$LiAlH_4$. The mixt was stirred at room temp for 29 hr. The reaction was hydrolyzed with $H_2O$ and extracted with $Et_2O$. The $Et_2O$ soln was evapd *in vacuo* to yield 3.0 g of crude product. Tlc showed a number of spots (silica gel-$C_6H_6$). The crude reaction product was chromatographed on a 28 × 3 cm column of silica gel ($C_6H_6$ elution, 60-ml fractions). Fractions 6-12 gave 500 mg of the starting amino ketone (15%) (nmr, ir). Fractions 22-29 (10% $Et_2O$) gave 500 mg of product (nmr, ir, elemental analysis of the HCl salt). Other fractions were unidentified, although final 100% $Et_2O$ elution gave 800 mg of material that appeared to be a trialkylamine. The HCl salt of the product was prepd in EtOH-$Et_2O$ as white crystals, mp 119-122° (15% yield).

A 100-mg probe run had given a nearly quantitative yield of product 17.

**Acknowledgment.** The authors gratefully acknowledge many helpful discussions with Dr. R. E. Strube of the Walter Reed Army Institute of Research. Dr. Strube also suggested a number of the aryl substrates and made them available for this work.

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# Antimalarial Phenanthrene Amino Alcohols. 2. Trifluoromethyl-Containing 9-Phenanthrenemethanols[†,1]

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*Received November 29, 1971*

A series of mono-, di-, tri-, and tetrasubstituted 9-phenanthrene amino alcohols has been prepd in which each compd bears at least one $CF_3$ group. A number of these compds, tri- and tetrasubstituted with a combination of $CF_3$ and Cl groups, are the most active, nontoxic amino alcohols to emerge from the vast primary screen (*Plasmodium berghei*, mouse) of the Army's Research Program on Malaria. The most effective member of the series, 6,7-dichloro-2,4-bis(trifluoromethyl)-α-(di-*n*-propylaminomethyl)-9-phenanthrenemethanol·HCl (**159**), is 100% curative at 5 mg/kg and active at concentrations as low as 1.25 mg/kg.

Antimalarial enhancement of 9-phenanthrenemethanols by introduction of $CF_3$ groups or a combination of $CF_3$ and halogen was described earlier.[1] In an effort to approach the optimal substitution pattern for this series we have synthesized the compds included in Table I.

**Chemistry.** The preparative routes were essentially those described in paper 1.[1] Details have been tabulated in the Experimental Section.

**Biology.** Table I includes murine antimalarial data for 48 new $CF_3$-contg 9-phenanthrene amino alcohols. The distribution of these compds among the curative, active, and inactive categories, at each dose, is shown in Table II.

Most of the new compds were active or curative at doses as low as 10 mg/kg. Conspicuous exceptions were the derivs with one or more nonhalogenic groups (**125, 126, 127, 131**). In fact, the 6-$CF_3$, 3-COOH deriv (**126**) was the only one in the entire series completely inactive at even the highest concentrations. It would seem that the preferred substituents are those which combine a positive Hansch $\pi$ constant[2] with a positive Hammett $\sigma$ constant.[3]

The most active compds (**113, 129, 135-139, 142, 159**), with 60-100% cures at 20 mg/kg, were mainly tri- and tetrasubstituted with a combination of Cl and $CF_3$ groups. The best of these (**135, 137, 138, 159**), with 60-100% cures at 10 mg/kg, all had two of their substituents at positions 2 and 4.

Among the side chains, the piperidyl, Pr, Bu, and Am derivs were all quite good. Compds with the heptyl side chain retained considerable activity but were less effective than the others.

The compds **135, 137, 138,** and **159** are the most active, nontoxic amino alcohols to emerge from the vast primary screen of the Army's Research Program on Malaria.

### Experimental Section‡

**4,5-Dichloro-2-nitrophenylacetic Acid. Method A.** Commercial 3,4-dichlorobenzoic acid (Eastman), suspended in concd $H_2SO_4$, was nitrated with mixed acid (modification of the method of Claus and Bucher[4]) to give 77% of 4,5-dichloro-2-nitrobenzoic acid. This material was identical with that obtd on oxidation ($KMnO_4$ in aqueous $Me_2CO$) of authentic 4,5-dichloro-2-nitrobenzaldehyde[9] thereby proving its structure. This nitrobenzoic acid was converted to the corresponding nitrophenylacetic acid in the usual manner (Table III, footnote *y*); mp 133-136° ($C_6H_6$-ligroin), yield 68%. *Anal.* ($C_8H_5Cl_2NO_4$) C, H, N.

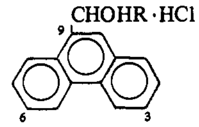
**Method B.** To a mixt of 34 ml of $HNO_3$ (*d* 1.42) and 375 ml of concd $H_2SO_4$ at −20° was added, in one portion, 95 g (0.46 mole) of 3,4-dichlorophenylacetic acid (Research Organic/Inorganic Chemical Corp., Sun Valley, Calif.). The reaction temp rose to −5° and was then maintained at −10° to −5° for 0.5 hr and at −5° to 0° for 1 hr. The resulting white mass was poured into 1.8 kg of crushed ice and the white solid was washed, dried, extd with boiling ligroin (ext discarded), and crystd from aqueous HOAc; yield 95 g (83%), mp 132-134°. The ir spectrum of this material was identical with that of the analytical sample obtd *via* method A.

**3,5-Bis(trifluoromethyl)benzaldehyde.** A mixt of 3,5-bis(tri-

†This investigation was supported by the U.S. Army Medical Research and Development Command under Contract No. DADA17-70-C-0101 and is Contribution No. 1029 from the Army Research Program on Malaria.

‡Satisfactory spectra were obtd where required for structural detn; ir as Nujol mulls on Perkin-Elmer 137B Infracord; nmr (by Sadtler Research Laboratories, Philadelphia, Pa.) on Varian A-60A. Mp's were detd in capillary tubes in an electrically heated Thiele-Dennis apparatus and are uncorr. Where analyses (Microanalysis, Inc., Wilmington, Del.) are indicated only by symbols of the elements analytical results were within ±0.4% of the theor values.

