300-ml glass liner of a screw-top Monel metal bomb 0.01 mole of a 2-naphthyl ketone was dissolved in 100 ml of dimethylformamide. Following the addition of a solution of 1.5 g formula weights of KCN in the least amount of water, 4.0 equiv of $(NH_4)_2CO_3$ was introduced and the bomb was rapidly closed. The resulting reaction mixture was placed in an oven (115°) for 24 hr, then made alkaline by the addition of 10% aqueous NaOH. Any unreacted ketone was subsequently removed by ether extraction. Acidification of the aqueous layer with concentrated HCl precipitated the desired hydantoin, which was recrystallized to white needles from EtOH–H_2O. Results are indicated in Table II.

TABLE I

SUBSTITUTED 2-NAPHTHYL KETONES

R	Bp (mm) or mp,[a] °C	Yield, %	Calcd, % C	Calcd, % H	Found,[b] % C	Found,[b] % H
sec-C_4H_9	168–170 (7)	62	84.86	7.60	85.05	7.71
t-C_4H_9	189–191 (15)	39	84.86	7.60	84.57	7.68
i-C_5H_{11}	45–45.4	61	84.91	8.02	84.63	8.16
n-$C_{12}H_{25}$	51–52	73	85.10	9.98	85.18	9.88

[a] All melting points were determined by the capillary method and are corrected. [b] Carbon and hydrogen microanalyses were performed by the Huffman Laboratories, Inc., Wheatridge, Colo.

(1) The University of Tennessee Medical Units, Memphis, Tenn.
(2) H. R. Henze and L. Nunn, *J. Org. Chem.*, **12**, 540 (1947).
(3) H. H. Merritt and T. J. Putnam, *Epilepsia*, 51 (1945).

TABLE II

5-SUBSTITUTED 5-(2-NAPHTHYL)HYDANTOINS

R	Mp, °C[a]	Yield, %	Calcd, % C	Calcd, % H	Calcd, % N	Found, %[b] C	Found, %[b] H	Found, %[b] N
CH_3	247–248	83	69.99	5.04	11.66	70.31	4.97	11.53
n-C_3H_7	239–240	78	71.62	6.01	10.44	71.84	6.09	10.30
i-C_3H_7	261–263	72	...	...	10.44	...	...	10.29
n-C_4H_9	201–202	76	72.32	6.43	9.92	72.21	6.49	9.85
i-C_4H_9	217–218	69	...	...	9.92	...	...	10.04
sec-C_4H_9	256–257	57	...	...	9.92	...	...	10.01
t-C_4H_9	292–293 dec	43	72.32	6.43	9.92	71.99	6.42	10.09
n-C_5H_{11}	188–189	72	72.95	6.80	9.45	72.96	6.66	9.39
i-C_5H_{11}	244–245	87	...	...	9.45	...	...	9.32
n-C_6H_{13}	177–178	85	...	...	9.03	...	...	9.01
n-C_7H_{15}	167–168	95	...	...	8.63	...	...	8.74
n-C_8H_{17}	169–170	64	...	...	8.27	...	...	8.24
n-$C_{10}H_{21}$	167–168	73	...	...	7.65	...	...	7.62
n-$C_{12}H_{25}$	169–170	70	...	...	7.10	...	...	7.09
C_6H_5	281–282	63	...	...	9.27	...	...	9.32
1-$C_{10}H_7$	323–324	68	78.39	4.58	7.95	77.82	4.29	8.33
2-$C_{10}H_7$	313–314	64	78.39	4.58	7.95	78.39	4.51	7.92

[a] All melting points were determined by the capillary method and are corrected. [b] Carbon, hydrogen, and nitrogen microanalyses were performed by the Huffman Laboratories, Inc., Wheatridge, Colo.

Heterocycles. II.[1] Synthesis of 3-Carbomethoxy-3-methyl-7,8-benzothiochromanone

TOSIO MORIWAKE

Department of Industrial Chemistry, School of Engineering, Okayama University, Okayama, Japan

Received December 4, 1965

During an attempted syntheses of 11-thia steroid homologs, the title compound was synthesized as an intermediate. The method of synthesis is analogous to the route used by Bachmann, *et al.*,[2] for the preparation of equilenin.

