chloride solution was added to the stirred diethylcadmium mixture over the course of one hour at room temperature. A one-hour reflux period was employed after the addition was completed. The cooled suspension was treated with ice and 2% hydrochloric acid. The benzene layer and one benzene extract were combined and washed twice with water, twice with dilute sodium hydroxide solution and once with water. The benzene solution was dried over anhydrous sodium sulfate and evaporated at reduced pressure. The residual oil was distilled. Three fractions were collected: (1) b.p. 137–139° (1.5 mm.), wt. 1.0 g., $n^{25}\text{D}$ 1.4678; (2) b.p. 140–150° (1.5 mm.), wt. 14.9 g., $n^{25}\text{D}$ 1.4674; (3) b.p. 134–145° (1.5 mm.), wt. 0.9 g., $n^{25}\text{D}$ 1.4678. The residue in the distilling flask weighed 2.7 g. The yield was 16.8 g. (81%).

Anal. Calcd. for $C_{14}H_{24}O$: C, 80.71; H, 11.61. Found: C, 80.71; H, 11.37; IR (3% in chloroform), 5.84, 6.88, 7.26, 8.92, 10.20, 11.20, 11.88 *u*.

A second run on a 0.158-mole scale gave 25.9 g. (78%), b.p. 152–158° (2.5 mm.), $n^{25}\text{D}$ 1.4672. **The semicarbazone** of the ketone was crystallized from petroleum ether (60–68°), m.p. 86–89°.

Anal. Calcd. for $C_{15}H_{27}ON_3$: C, 67.88; H, 10.26; N, 15.83. Found: C, 68.73; H, 10.05; N, 15.69.

2,6,19,23-Tetramethyl-10,15-diethyltetracosa-2,6,10,14,-18,22-hexaene (VI).—This reaction followed the directions of Schmidt[6] for the conversion of geranylacetone to squalene. A mixture of 3.87 g. of magnesium, 25.9 g. of 7,11-dimethyl-6,10-dodecadien-3-one and 16.8 ml. of 1,4-dibromobutane (b.p. 83–84° (14 mm.), $n^{25}\text{D}$ 1.5.73) was heated and then 83 ml. of ether added. A vigorous reaction took place. The crude Barbier product (29 g.) was dissolved in 150 ml. of pyridine, the solution cooled to 0°, and 12 ml. of thionyl chloride added. A considerable separation of pyridine hydrochloride was observed. After one hour at 0°, the dark brown colored reaction mixture was poured into dilute hydrochloric acid. The suspension was extracted with ether. The ethereal solution was washed with dilute hydrochloric acid, once with water, twice with dilute sodium hydroxide solution (strong color development), once with sodium sulfite solution and twice with water. The ethereal solution was dried over anhydrous sodium sulfate, the ether evaporated, and the oil distilled. Five fractions were taken: (1) b.p. 38–63° (2.5 mm.), wt. 4.64 g.; (2) b.p. 100–152° (1.0–3.0 mm.), wt. 8.14 g.; (3) b.p. 160–215° (2.5 mm.), wt. 3.88 g.; (4) b.p. 220–238° (1.2 mm.), wt. 8.30 g.; (5) b.p. 218–234° (0.8 mm.), wt. 2.78 g. Fractions 4 and 5 were combined and distilled. Four fractions were collected: (1) b.p. 140–192° (0.05 mm.), wt. 2.99 g.; (2) b.p. 192–200° (0.05 mm.), wt. 2.90 g., $n^{25}\text{D}$ 1.4943; (3) b.p. 201–203° (0.05 mm.), wt. 2.80 g., $n^{25}\text{D}$ 1.4950; (4) b.p. 201–208° (0.05 mm.), wt. 1.36, $n^{25}\text{D}$ 1.4963. Fraction 3 was taken for analysis.

Anal. Calcd. for $C_{32}H_{54}$: C, 87.59; H, 12.41. Found: C, 87.47; H, 12.36; IR (3% in chloroform), 6.90, 7.26, 11.18, 11.90 μ.

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The Preparation and Cyclization of Substituted Acetoacetanilides

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In connection with other work in progress it became necessary to synthesize a number of hitherto unreported α- and phenyl-substituted acetoacetanilides, and from these the corresponding 4-methylcarbostyrils. The former were prepared by previously described alkylations of acetoacetanilide[1,2] and by acetoacetylation of aromatic amines,[3] the latter by cyclodehydration of the acetoacetanilides with sulfuric acid, either slowly by standing at room temperature[1] or more rapidly by heating at 75–100°.[2,4]

The chief obstacle encountered was effecting the ring closure of acetoacetanilides substituted by a benzyl or phenyl group. Previous workers state either that such compounds could not be cyclized,[1,2] that they could not be characterized after cyclization,[5] or that cyclization proceeded only with concomitant sulfonation of a phenyl group.[6] The single instance of success reported is by Kaslow and Hayek,[7] who describe the preparation of 4-methyl-6-phenylcarbostyril by heating 4-phenylacetoacetanilide in mineral oil to 275°, or in unsatisfactory yield by the use of phosphoric acid (methods which did not accomplish the desired result when applied to our compounds); however, they found both these and conventional procedures failed with 2-phenylacetoacetanilide.