Table I. Antimalarial Activity[a]




| No. | Substituents | R[b] | ΔMST or C[c], Dose, mg/kg: 5 | 10 | 20 | 40 | 80 | 160 | 320 | 640 |
|---|---|---|---|---|---|---|---|---|---|---|
| 143 | 2-$CF_3$ | $CH_2NBu_2$ | | 4.7 | 9.7 | 13.7 | 3C | 5C | 5C | 5C |
| 113 | 2-$CF_3$ | Pip | | | 4C | 5C | 5C | 5C | 4C[d] | 3C[d] |
| 114 | 4-$CF_3$ | Pip | | | 1.7 | 4.9 | 2C | 5C | 5C | 5C |
| 115 | 5-$CF_3$ | Pip | | | 2.1 | 8.3 | 3C | 4C | 5C | 5C |
| 116 | 7-$CF_3$ | Pip | | | 0.5 | 5.1 | 9.1 | 1C | 4C | 5C |
| 144 | 1-Br, 6-$CF_3$ | $CH_2NHep_2$ | | | 1.0 | 6.0 | 6.2 | 1C | 1C | 3C |
| 117 | 2-Cl, 5-$CF_3$ | Pip | 3.8 | 17.3 | 2C | 2C | 4C | 5C | 5C | |
| 118 | 2-Cl, 7-$CF_3$ | Pip | 0.5 | 0.5 | 0.6 | 9.2 | 14.7 | 17.7 | 5C | 5C |
| 119 | 7-Cl, 2-$CF_3$ | Pip | 1.1 | 1C | 1C | 5C | 5C | 5C | 5C | 5C |
| 120 | 7-Cl, 4-$CF_3$ | Pip | | 10.3 | 12.5 | 1C | 2C | 5C | 5C | 5C |
| 145 | 2-Br, 6-$CF_3$ | $CH_2NBu_2$ | | | 1C | 3C | 3C | 5C | 5C | 5C |
| 121 | 2-Br, 6-$CF_3$ | Pip | 1.8 | 17.2 | 1C | 2C | 4C | 5C | 5C | 5C |
| 146 | 4-Br, 6-$CF_3$ | $CH_2NBu_2$ | | | 2.0 | 9.6 | 10.6 | 1C | 2C | 5C |
| 147 | 2-Cl, 6-$CF_3$ | $CH_2NBu_2$ | 5.3 | 7.5 | 1C | 1C | 2C | 3C | 4C | 5C |
| 148 | 2-Cl, 6-$CF_3$ | $CH_2NHep_2$ | | | 1.9 | 9.7 | 2C | 3C | 5C | 5C |
| 122 | 2-Cl, 6-$CF_3$ | Pip | | 0.3 | 1C | 3C | 4C | 5C | 5C | 5C |
| 123 | 2,6-$(CF_3)_2$ | Pip | | | 15.8 | 1C | 3C | 5C | 5C | 5C |
| 124 | 4,6-$(CF_3)_2$ | Pip | | 1.1 | 14.7 | 1C | 1C | 1C | 5C | 5C |
| 125 | 3-$CH_3$, 6-$CF_3$ | Pip | | | 0.1 | 0.3 | 3.7 | 9.5 | 3C | 3C |
| 126 | 3-COOH, 6-$CF_3$ | Pip | | | 0.1 | 0.1 | 0.3 | 0.3 | 0.3 | 0.5 |
| 127 | 3-$SO_2CH_3$, 6-$CF_3$ | Pip | | 0.3 | 0.3 | 2.7 | 5.9 | 13.1 | 5C | |
| 128 | 7-Cl, 3-$CF_3$ | Pip | | 1.9 | 13.9 | 4C | 5C | 5C | 5C | 5C |
| 149 | 1,2-$Cl_2$, 6-$CF_3$ | $CH_2NBu_2$ | | 5.3 | 8.1 | 11.1 | 14.3 | 3C | 5C | 5C |
| 129 | 1,2-$Cl_2$, 6-$CF_3$ | Pip | 0.7 | 13.5 | 4C | 5C | 5C | 5C | 5C | 5C |
| 150 | 1,3-$Cl_2$, 6-$CF_3$ | $CH_2NBu_2$ | 7.1 | 12.3 | 2C | 4C | 5C | 5C | | |
| 151 | 1,3-$Cl_2$, 6-$CF_3$ | $CH_2NHep_2$ | | 0.4 | 0.5 | 1.1 | 4.7 | 2C | 5C | 5C |
| 130 | 1,3-$Cl_2$, 6-$CF_3$ | Pip | 0.4 | 10.0 | 17.8 | 3C | 5C | 5C | 5C | 5C |
| 131 | 1,3-$(CH_3)_2$, 6-$CF_3$ | Pip | | 0.3 | 0.5 | 0.9 | 11.7 | 13.7 | 5C | 5C |
| 132 | 1,3-$Br_2$, 6-$CF_3$ | Pip | | 0.3 | 1C | 3C | 5C | 5C | 5C | 5C |
| 133 | 2,3-$Cl_2$, 6-$CF_3$ | Pip | 0.6 | 7.0 | 1C | 4C | 5C | 5C | 5C | |
| 134 | 2,3-$Br_2$, 6-$CF_3$ | Pip | | 0.3 | 0.5 | 1.9 | 6.9 | 3C | 4C | |
| 152 | 2,4-$Cl_2$, 6-$CF_3$ | $CH_2NBu_2$ | | 6.5 | 15.1 | 20.1 | 2C | 5C | 5C | 5C |
| 135 | 2,4-$Cl_2$, 6-$CF_3$ | Pip | 5.5 | 3C | 4C | 5C | 5C | 5C | 5C | 5C |
| 153 | 2,4-$Br_2$, 6-$CF_3$ | $CH_2NBu_2$ | 6.9 | 8.9 | 13.3 | 4C | 5C | 5C | 5C | 5C |
| 154 | 3,4-$Cl_2$, 6-$CF_3$ | $CH_2NPr_2$ | | 5.5 | 1C | 2C | 5C | 5C | 5C | 5C |
| 155 | 3,4-$Cl_2$, 6-$CF_3$ | $CH_2NBu_2$ | 5.1 | 12.3 | 15.9 | 1C | 5C | 5C | 5C | 5C |
| 156 | 3,4-$Cl_2$, 6-$CF_3$ | $CH_2NAm_2$ | | 7.5 | 13.1 | 5C | 5C | 5C | 5C | 5C |
| 157 | 3,4-$Cl_2$, 6-$CF_3$ | $CH_2NHep_2$ | | 0.9 | 2.3 | 6.9 | 3C | 5C | 5C | 5C |
| 136 | 3,4-$Cl_2$, 6-$CF_3$ | Pip | 1.3 | 11.5 | 3C | 5C | 5C | 5C | 5C | 5C |
| 137 | 6-Cl, 2,4-$(CF_3)_2$ | Pip | 10.3 | 3C | 5C | 5C | 5C | 5C | 5C | 5C |
| 138 | 7-Cl, 2,4-$(CF_3)_2$ | Pip | 4.1 | 5C | 5C | 5C | 5C | 5C | 5C | 5C |
| 139 | 2,4,6-$(CF_3)_3$ | Pip | | 1.9 | 3C | 5C | 5C | 5C | 5C | 5C |
| 140 | 5,7-$Cl_2$, 3-$CF_3$ | Pip | 0.5 | 1C | 2C | 5C | 5C | 5C | 5C | 5C |
| 158 | 6,7-$Cl_2$, 3-$CF_3$ | $CH_2NPr_2$ | | 13.1 | 2C | 4C | 5C | 5C | 5C | 5C |
| 141 | 6,7-$Cl_2$, 3-$CF_3$ | Pip | | 1.7 | 11.9 | 2C | 5C | 5C | 5C | 5C |
| 159 | 6,7-$Cl_2$, 2,4-$(CF_3)_2$ | $CH_2NPr_2$ | 5C[e] | 5C | 5C | 5C | 5C | 5C | 5C | 5C |
| 142 | 6,7-$Cl_2$, 2,4-$(CF_3)_2$ | Pip | | 1C | 3C | 5C | 5C | 5C | 5C | 5C |
| 160 | 2,3-$Br_2$, 6-$CF_3$ | $CH_2NBu_2$ | | 6.1 | 12.3 | 5C | 5C | 5C | 5C | 5C |

