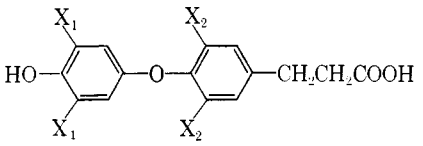
TABLE I



I

I			Yield,	Found, %		Calcd., %			Recrystn.
X_1	X_2	M.p., °C.	%	C	H	C	H	Formula	solvents
H	I	247–248[a]	78					$C_{16}H_{12}I_2O_4$	H_2O–EtOH
H	Br	200–202	64	43.19	2.89	43.30	2.91	$C_{15}H_{12}Br_2O_4$	H_2O–EtOH
H	Cl	200–201	41	55.14	3.63	55.06	3.70	$C_{15}H_{12}Cl_2O_4$	EtOAc–C_6H_6
Br	I	207–209	94[b]	28.09	1.74	26.97	1.51	$C_{15}H_{10}Br_2I_2O_4$	C_6H_6
I	Br	179–181	100[b]	26.81	1.58	26.97	1.51	$C_{15}H_{10}Br_2I_2O_4$	C_6H_6
Br	Br	183–184	56[b]	31.89	2.02	31.39	1.76	$C_{15}H_{10}Br_4O_4$	C_6H_6
I	Cl	188–189	69[b]	31.55	1.90	31.11	1.74	$C_{15}H_{10}Cl_2I_2O_4$	C_6H_6

[a] Lit.[8] m.p. 250°. [b] Crude yield.

Synthesis of 2,2-Diphenyl-5-cyanocyclopentanone

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The structural relationships of substituted 2,2-diphenylcyclopentanones to the methadone class of analgetics have been discussed.[2-4] A previous report[5] mentions several unsuccessful attempts to synthesize 2,2-diphenyl-5-cyanocyclopentanone. This keto nitrile has now been prepared from methyl 2,2-diphenyladipate.

Experimental[6]

Methyl 2,2-diphenyladipate was synthesized as reported[5] except 5-chloro-2,2-diphenylpentanenitrile was converted to the corresponding dinitrile in 99% yield in 3 hr. by using dimethyl sulfoxide as solvent.[7]

5-Carbomethoxy-5,5-diphenylpentanoic Acid.—A solution of 73.4 g. (0.225 mole) of methyl 2,2-diphenyladipate in 200 ml. of methanol was heated under reflux with vigorous stirring. After dropwise addition of 117.5 ml. of 2 *N* NaOH (0.235 mole) over 1 hr., the solution was refluxed for an additional 2 hr. The methanol was removed by distillation and the remaining solution was diluted with 500 ml. of water. Acidification with concentrated HCl gave a yellow oil which soon solidified. The crude product, 67.8 g. (96.6%), melted at 103–108°. A sample recrystallized from methanol had m.p. 107–110° (lit.[8] 105–106°). The method of Salmon-Legagneur and Neveu[8] gave inseparable mixtures.[5]

Methyl 5-Carbamoyl-2,2-diphenylpentanoate.—A mixture of 37 g. (0.222 mole) of thionyl chloride and 63 g. (0.202 mole) of the above acid ester stood overnight, was heated at 80° for 1 hr., and the excess thionyl chloride was removed under reduced pressure. The acid chloride was dissolved in 100 ml. of dry dioxane then dropped into 1000 ml. of concentrated NH_4OH at 0° over 1 hr. After warming to room temperature, filtration gave 64.6 g. (99%) of crude product melting at 88–100°. Recrystallization of a sample from methanol–water raised the m.p. to 98–100°.

Anal. Calcd. for $C_{19}H_{17}NO$: C, 82.87; H, 6.22; N, 5.09. Found: C, 82.70; H, 6.51; N, 5.03.

Methyl 5-Cyano-2,2-diphenylpentanoate.—Dehydration of the above amide ester with phosphorus oxychloride[9] gave the cyano ester in 79% yield. It had b.p. 220–225° (6 mm.) and m.p. 65–66.5° after recrystallization from methanol.

Anal. Calcd. for $C_{19}H_{19}NO_2$: C, 77.82; H, 6.48; N, 4.78. Found: C, 77.67; H, 6.81; N, 4.83.

2,2-Diphenyl-5-cyanocyclopentanone.—To a stirred, refluxing solution of 0.0793 mole of potassium *t*-butoxide in 150 ml. of dry *t*-butyl alcohol was added a solution of 21.7 g. (0.0741 mole) of methyl 2,2-diphenyl-5-cyanopentanoate in 350 ml. of *t*-butyl alcohol over 2.5 hr. After completion of the addition, the solution was refluxed for 8 hr. About two-thirds of the solvent was removed under reduced pressure and a white solid formed. After cooling, a solution of 5 ml. of acetic acid in 200 ml. of water was added, and the solid redissolved. Concentration of the resulting solution to about half its volume gave white crystals which were filtered. The product, 17.6 g. (91.2%), melted at 97–101°. After several recrystallizations from methanol, the m.p. was 103.5–106°.