In order to circumvent both the comparative difficulty of ring closure and the ease of sulfonation that such behavior implies, aqueous rather than the usual concentrated sulfuric acid was employed as a cyclodehydrating agent. Thus, with an excess of 74% sulfuric acid at 96° for a half-hour, α-acetyl-β-phenylpropionanilide gave an excellent (89%) yield of 3-benzyl-4-methylcarbostyril. 2-Methylacetyl-β-phenylpropionanilide and α-acetyl-γ-phenylbutyranilide were likewise cyclized in the same way.

Although this apparently general method could not be fruitfully applied to 2-phenylacetoacetanilide, the latter compound was eventually cyclodehydrated by refluxing with phosphorus pentoxide in xylene, albeit in very low (8.5%) yield. The closely related α-methyl-2-phenylacetoacetanilide, however, resisted cyclization in this fashion or by any other procedure employed.

Our results are summarized in Tables I and II. Unless otherwise noted, all compounds cited gave negative ferric chloride tests and were crystallized from aqueous ethanol, whence they separated as colorless or white needles. Melting points are uncorrected.

Experimental

3-Benzyl-4-methylcarbostyril.—α-Acetyl-β-phenylpropionanilide[1] (4.0 g.) was mixed with 50 ml. of 74% sulfuric acid (conveniently prepared by combining two volumes of concentrated sulfuric acid with one volume of water). The mixture was heated at 96° for 0.5 hr. The anilide gradually dissolved, giving an orange-red solution; toward the end of the reaction period a yellow solid began to precipitate. The mixture was poured into 200 ml. of cold water, and the residue which formed filtered off and washed with cold water. Recrystallization from a benzene–ethanol mixture gave white needles melting at 238–240°. Further crops were obtained by successive concentrations and refrigeration of the mother liquor from the first crystallization. The total yield of product was 3.3 g. (89%).

3-Benzyl-4,8-dimethylcarbostyril.—2-Methyl-α-acetyl-β-phenylpropionanilide (2.0 g.) and 40 ml. of 74% sulfuric acid were heated on a steam-bath for 1.5 hours. There were two phases present at all times, and the mixture became deep red as the reaction proceeded. The mixture was stirred occasionally during the heating period. It was

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[1] A. L. Searles and H. G. Lindwall, THIS JOURNAL, **68**, 988 (1946).

[2] D. J. Cook and W. C. Lawall, *ibid.*, **70**, 1918 (1948).

[3] H. E. Fierz-David and E. Ziegler, *Helv. Chim. Acta*, **11**, 776 (1928).

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[6] E. Ritchie, *J. Proc. Roy. Soc. N. S. Wales*, **78**, 147 (1945).

[7] C. E. Kaslow and M. Hayek, THIS JOURNAL, **73**, 4986 (1951).

TABLE I

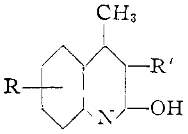
ACETOACETANILIDES, $C_6H_5NHCOCH_2COCH_3$

Substituent(s)	Yield, %	M.p., °C.	Formula	Nitrogen, % Calcd.	Nitrogen, % Found
2-Methyl-5-nitro[a]	72	119–119.5	$C_{11}H_{12}O_4N_2$	11.9	11.9
2-Chloro-α-methyl	48	94–94.5	$C_{11}H_{12}O_2NCl$	6.21	6.15
4,α-Dimethyl[b]	65	88–89	$C_{12}H_{15}O_2N$	6.83	6.84
2,α-Dimethyl	60	109.5–111[c]	$C_{12}H_{15}O_2N$	6.83	6.53
2-Phenyl-α-methyl	98	115–115.5	$C_{17}H_{17}O_2N$	5.24	5.49
2-Methyl-α-benzyl	77	154.5–155.5	$C_{18}H_{19}O_2N$[d]	4.98	4.92
α-(2′-Phenylethyl)	35	101.5–102	$C_{18}H_{19}O_2N$[e]	4.98	4.90
α-(4′-Nitrobenzyl)[f]	65	141–143	$C_{17}H_{16}O_4N_2$	8.97	8.95
α-Isopropyl[g]	81	139–140	$C_{13}H_{17}O_2N$	6.40	6.39
α-Cyclopentyl	67	150.5–151.5	$C_{15}H_{19}O_2N$	5.71	6.00
α-Amyl[b]	72	72–73[h]	$C_{15}H_{21}O_2N$	5.67	5.49
α-Hexyl	85	70–71[c]	$C_{16}H_{23}O_2N$	5.36	5.14
α-Heptyl[b]	58	64–66	$C_{17}H_{25}O_2N$	5.09	4.85

[a] Straw-colored rods which give a magenta solution with aqueous ethanolic ferric chloride. [b] Crystallized from low-boiling petroleum ether. [c] With emollescence. [d] Calcd.: C, 76.8; H, 6.81. Found: C, 77.1; H, 7.04. [e] Calcd.: C, 76.8; H, 6.81. Found: C, 76.9; H, 6.60. [f] Crystallized from a benzene–ethanol mixture. [g] Crystallized from aqueous methanol. [h] A less stable form, m.p. 55–56°, is often encountered; on long standing or melting and resolidification it is converted into the higher-melting modification.