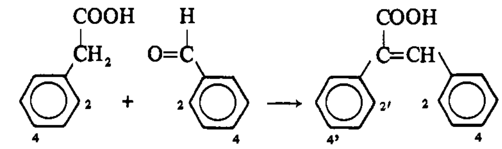
[a]Tests were carried out in five mice, infected with a lethal dose of *P. berghei*, by Dr. L. Rane and coworkers, Malaria Screening Laboratory, University of Miami, Miami, Fla. For details of test procedure, see Osdene, *et al.*[16] Test data were supplied by Drs. T. R. Sweeney and R. E. Strube of Walter Reed Army Institute of Research. [b]Pip = 2-piperidyl. [c]ΔMST, mean survival time over controls (6.2 ± 0.49 days); C, number of cures (mice surviving to 60 days); a compd is considered to be "active" when the MST of the treated group is more than twice that of the control group. [d]1 and 2 toxic deaths at 320 mg/kg and 640 mg/kg, respectively (deaths occurring before day 6 after infection are attributed to drug action and counted as "toxic deaths"). [e]ΔMST at 2.50 and 1.25 mg/kg = 12.0 and 6.8 days, respectively.

Table II. $CF_3$-Containing 9-Phenanthrenemethanols. Activity Distribution at Each Dose

| Dose, mg/kg | No. tested | No. curative[a] | No. active[a] | No. inactive | Dose, mg/kg | No. tested | No. curative[a] | No. active[a] | No. inactive |
|---|---|---|---|---|---|---|---|---|---|
| 5 | 17 | 1 | 3 | 13 | 80 | 48 | 37 | 7 | 4 |
| 10 | 37 | 7 | 14 | 16 | 160 | 48 | 43 | 4 | 1 |
| 20 | 48 | 21 | 13 | 14 | 320 | 48 | 47 | 0 | 1 |
| 40 | 48 | 31 | 8 | 9 | 640 | 43 | 42 | 0 | 1 |

[a]See footnote *c*, Table I.

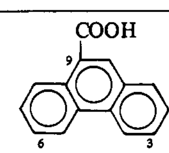
Table III. Nitro α-Phenylcinnamic Acids[aa]