Anal. Calcd. for $C_{18}H_{15}NO$: C, 82.76; H, 5.75; N, 5.36. Found: C, 82.61; H, 6.01; N, 5.28.

The infrared spectrum (CCl_4 solution) had absorption peaks at 4.42 (CN) and 5.64 μ (CO).

Hydrolysis with 80% sulfuric acid for 1 hr. then dilution to 40% and refluxing for 6 hr. gave 2,2-diphenylcyclopentanone, m.p. 86–88°. A mixture melting point of this material with an authentic sample[3] was not depressed.

(1) Taken from the Senior Honors thesis of S. A. I., Moravian College, 1964.

(2) P. N. Craig and I. H. Witt, *J. Am. Chem. Soc.*, **72**, 4925 (1950).

(3) N. R. Easton and S. J. Nelson, *ibid.*, **75**, 640 (1953).

(4) N. R. Easton, H. E. Reiff, G. Svarnas, and V. B. Fish, *ibid.*, **74**, 260 (1952).

(5) S. S. Kulp, V. B. Fish, and N. R. Easton, *J. Med. Chem.*, **6**, 516 (1963).

(6) Melting points are corrected and were determined in a Mel-Temp apparatus.

(7) L. Friedman and H. Shechter, *J. Org. Chem.*, **25**, 879 (1960).

(8) F. Salmon-Legagneur and C. Neveu, *Bull. soc. chim. France*, [5] **23**, 929 (1956).

(9) A. R. Surrey, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 535.

Some 2,3-Disubstituted Quinazolones[1]

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In a series of 2,3-disubstituted quinazolones[2] possessing hypnotic activity,[3] 2-methyl-3-(*o*-tolyl)-4-quinazolone was found to be a potent anticonvulsant, superior to sodium phenobarbital against pentylenetetrazole seizures.[4] Furthermore, Darwin,

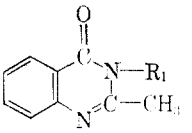
(1) The authors wish to express their thanks to the State Medical Research Council (U.P.) for a research grant and to the Indian Council of Medical Research for financial assistance to R. K.

(2) I. K. Kacker and S. H. Zaheer, *J. Indian Chem. Soc.*, **28**, 344 (1951).

(3) M. L. Gujral, R. P. Kohli, and P. N. Saxena, *J. Assoc. Physicians India*, **2**, 29 (1955).

(4) M. L. Gujral, P. N. Saxena, and R. P. Kohli, *Indian J. Med. Res.*, **45**, 207 (1957).

TABLE I
2-METHYL-3-R_1-4-QUINAZOLONE



R_1	M.p., °C.	Yield, %	Formula	Calcd., % C	Calcd., % H	Calcd., % N	Found, % C	Found, % H	Found, % N
2-Pyridyl	164–165	65	$C_{14}H_{11}N_3O$	70.8	4.62	17.7	70.44	5.1	17.1
3-Pyridyl[a]	225–226	68	$C_{14}H_{11}N_3O \cdot HCl$	61.42	4.31	15.35	60.83	4.81	15.05
4-Pyridyl	144–146	58	$C_{14}H_{11}N_3O$	70.8	4.62	17.7	69.83	5.7	17.2
2-Pyridylmethyl	122	57	$C_{15}H_{13}N_3O$	71.7	5.1	16.7	71.87	5.5	16.0
3-Pyridylmethyl	116	49	$C_{15}H_{13}N_3O$	71.7	5.1	16.7	71.21	5.64	16.1
4-Pyridylmethyl	127	54	$C_{15}H_{13}N_3O$	71.7	5.1	16.7	71.28	5.47	16.4
5-Quinolyl	208–209	56	$C_{18}H_{13}N_3O$	75.26	4.53	14.63	74.92	4.71	15.06

[a] The free base could not be crystallized and hence was reported as hydrochloride of 2-methyl-3-pyridyl-4-quinazolone.

et al.,[5] have reported that inhibitors of monoamine oxidase possess pronounced anticonvulsant properties. 4-Aminoquinoline has been shown to be a potent inhibitor of this enzyme, as compared to 4-aminopyridine which was almost devoid of such inhibitory activity.[6] On the basis of these observations we have synthesized 2,3-disubstituted quinazolones from aminopyridines and 5-aminoquinoline following the method of Bogert, *et al.*[7]

Experimental[8]

Molar proportions of acetanthranil (m.p. 78–80°) and the appropriate amines were mixed together in a round-bottomed flask. The contents of the flask were first heated on a low flame and then on a full flame. On cooling, the jelly-like mass which separated out crystallized yielding 2,3-disubstituted quinazolones in good yield.

The various pyridine derivatives used were 2-amino-, 3-amino-, and 4-aminopyridines, and 2-aminomethyl-, 3-aminomethyl-, and 4-aminomethylpyridines. In addition, 5-aminoquinoline was also used for the preparation of a quinazolone. All quinazolones were crystallized from a mixture of ethyl alcohol and ether (1:1) except the one formed from 4-aminopyridine which was crystallized with methyl alcohol only. The characterization of these 2,3-disubstituted quinazolones was done by their sharp melting points and also by analysis. The results are summarized in Table I.