Experimental Section

Methyl 7,8-Benzothiochromanone-3-glyoxalate.—To a suspension of 3.2 g of sodium methoxide in 40 ml of benzene was added 7.1 g of dimethyl oxalate, and the mixture was refluxed for 10 min. To the ice-cooled solution was added a solution of 6.4 g of 7,8-benzothiochromanone[3] in 70 ml of benzene over a 10-min period, and the mixture was stirred at room temperature for 4 hr. Within a few minutes a light red solution resulted, which soon deposited a light yellow precipitate. The mixture was hydrolyzed with 100 ml of water. The benzene solution which separated was extracted twice with 60 ml of 2% NaOH solution and the combined aqueous solution was acidified with dilute HCl. The light yellow crystals were filtered off and dried. Recrystallization from ethanol gave 7.3 g (81%) of glyoxalate as pale yellow clusters which melted at 107–109°. Further recrystallizations from alcohol gave a pure sample of mp 108.5–109.5°.

Anal. Calcd for $C_{16}H_{12}O_4S$: C, 64.00; H, 4.03. Found: C, 64.08; H, 4.10.

3-Carbomethoxy-7,8-benzothiochromanone.—A mixture of 7.0 g of the above-mentioned glyoxalate and 3.5 g of powdered soft glass was heated at 180–200° for 1 hr with occasional stirring. After cooling, the dark brown product was dissolved in a mixture of benzene and acetone (1:1), and the solution was decanted from the glass. The solution was evaporated, and the residue was digested with methanol, whereupon crystallization took place. Recrystallization from ethyl acetate gave 5.1 g of product, mp 114–116°, as yellow needles.

Anal. Calcd for $C_{15}H_{12}O_3S$: C, 66.17; H, 4.44. Found: C, 66.21; H, 4.52.

3-Carbomethoxy-3-methyl-7,8-benzothiochromanone.—A warm solution of 3.6 g of 3-carbomethoxy-7,8-benzothiochromanone in 30 ml of benzene was added to a solution of sodium methoxide prepared from 1.6 g of sodium and 30 ml of methanol. The mixture was refluxed for 2 hr, cooled, and treated with 4 ml of methyl iodide. After 1 hr at room temperature, an additional 4 ml of methyl iodide was added. The resulting mixture was stirred at room temperature for 30 min, then refluxed for 2 hr, cooled, neutralized with acetic acid, and evaporated nearly to dryness. The residue was treated with benzene and water, and the organic solution after separating was washed with 5% NaOH solution with water, dried, and evaporated. Recrystallization of the residue from ethanol gave 3.5 g (92%) of the product, mp 112–113°, as tan needles.

Anal. Calcd for $C_{16}H_{14}O_3S$: C, 67.12; H, 4.93. Found: C, 67.30; H, 5.14.

(1) T. Moriwake, *J. Med. Chem.*, **9**, 163 (1966).

(2) W. E. Bachmann, W. Cole, and A. L. Wilds, *J. Am. Chem. Soc.*, **61**, 974 (1939); **62**, 824 (1940); see also ref 1.

(3) F. Krollpfeiffer and H. Schultze, *Ber.*, **56**, 1821 (1923).

Synthesis of Some 3-Arylacetyl- and 1,3-Di(arylacetyl)indoles[1]

THOMAS E. YOUNG AND MICHAEL F. MIZIANTY[2]

William H. Chandler Chemistry Laboratory, Lehigh University, Bethlehem, Pennsylvania

Received December 13, 1965

The recent demonstration of anticonvulsant activity[3] of certain 3-acylindoles has prompted us to report eighteen new 3-arylacetylindoles, of which compounds Ia–n (Table I) were all prepared by acylation of the corresponding indolylmagnesium bromides with the appropriate arylacetyl chloride, a method first described by Oddo[4] and briefly elaborated by others.[5] The 1,3-diacyl derivatives (II) were also produced as coproducts, and could be obtained pure in several cases (Table II). The 3-arylacetyl-2-methylindoles (Io–r, Table I) were prepared by reac-

(1) This investigation was supported by research Grant C-4425 from the National Cancer Institute, National Institutes of Health, U. S. Public Health Service.

(2) Abstracted in part from the Ph.D. Dissertation of M. F. M., Lehigh University, 1963.

(3) H. H. Keasling, R. E. Willette, and J. Szmuszkovicz, *J. Med. Chem.*, **7**, 94 (1964).

(4) B. Oddo and L. Sessa, *Gazz. Chim. Ital.*, **41I**, 234 (1911).

(5) N. P. Buu-Hoi, E. Bisagni, and C. Routier, *J. Chem. Soc.*, 625 (1957); S. Takagi, A. Sugii, and K. Machida, *Pharm. Bull* (Tokyo), **5**, 617 (1957); T. E. Young, *J. Org. Chem.*, **27**, 509 (1962); T. E. Young and M. F. Mizianty, *ibid.*, **29**, 2030 (1964).