| No. | Phenylcinnamic acid | Phenylacetic acid | Benzaldehyde | Temp, °C | Mp, °C (solvent) | Yield, % | Formula[bb] |
|---|---|---|---|---|---|---|---|
| 1 | 2'-$NO_2$, 3-$CF_3$ | 2-$NO_2$[a] | 3-$CF_3$[b] | 95 | 174–175 ($C_6H_6$-petr ether) | 63 | $C_{16}H_{10}F_3NO_4$[g] |
| 2 | 2-$NO_2$, 3'-$CF_3$ | 3-$CF_3$[c] | 2-$NO_2$[a] | 100 | 116–117 ($C_6H_6$-hexane) | 59 | $C_{16}H_{10}F_3NO_4$ |
| 3 | 2-Br, 2'-$NO_2$, 4'-$CF_3$ | 2-$NO_2$, 4-$CF_3$[d] | 2-Br[a] | 80 | 250 (aq EtOH) | 57[e] | $C_{16}H_9BrF_3NO_4$ |
| 4 | 5-Cl, 2-$NO_2$, 3'-$CF_3$ | 3-$CF_3$[c] | 5-Cl, 2-$NO_2$[a] | 20 | 157.5–158.5 (aq AcOH) | 63 | $C_{16}H_9ClF_3NO_4$[h] |
| 5 | 2'-$NO_2$, 5'-Cl, 3-$CF_3$ | 5-Cl, 2-$NO_2$[x] | 3-$CF_3$[b] | 60 | 188–190 (aq EtOH) | 65 | $C_{16}H_9ClF_3NO_4$[i] |
| 6 | 3-Br, 2'-$NO_2$, 4'-$CF_3$[j] | 2-$NO_2$, 4-$CF_3$[d] | 3-Br[a] | 45 | 177–179 (aq MeOH) | 88 | $C_{16}H_9BrF_3NO_4$ |
| 7 | 5-Br, 2-$NO_2$, 4'-$CF_3$[j] | 4-$CF_3$[c] | 5-Br, 2-$NO_2$[k] | 100 | 218–220 ($C_6H_6$) | 72 | $C_{16}H_9BrF_3NO_4$ |
| 8 | 5-Cl, 2-$NO_2$, 4'-$CF_3$ | 4-$CF_3$[c] | 5-Cl, 2-$NO_2$[a] | 50 | 189–190 ($C_6H_6$) | 64 | $C_{16}H_9ClF_3NO_4$ |
| 9 | 2'-$NO_2$, 3,4'-$(CF_3)_2$ | 2-$NO_2$, 4-$CF_3$[d] | 3-$CF_3$[b] | 50 | 209–210 (aq EtOH) | 63 | $C_{17}H_9F_6NO_4$ |
| 10 | 4-$CH_3$, 2'-$NO_2$, 4'-$CF_3$ | 2-$NO_2$, 4-$CF_3$[d] | 4-$CH_3$[a] | 70 | 222–224 ($C_6H_6$) | 38 | $C_{17}H_{12}F_3NO_4$ |
| 11 | 4-$SO_2CH_3$, 2'-$NO_2$, 4'-$CF_3$ | 2-$NO_2$, 4-$CF_3$[d] | 4-$SO_2CH_3$[l] | 70 | 182–183 (aq EtOH) | 56 | $C_{17}H_{12}F_3NO_6S$ |
| 12 | 5'-Cl, 2'-$NO_2$, 4-$CF_3$ | 5-Cl, 2-$NO_2$[x] | 4-$CF_3$[b] | 65 | 202–203 ($C_6H_6$-ligroin) | 95 | $C_{16}H_9ClF_3NO_4$ |
| 13 | 2,3-$Cl_2$, 2'-$NO_2$, 4'-$CF_3$ | 2-$NO_2$, 4-$CF_3$[d] | 2,3-$Cl_2$[t] | 80 | 223–225 (AcOH) | 89 | $C_{16}H_8Cl_2F_3NO_4$ |
| 14 | 2,4-$Cl_2$, 2'-$NO_2$, 4'-$CF_3$ | 2-$NO_2$, 4-$CF_3$[d] | 2,4-$Cl_2$[n] | 65 | 243–244 ($C_6H_6$) | 84[o] | $C_{16}H_8Cl_2F_3NO_4$ |
| 15 | 2,4-$(CH_3)_2$, 2'-$NO_2$, 4'-$CF_3$ | 2-$NO_2$, 4-$CF_3$[d] | 2,4-$(CH_3)_2$[a] | 70 | 222–224 (aq EtOH) | 22 | $C_{18}H_{14}F_3NO_4$ |
| 16 | 2,4-$Br_2$, 2'-$NO_2$, 4'-$CF_3$ | 2-$NO_2$, 4-$CF_3$[d] | 2,4-$Br_2$[u] | 61 | 233–235 ($C_6H_6$) | 47 | $C_{16}H_8Br_2F_3NO_4$ |
| 17 | 4,5-$Cl_2$, 2-$NO_2$, 4'-$CF_3$ | 4-$CF_3$[c] | 4,5-$Cl_2$, 2-$NO_2$[p] | 60 | 195–198 ($C_6H_6$) | 62 | $C_{16}H_8Cl_2F_3NO_4$ |
| 18 | 4,5-$Br_2$, 2-$NO_2$, 4'-$CF_3$ | 4-$CF_3$[c] | 4,5-$Br_2$,[z] 2-$NO_2$ | 77 | 196–198 (AcOH) | 65 | $C_{16}H_8Br_2F_3NO_4$ |
| 19 | 3,5-$Cl_2$, 2'-$NO_2$, 4'-$CF_3$ | 2-$NO_2$, 4-$CF_3$[d] | 3,5-$Cl_2$[a] | 90 | 212–214 ($C_6H_6$) | 86 | $C_{16}H_8Cl_2F_3NO_4$ |
| 20 | 3,5-$Br_2$, 2'-$NO_2$, 4'-$CF_3$ | 2-$NO_2$, 4-$CF_3$[d] | 3,5-$Br_2$[v] | 60 | 217–218 ($C_6H_6$) | 57 | $C_{16}H_8Br_2F_3NO_4$[q] |
| 21 | 4'-Cl, 2'-$NO_2$, 3,5-$(CF_3)_2$ | 4-Cl, 2-$NO_2$[s] | 3,5-$(CF_3)_2$[f] | 60 | 228–229 ($C_6H_6$) | 72 | $C_{17}H_8ClF_6NO_4$[r] |
| 22 | 5'-Cl, 2'-$NO_2$, 3,5-$(CF_3)_2$ | 5-Cl, 2-$NO_2$[x] | 3,5-$(CF_3)_2$[f] | 55 | 212–213 ($C_6H_6$) | 75 | $C_{17}H_8ClF_6NO_4$ |
| 23 | 2'-$NO_2$, 3,4',5-$(CF_3)_3$ | 2-$NO_2$, 4-$CF_3$[d] | 3,5-$(CF_3)_2$[f] | 60 | 185 ($C_6H_6$) | 63 | $C_{18}H_8F_9NO_4$ |
| 24 | 3',5'-$Cl_2$, 2'-$NO_2$, 4-$CF_3$ | 3,5-$Cl_2$, 3-$NO_2$[y] | 4-$CF_3$[b] | 75 | 234–236 (EtOH) | 60 | $C_{16}H_8Cl_2F_3NO_4$ |
| 25 | 4',5'-$Cl_2$, 2'-$NO_2$, 4-$CF_3$ | 4,5-$Cl_2$, 2-$NO_2$[f] | 4-$CF_3$[b] | 45 | 186–187 (aq EtOH) | 66 | $C_{16}H_8Cl_2F_3NO_4$ |
| 26 | 4',5'-$Cl_2$, 2'-$NO_2$, 3,5$(CF_3)_2$ | 4,5-$Cl_2$, 2-$NO_2$[f] | 3,5-$(CF_3)_2$[f] | 80 | 210–214[m] | 80 | $C_{17}H_7Cl_2F_6NO_4$[m] |
| 27 | 2'-$NO_2$, 3,4,5-$Br_3$, 4'-$CF_3$ | 2-$NO_2$, 4-$CF_3$[d] | 3,4,5-$Br_3$[w] | 60 | 257.5–258.5 ($CHCl_3$-hexane) | 58 | $C_{16}H_7Br_3F_3NO_4$ |