TABLE II

4-METHYLCARBOSTYRILS



Substituents R	Substituents R′	Yield, %	M.p., °C.	Formula	Nitrogen, % Calcd.	Nitrogen, % Found
8-Chloro	Methyl	80	208–209	$C_{11}H_{10}ONCl$	6.43	6.79
6-Methyl	Methyl	91	277–277.5	$C_{12}H_{13}ON$	7.48	6.97
8-Methyl	Methyl[a]	71	216.5–217.5	$C_{12}H_{13}ON$	7.48	7.18
8-Methyl	Benzyl	91	226.5–227.5	$C_{18}H_{17}ON$	5.32	5.44
H	2′-Phenylethyl	25	211–211.5	$C_{18}H_{17}ON$	5.32	5.50
H	4′-Nitrobenzyl	81	294–296	$C_{17}H_{14}O_3N_2$[b]	9.52	9.95
H	Isopropyl	77	244–245	$C_{13}H_{15}ON$	6.96	6.78
H	Amyl	68	163–164.5[c]	$C_{15}H_{19}ON$	6.11	5.84
H	Hexyl[d]	82	154–154.5	$C_{16}H_{21}ON$	5.76	5.91
H	Heptyl	89	161.5–163.5	$C_{17}H_{23}ON$	5.45	5.55
8-Methyl	Ethyl	63	192.5–193[c]	$C_{13}H_{15}ON$	6.96	6.83
H	Benzyl[e]	89	238–240	$C_{17}H_{15}ON$	5.62	5.63
8-Phenyl	H	8.5	224.5–225	$C_{16}H_{13}ON$	5.95	5.63

[a] Crystallized from benzene. [b] Calcd.: C, 69.4; H, 4.90. Found: C, 69.3; H, 4.74. [c] With emollescence. [d] Crystallized from aqueous methanol. [e] Crystallized from a benzene–ethanol mixture.

then poured into a slurry of water and crushed ice, stirred briefly and filtered; the filtrate was discarded. The precipitate was suspended in 300 ml. of cold water and allowed to stand for 36 hr. Filtration yielded a pale tan solid which weighed 1.7 g. (91%) after air-drying. This was triturated with three 20-ml. portions of 50% ethereal acetone to remove small amounts of colored impurities and then crystallized twice from aqueous ethanol. Clusters of white needles, m.p. 226.5–227.5°, were obtained in this way.

8-Phenyl-4-methylcarbostyril.—2-Aminobiphenyl (33.8 g., 0.200 mole) was dissolved in 300 ml. of anhydrous xylene by gentle warming. The resulting solution was brought to a boil, and to it was added a solution of pyridine (1 ml.) in ethyl acetoacetate (41.6 g., 0.320 mole). Heating was continued at such a rate that only that fluid boiling less than 80° was removed from the system. After one hour, the rate of boiling was increased, and 220 ml. of liquid was distilled off in a 0.5-hr. period. The residual solution was refrigerated, whereupon a pale straw-colored solid precipitated. This was filtered off and washed with cold petroleum ether; the yield of 2-phenylacetoacetanilide was 44.7 g. (88%).[8] White needles (42.1 g., 94% recovery) of m.p. 83.5–85° were obtained after crystallization from 50% aqueous ethanol.

A mixture of the 2-phenylacetoacetanilide so obtained (1.27 g.), phosphorus pentoxide (1.3 g.) and anhydrous xylene (25 ml.) was refluxed for one hour. By this time a sticky orange precipitate was in evidence. After cooling, excess water was added, and the mixture neutralized with potassium hydroxide; it was then steam distilled to remove the xylene. The residual mixture was refrigerated and filtered. The orange precipitate remaining was leached with three 5-ml. portions of acetone and then twice crystallized from aqueous ethanol, using decolorizing charcoal. This gave 0.100 g. (8.5%) of colorless needles, m.p. 224.5–225°.

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Ethylpseudocymene

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In a previous publication[1] we described the dehydration of 1-ethynylcyclohexanol to cyclohexenylacetylene by passage over an aluminum oxide

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[8] Ritchie, ref. 6, obtained a 60% yield using a shorter reaction time and without a solvent and catalyst. The compound gives a deep violet color with aqueous ethanolic ferric chloride.

[1] H. Sobotka and J. D. Chanley, THIS JOURNAL, **70**, 3914 (1948).