(5) J. P. Darwin, A. Shore, and B. B. Brodie, *Ann. N. Y. Acad. Sci.*, **80**, 643 (1959).

(6) P. N. Kaul, *J. Pharm. Pharmacol.*, **14**, 243 (1962).

(7) T. A. Williamson, "Heterocyclic Compounds," Vol. 6, R. C. Elderfield, Ed., John Wiley and Sons, Inc., New York, N. Y., 1957, p. 334.

(8) Melting points were taken in a capillary tube and are uncorrected.

9-Thienylanthracenes[1]

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The title compounds were prepared as part of an air pollution study program to make new polycyclic aromatic compounds available for carcinogenicity testing. The synthetic routes to these compounds involve extensions to useful reactions previously recorded.[4]

(1) This investigation was supported by research Grant AP-00088-06 from the Division of Air Pollution, Bureau of State Services, Public Health Service.

(2) Taken from the Doctorate theses of S. G. Quo and P. Polss presented to the Virginia Polytechnic Institute in 1959 and 1962, respectively.

(3) N. D. E. A. Fellow 1960–1963, Eastman Kodak Fellow 1963–1964.

(4) F. A. Vingiello, S. G. Quo, and J. Sheridan, *J. Org. Chem.*, **26**, 2669 (1961).

Experimental[5,6]

2-(2-Thenoyl)diphenylmethane. A.—A Grignard reagent was prepared from 7.2 g. (0.30 g.-atom) of magnesium and a solution of 50 g. (0.30 mole, 30 ml.) of 2-bromothiophene in anhydrous ether. After completion of reaction, most of the ether was distilled while 47 g. (0.24 mole) of 2-cyanodiphenylmethane dissolved in anhydrous benzene was added. The mixture was heated under reflux for 18 hr. and worked-up in the usual way. The product was a viscous oil, b.p. 192–195° (0.5 mm.), 59 g. (88%). It was crystallized from ethanol, m.p. 43–44°.

Anal. Calcd. for $C_{18}H_{14}OS$: C, 77.66; H, 5.07; S, 11.52. Found: C, 77.53; H, 4.97; S, 11.52.

The product was oxidized quantitatively using sodium dichromate in glacial acetic acid to give 2-(2-thenoyl)benzophenone, m.p. 135–136° (from ethanol).

Anal. Calcd. for $C_{18}H_{12}O_2S$: C, 73.94; H, 4.14. Found: C, 73.69; H, 4.24.

B.—A Grignard reagent was prepared from 37 g. (0.15 mole of 2-bromodiphenylmethane and 3.9 g. (0.16 g.-atom) of magnesium in dry ether. After most of the magnesium had reacted, the ethereal solution of the Grignard reagent was transferred, under nitrogen, to a separatory funnel and added slowly to a boiling solution of 22 g. (0.15 mole) of 2-thenoyl chloride in dry benzene. Solvent was removed until the boiling temperature was 66°, and the mixture was heated for 4.5 hr., then decomposed and worked-up to give 16 g. (38%) of product, identical with that obtained by A.

2-(3-Thenoyl)diphenylmethane. A.—This compound could not be prepared as was the 2-isomer, but resort had to be had in the entrainment method using ethyl bromide. The product, b.p. 180–185° (0.5 mm.), was a viscous oil obtained in 58% yield.

Anal. Calcd. for $C_{18}H_{14}OS$: C, 77.66; H, 5.07; S, 11.52. Found: C, 77.64; H, 5.09; S, 11.24.

B.—The compound was prepared essentially as was the 2-isomer. The product, b.p. 127° (0.20 mm.) (spinning band column), was a viscous oil obtained in yield 37%.

9-(2-Thienyl)anthracene.—A mixture of 34 g. (0.122 mole) of 2-(2-thenoyl)diphenylmethane, 1200 ml. of glacial acetic acid, and 600 ml. of 48% hydrobromic acid was heated under reflux for 44 hr. The solution was cooled, diluted with water, and refrigerated overnight giving 20 g. (65%) of crystals, m.p. 113–114°. Recrystallization from absolute ethanol gave an analytical sample as yellow needles, m.p. 113.5–114.0°, which fluoresced green under ultraviolet light.

Anal. Calcd. for $C_{18}H_{12}S$: C, 83.03; H, 4.65; S, 12.32. Found: C, 82.81; H, 4.97; S, 12.18.

The same product was obtained using phosphorus pentoxide or hydrogen phenyl phosphate as the acid catalyst.

The product formed a deep violet 1:2 adduct with 2,4,7-trinitrofluorenone, m.p. 166–167°.

Anal. Calcd. for $C_{44}H_{22}N_6O_{14}S$: C, 59.33; H, 2.49; N, 9.43; S, 3.60. Found*: C, 59.27; H, 2.41; N, 9.44; S, 3.67.

(5) Analyses by Geller Laboratories, Bardonia, N. Y., except those marked with an asterisk which were performed by Galbraith Laboratories, Knoxville, Tenn.

(6) Melting points are corrected, boiling points are not.