[a]Aldrich Chemical Co., Milwaukee, Wis. [b]Prepd *via* adaptation of method described in ref 5. [c]Pierce Chemical Co., Rockford, Ill. [d]See ref 6. [e]Isolated as a by-product was the decarboxylated compd, 2-bromo-2'-nitro-4'-trifluoromethylstilbene, mp 114° (MeOH). *Anal.* ($C_{15}H_9BrF_3NO_2$) C, H, N. [f]Experimental Section. [g]C: calcd, 56.89; found, 57.50. [h]H: calcd, 3.77; found, 3.30. [i]C: calcd, 51.70; found, 51.23. [j]Compds 6 and 7 are both intermediates in the synthesis of 2-bromo-6-trifluoromethylphenanthrene-9-carboxylic acid (37). Although prepn of 7 involves the relatively expensive *p*-trifluoromethylphenylacetic acid, use of 7 instead of 6 eliminates isomer possibilities during subsequent prepn of 37. [k]See ref 7. [l]See ref 8. [m]Used without purification. [n]Eastman Organic Chemicals, Rochester, N. Y. [o]At 100°, the yield was 72%. [p]See ref 9. [q]H: calcd, 2.83; found, 3.29. [r]C: calcd, 46.36; found, 47.00. [s]From commercial 2,5-dichloronitrobenzene in 33% yield, *via* adaptation of method of Simet;[6] mp 164–166° (aq EtOH). *Anal.* ($C_8H_6ClNO_4$) C, H, N. [t]See ref 10. [u]See ref 11. [v]See ref 12. [w]See ref 13. [x]Prepd from commercial 5-chloro-2-nitrobenzoic acid in usual manner (see footnote *y*), mp 156–158° (sublimation at 135–140°, 1 mm). *Anal.* ($C_8H_6ClNO_4$) C, H, N. [y]Prepd from 3,5-dichloro-2-nitrobenzoic acid[14] *via* the method described for 4-trifluoromethoxy phenylacetic acid in paper 1;[1] mp 163–164° ($C_6H_6$). *Anal.* ($C_8H_5Cl_2NO_4$) C, H, Cl, N. [z]Obtd in 66% yield by nitration of 3,4-dibromobenzaldehyde in an adaptation of the method of Alford and Schofield,[15] mp 105–107° (hexane). *Anal.* ($C_7H_3Br_2NO_3$) C, H, N. [aa]The compds in this table were all made *via* method B ($Ac_2O$ + $K_2CO_3$) of paper 1.[1] [bb]All compds were analyzed for C, H, N.

Table IV. Phenanthrene-9-carboxylic Acids



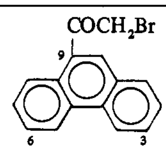
| No. | Starting[a] material | Substituents | Mp, °C (solvent) | Yield, % | Formula[m] |
|---|---|---|---|---|---|
| 28 | 1 | 2-$CF_3$[b] | 214–216 ($C_6H_6$) | 31 | $C_{16}H_9F_3O_2$ |
| 29 | 1 | 4-$CF_3$[b] | 228–230 ($C_6H_6$) | 6 | $C_{16}H_9F_3O_2$ |
| 30 | 2 | 5-$CF_3$[c] | 219–220 ($C_6H_6$) | 12 | $C_{16}H_9F_3O_2$ |
| 31 | 2 | 7-$CF_3$[c] | 247–249 ($C_6H_6$) | 12 | $C_{16}H_9F_3O_2$ |
| 32 | 3 | 1-Br, 6-$CF_3$ | 287–288 (*i*-PrOH) | 36 | $C_{16}H_8BrF_3O_2$ |
| 33 | 4 | 2-Cl, 5-$CF_3$[e] | 239–240.5 ($Me_2CO$)[e] | 20 | $C_{16}H_8ClF_3O_2$[d] |
| 34 | 4 | 2-Cl, 7-$CF_3$[e] | 215–255 ($Me_2CO$)[e] | 20 | $C_{16}H_8ClF_3O_2$ |
| 35 | 5 | 7-Cl, 2-$CF_3$[e] | 206–230 (EtOH-ligroin)[e] | | $C_{16}H_8ClF_3O_2$ |
| 36 | 5 | 7-Cl, 4-$CF_3$[e] | 206–230 (EtOH-ligroin)[e] | | $C_{16}H_8ClF_3O_2$ |
| 37 | 7 | 2-Br, 6-$CF_3$ | 288–289.5 (EtOH) | 51 | $C_{16}H_8BrF_3O_2$ |
| 37 | 6 | 2-Br, 6-$CF_3$[f] | 289.5–290.5 (EtOH) | 65 | $C_{16}H_8BrF_3O_2$ |
| 38 | 6 | 4-Br, 6-$CF_3$[f] | 246–247 (AcOH) | 65 | $C_{16}H_8BrF_3O_2$ |
| 39 | 8 | 2-Cl, 6-$CF_3$ | 276–277 ($C_6H_6$-EtOH) | 79 | $C_{16}H_8ClF_3O_2$ |
| 40 | 9 | 2,6-$(CF_3)_2$[g] | 288–289 (aq AcOH) | 20 | $C_{17}H_8F_6O_2$ |
| 41 | 9 | 4,6-$(CF_3)_2$[g] | 211–211.5 (aq AcOH) | 40 | $C_{17}H_8F_6O_2$ |
| 42 | 10 | 3-$CH_3$, 6-$CF_3$ | 278–279 (dioxane) | 40 | $C_{17}H_{11}F_3O_2$ |
| 43 | 11 | 3-$SO_2CH_3$, 6-$CF_3$ | 314–315 (AcOH) | 40 | $C_{17}H_{11}F_3SO_4$ |

Table IV. *Continued*

| No. | Starting[a] material | Substituents | Mp, °C (solvent) | Yield, % | Formula[m] |
|---|---|---|---|---|---|
| 44 | 12 | 7-Cl, 3-$CF_3$ | 308.5–310 (dioxane–hexane) | 58 | $C_{16}H_8ClF_3O_2$ |
| 45 | 13 | 1,2-$Cl_2$, 6-$CF_3$ | 297–298 (EtOH) | 45 | $C_{16}H_7Cl_2F_3O_2$ |
| 46 | 14 | 1,3-$Cl_2$, 6-$CF_3$ | 287.5–288.5 (aq EtOH) | 37 | $C_{16}H_7Cl_2F_3O_2$ |
| 47 | 15 | 1,3-$(CH_3)_2$, 6-$CF_3$ | 308.5–309 (AcOH) | 43 | $C_{18}H_{13}F_3O_2$ |
| 48 | 16 | 1,3-$Br_2$, 6-$CF_3$ | 298–300 (aq EtOH) | 71 | $C_{16}H_7Br_2F_3O_2$ |
| 49 | 17 | 2,3-$Cl_2$, 6-$CF_3$ | 320–323 (EtOAc) | 31 | $C_{16}H_7Cl_2F_3O_2$ |
| 50 | 18 | 2,3-$Br_2$, 6-$CF_3$ | 318–320 (dioxane) | 33 | $C_{16}H_7Br_2F_3O_2$ |
| 51 | 19 | 2,4-$Cl_2$, 6-$CF_3$ | 238–239 (aq EtOH) | 69 | $C_{16}H_7Cl_2F_3O_2$ |
| 52 | 20 | 2,4-$Br_2$, 6-$CF_3$ | 250–251 (aq dioxane) | 35 | $C_{16}H_7Br_2F_3O_2$[h] |
| 53 | 21 | 6-Cl, 2,4-$(CF_3)_2$ | 218 ($C_6H_6$) | 60 | $C_{17}H_7ClF_6O_2$ |
| 54 | 22 | 7-Cl, 2,4-$(CF_3)_2$ | 252 ($C_6H_6$) | 72 | $C_{17}H_7ClF_6O_2$[i] |
| 55 | 23 | 2,4,6-$(CF_3)_3$ | 215 ($C_6H_6$) | 52 | $C_{18}H_7F_9O_2$ |
| 56 | 24 | 5,7-$Cl_2$, 3-$CF_3$ | 284–286 (EtOH–dioxane) | 17 | $C_{16}H_7Cl_2F_3O_2$ |
| 57 | 25 | 6,7-$Cl_2$, 3-$CF_3$ | 339–340 (dioxane) | 45 | $C_{16}H_7Cl_2F_3O_2$[l] |
| 58 | 26 | 6,7-$Cl_2$, 2,4-$(CF_3)_2$ | 252–253 (AcOH) | 45 | $C_{17}H_6Cl_2F_6O_2$[j] |
| 59 | 27 | 2,3,4-$Br_3$, 6-$CF_3$ | 278–279 ($C_6H_6$) | 43 | $C_{16}H_6Br_3F_3O_2$[k] |

[a]The nitrocinnamic acids (Table III) were reduced to the corresponding amino derivs using method B ($FeSO_4$ + NaOH) of paper 1.[1] The resulting Na salts were subjected to Pschorr cyclization without purification. [b]These isomeric acids were sepd by fractional crystn from $C_6H_6$, the 4 isomer (29) being the less sol fraction. [c]See footnote *b*; 7 isomer less sol. [d]C: calcd, 59.20; found, 59.74. [e]Obtd as mixt and used as such in the pyridylation step at which stage isomer sepn was effected. [f]Cyclization of 6 gave a mixt of the isomeric acids 37 and 38. Isomer sepn was initially effected by repeated frac crystn from AcOH. It was later found more expedient to carry the mixt through to the target compds 145 and 146 and to make the sepn at that stage. [g]Sepn of 40 and 41 was carried out by extg 40 from the mixt with $Et_2O$. [h]C: calcd, 42.87; found, 43.35. [i]C: calcd, 51.90; found, 52.45. [j]Used without purification. [k]H: calcd, 1.15; found, 0.70. [l]H: calcd, 1.96; found, 2.72. [m]All compds were analyzed for C, H.

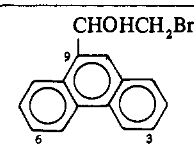
Table V. 9-Bromoacetylphenanthrenes



| No. | Substituents | Mp, °C (solvent)[a] | Yield, % |
|---|---|---|---|
| 91 | 2-$CF_3$ | 65–67 (petr ether) | 78 |
| 92 | 1-Br, 6-$CF_3$ | 168–170 (aq dioxane) | 71 |
| 93 | 2-Cl, 6-$CF_3$ | 172–173 ($CCl_4$) | 86 |
| 94 | 1,2-$Cl_2$, 6-$CF_3$ | 161–163 | 78 |
| 95 | 1,3-$Cl_2$, 6-$CF_3$ | 191.5–193 (EtOH–$C_6H_6$) | 62 |
| 96 | 2,4-$Cl_2$, 6-$CF_3$ | 164–165 (aq EtOH) | 49 |
| 97 | 2,4-$Br_2$, 6-$CF_3$ | 172–173 ($C_6H_6$-hexane) | 80 |
| 98 | 3,4-$Cl_2$, 6-$CF_3$ | 135–137 (EtOH) | 57 |
| 99 | 6,7-$Cl_2$, 3-$CF_3$ | 204–210 | 75 |
| 100 | 6,7-$Cl_2$, 2,4-$(CF_3)_2$ | 145–160 | 78 |
| 101 | 2,3,4-$Br_3$, 6-$CF_3$ | 117–119 (hexane) | 76 |

[a]Compds 94, 99, and 100 were used without purification. The remaining compds were crystd but used without analysis.

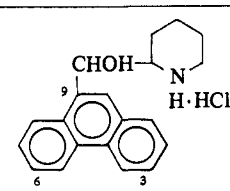
Table VI. α-Bromomethyl-9-phenanthrenemethanols



| No. | Substituents | Mp, °C (solvent) | Yield, % |
|---|---|---|---|
| 102 | 2-$CF_3$ | 115–120 | 100[a] |
| 103 | 1-Br, 6-$CF_3$ | 175–176 (EtOH) | 87[b] |
| 104 | 2-Cl, 6-$CF_3$ | 137 (EtOH) | 65[b,c] |
| 105 | 1,2-$Cl_2$, 6-$CF_3$ | 151–156 ($H_2O$ wash) | 81[a] |
| 106 | 1,3-$Cl_2$, 6-$CF_3$ | 172.5–174 (EtOH–$C_6H_6$) | 66[b,c] |
| 107 | 2,4-$Cl_2$, 6-$CF_3$ | 146–148 ($C_6H_6$-hexane) | 85[b] |
| 108 | 2,4-$Br_2$, 6-$CF_3$ | 130–135 | 84[a] |
| 109 | 3,4-$Cl_2$, 6-$CF_3$ | 140–142 (hexane) | 92[b] |
| 110 | 6,7-$Cl_2$, 3-$CF_3$ | 193–200 | 82[a] |
| 111 | 6,7-$Cl_2$, 2,4-$(CF_3)_2$ | 125–127 | 50[a] |
| 112 | 2,3,4-$Br_3$, 6-$CF_3$ | 138–143 ($H_2O$ wash) | 87[a] |

[a]Used without purification. [b]Used without analysis. [c]Isolated and used in the next step as the epoxide.

Table VII. α-(2-Piperidyl)-9-phenanthrenemethanol Hydrochlorides



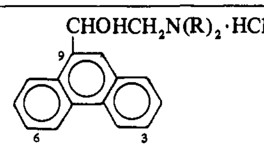
| No. | Substituents | Mp, °C (solvent) | Yield, % | Formula | Analyses |
|---|---|---|---|---|---|
| 113 | 2-$CF_3$ | 301–303 (aq MeOH) | 35 | $C_{21}H_{21}ClF_3NO$[a] | C, N, H[b] |
| 114 | 4-$CF_3$ | 270–272 (MeOH) | 37 | $C_{21}H_{21}ClF_3NO$ | C, H, N |
| 115 | 5-$CF_3$ | 305 (aq EtOH) | 50 | $C_{21}H_{21}ClF_3NO$ | H, N, C[c] |
| 116 | 7-$CF_3$ | 269–270 ($C_6H_6$–petr ether) | 55 | $C_{21}H_{21}ClF_3NO$[a] | H, N, C[d] |
| 117 | 2-Cl, 5-$CF_3$ | 304–305 (EtOH) | 56 | $C_{21}H_{20}Cl_2F_3NO$ | C, H, F, N |
| 118 | 2-Cl, 7-$CF_3$ | 292–293 ($Me_2CO$) | 64 | $C_{21}H_{20}Cl_2F_3NO$[a] | C, H, N |
| 119 | 7-Cl, 2-$CF_3$ | 327–329 (EtOH) | 58 | $C_{21}H_{20}Cl_2F_3NO$ | C, H, F, N |
| 120 | 7-Cl, 4-$CF_3$ | 312–313 (EtOH) | 58 | $C_{21}H_{20}Cl_2F_3NO$ | C, H, F, N |
| 121 | 2-Br, 6-$CF_3$ | 320–322 (aq EtOH) | 33 | $C_{21}H_{20}BrClF_3NO$ | C, H, F, N |
| 122 | 2-Cl, 6-$CF_3$ | 313 (aq EtOH) | 71 | $C_{21}H_{20}Cl_2F_3NO$ | C, H, N |
| 123 | 2,6-$(CF_3)_2$ | 302–304 (EtOH) | 75 | $C_{22}H_{20}ClF_6NO$ | H, N, C[e] |
| 124 | 4,6-$(CF_3)_2$ | 264–265 ($Me_2CO$) | 33 | $C_{22}H_{20}ClF_6NO$ | C, H, Cl, N |

Table VII. *Continued*

| No. | Substituents | Mp, °C (solvent) | Yield, % | Formula | Analyses |
|---|---|---|---|---|---|
| 125 | 3-$CH_3$, 6-$CF_3$ | 262-264 (EtOH) | 76 | $C_{22}H_{23}ClF_3NO$ | C, H, N |
| 126 | 3-COOH, 6-$CF_3$ | 320-321 (EtOH) | 68 | $C_{22}H_{21}ClF_3NO_3$[a] | C, H, N |
| 127 | 3-$SO_2CH_3$, 6-$CF_3$ | 316-318 (EtOH) | 44 | $C_{22}H_{23}ClF_3NO_3S$[a] | C, H, N |
| 128 | 7-Cl, 3-$CF_3$ | 329-330 (aq EtOH) | 69 | $C_{21}H_{20}Cl_2F_3NO$[a] | C, H, F, N |
| 129 | 1,2-$Cl_2$, 6-$CF_3$ | 350 (EtOH-10% HCl) | 42 | $C_{21}H_{19}Cl_3F_3NO$ | C, H, N |
| 130 | 1,3-$Cl_2$, 6-$CF_3$ | 326-327 (aq EtOH) | 23 | $C_{21}H_{19}Cl_3F_3NO$ | C, H, N |
| 131 | 1,3-$(CH_3)_2$, 6-$CF_3$ | 283-283.5 (EtOH-2% HCl) | 67 | $C_{23}H_{25}ClF_3NO$ | C, H, N |
| 132 | 1,3-$Br_2$, 6-$CF_3$ | 311-313 (MeOH) | 45 | $C_{21}H_{19}Br_2ClF_3NO$ | C, H, N |
| 133 | 2,3-$Cl_2$, 6-$CF_3$ | 325-327 (aq EtOH) | 36 | $C_{21}H_{19}Cl_3F_3NO$ | C, H, Cl, N |
| 134 | 2,3-$Br_2$, 6-$CF_3$ | 322-324 (EtOH) | 59 | $C_{21}H_{19}Br_2ClF_3NO$ | C, H, N |
| 135 | 2,4-$Cl_2$, 6-$CF_3$ | 325.5-327 (aq MeOH) | 53 | $C_{21}H_{19}Cl_3F_3NO$ | C, H, Cl, N |
| 136 | 3,4-$Cl_2$, 6-$CF_3$ | 294-295 (EtOH-10% HCl) | 68 | $C_{21}H_{19}Cl_3F_3NO$ | C, H, N |
| 137 | 6-Cl, 2,4-$(CF_3)_2$ | 327 (EtOH) | 68 | $C_{22}H_{19}Cl_2F_6NO$ | C, H, N |
| 138 | 7-Cl, 2,4-$(CF_3)_2$ | 338 (EtOH) | 67 | $C_{22}H_{19}Cl_2F_6NO$ | C, H, N |
| 139 | 2,4,6-$(CF_3)_3$ | 295-296 (EtOH) | 56 | $C_{23}H_{19}ClF_9NO$ | C, H, N |
| 140 | 5,7-$Cl_2$, 3-$CF_3$ | 301-303 (EtOH) | 65 | $C_{21}H_{19}Cl_3F_3NO$ | C, H, N |
| 141 | 6,7-$Cl_2$, 3-$CF_3$ | 345-346 (EtOH) | 66 | $C_{21}H_{19}Cl_3F_3NO$[f] | C, H, Cl, N |
| 142 | 6,7-$Cl_2$, 2,4-$(CF_3)_2$ | 332-334 (EtOH) | 63 | $C_{22}H_{18}Cl_3F_6NO$ | C, H, Cl, N |

[a]Isolated and analyzed as the hemihydrate. [b]H: calcd, 5.47; found, 6.11. [c]C: calcd, 63.71; found, 63.11. [d]C: calcd, 62.29; found, 61.65. [e]C: calcd, 56.97; found, 56.49. [f]Isolated and analyzed as the monohydrate. Also isolated was a hemihydrate (141A), mp 354-356°. *Anal.* C, H.

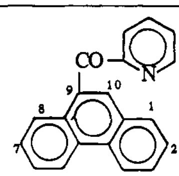
Table VIII. α-(Di-*n*-alkylaminomethyl)-9-phenanthrenemethanol Hydrochlorides




| No. | Substituents | R | Mp, °C (solvent) | Method[a] | Yield, % | Formula[b] |
|---|---|---|---|---|---|---|
| 143 | 2-$CF_3$ | Bu | 179-180 ($C_6H_6$-hexane) | B | 18 | $C_{25}H_{31}ClF_3NO$ |
| 144 | 1-Br, 6-$CF_3$ | Hep | 194-195 ($C_6H_6$-ligroin) | B | 44 | $C_{31}H_{42}BrClF_3NO$ |
| 145 | 2-Br, 6-$CF_3$ | Bu | 248-249 ($Me_2CO$) | A[d] | 13 | $C_{25}H_{30}BrClF_3NO$ |
| 146 | 4-Br, 6-$CF_3$ | Bu | 207-208 ($C_6H_6$) | A[d] | 13 | $C_{25}H_{30}BrClF_3NO$ |
| 147 | 2-Cl, 6-$CF_3$ | Bu | 253 ($Me_2CO$) | A | 63 | $C_{25}H_{30}Cl_2F_3NO$ |
| 148 | 2-Cl, 6-$CF_3$ | Hep | 226-227 ($Me_2CO$) | A | 35 | $C_{31}H_{42}Cl_2F_3NO$ |
| 149 | 1,2-$Cl_2$, 6-$CF_3$ | Bu | 239.5-241 ($C_6H_6$-hexane) | B | 27 | $C_{25}H_{29}Cl_3F_3NO$ |
| 150 | 1,3-$Cl_2$, 6-$CF_3$ | Bu | 263-264 (hexane-$CHCl_3$) | A | 41 | $C_{25}H_{29}Cl_3F_3NO$ |
| 151 | 1,3-$Cl_2$, 6-$CF_3$ | Hep | 223-225 (aq EtOH) | A | 38 | $C_{31}H_{41}Cl_3F_3NO$ |
| 152 | 2,4-$Cl_2$, 6-$CF_3$ | Bu | 235-236 ($C_6H_6$) | B | 29 | $C_{25}H_{29}Cl_3F_3NO$ |
| 153 | 2,4-$Br_2$, 6-$CF_3$ | Bu | 236-236.5 ($C_6H_6$) | B | 24 | $C_{25}H_{29}Br_2ClF_3NO$ |
| 154 | 3,4-$Cl_2$, 6-$CF_3$ | Pr | 234-235 (EtOH-10% HCl) | B | 48 | $C_{23}H_{25}Cl_3F_3NO$ |
| 155 | 3,4-$Cl_2$, 6-$CF_3$ | Bu | 191-192 ($C_6H_6$-hexane) | B | 22 | $C_{25}H_{29}Cl_3F_3NO$ |
| 156 | 3,4-$Cl_2$, 6-$CF_3$ | Am | 140-142 ($C_6H_6$-hexane) | B | 18 | $C_{27}H_{33}Cl_3F_3NO$[c] |
| 157 | 3,4-$Cl_2$, 6-$CF_3$ | Hep | 128-130 ($C_6H_6$-hexane) | B | 17 | $C_{31}H_{41}Cl_3F_3NO$ |
| 158 | 6,7-$Cl_2$, 3-$CF_3$ | Pr | 282-283 (EtOH) | B | 81 | $C_{23}H_{25}Cl_3F_3NO$ |
| 159 | 6,7-$Cl_2$ 2,4-$(CF_3)_2$ | Pr | 222-223 ($Me_2CO$-ligroin) | B | 85 | $C_{24}H_{24}Cl_3F_6NO$ |
| 160 | 2,3-$Br_2$, 6-$CF_3$[e] | Bu | 234-235 ($C_6H_6$) | B | 23 | $C_{25}H_{29}Br_2ClF_3NO$ |

[a]Methods A and B used epoxides and bromohydrins, respectively, as starting materials. [b]All compds were analyzed for C, H, N. [c]C: calcd, 58.86; found, 59.36. H: calcd, 6.04; found, 5.54. [d]Isomers sepd by frac crystn from $C_6H_6$. [e]This compd was obtd when 4-debromination occurred during routine treatment of 112 with $Bu_2NH$.

Table IX. 2-Pyridyl 9-Phenanthryl Ketones




| No. | Substituents | Mp, °C (solvent) | Yield, % | Formula[a] |
|---|---|---|---|---|
| 60 | 2-$CF_3$ | 121-123 (petr ether) | 76 | $C_{21}H_{12}F_3NO$ |
| 61 | 4-$CF_3$ | 114-115 (hexane) | 70 | $C_{21}H_{12}F_3NO$ |
| 62 | 5-$CF_3$ | 115-116 (hexane) | 50 | $C_{21}H_{12}F_3NO$ |
| 63 | 7-$CF_3$ | 139-141 (aq EtOH) | 49 | $C_{21}H_{12}F_3NO$ |
| 64 | 2-Cl, 5-$CF_3$ | 147-148 (EtOH) | 72 | $C_{21}H_{11}ClF_3NO$ |
| 65 | 2-Cl, 7-$CF_3$ | 201-202 (EtOH) | 52 | $C_{21}H_{11}ClF_3NO$ |
| 66 | 7-Cl, 2-$CF_3$ | 193-194 (EtOH)[b] | 34 | $C_{21}H_{11}ClF_3NO$ |
| 67 | 7-Cl, 4-$CF_3$ | 142-153 (EtOH)[b] | 25 | $C_{21}H_{11}ClF_3NO$ |
| 68 | 2-Br, 6-$CF_3$ | 215-217 (aq EtOH) | 73 | $C_{21}H_{11}BrF_3NO$ |

Table IX. *Continued*

| No. | Substituents | Mp, °C (solvent) | Yield, % | Formula[a] |
|---|---|---|---|---|
| 69 | 2-Cl, 6-$CF_3$ | 205 (EtOH-$C_6H_6$) | 42 | $C_{21}H_{11}ClF_3NO$ |
| 70 | 2,6-$(CF_3)_2$ | 226-227 (EtOH) | 54 | $C_{22}H_{11}F_6NO$ |
| 71 | 4,6-$(CF_3)_2$ | 166-167.5 (EtOH) | 53 | $C_{22}H_{11}F_6NO$ |
| 72 | 3-$CH_3$, 6-$CF_3$ | 209-210 ($C_6H_6$) | 36 | $C_{22}H_{14}F_3NO$ |
| 73 | 3-COOH, 6-$CF_3$ | 275-278 (EtOH) | *d* | $C_{22}H_{12}F_3NO_3$ |
| 74 | 3-$SO_2CH_3$, 6-$CF_3$ | 250-252 (EtOH) | 88 | $C_{22}H_{14}F_3NO_3S$[c] |
| 75 | 7-Cl, 3-$CF_3$ | 231-232 (aq $Me_2CO$) | 60 | $C_{21}H_{11}ClF_3NO$ |
| 76 | 1,2-$Cl_2$, 6-$CF_3$ | 227-228 (EtOH) | 75 | $C_{21}H_{10}Cl_2F_3NO$ |
| 77 | 1,3-$Cl_2$, 6-$CF_3$ | 233-234 (aq $Me_2CO$) | 63 | $C_{21}H_{10}Cl_2F_3NO$ |
| 78 | 1,3-$(CH_3)_2$, 6-$CF_3$ | 187-188 (EtOH) | 60 | $C_{23}H_{16}F_3NO$ |
| 79 | 1,3-$Br_2$, 6-$CF_3$ | 237-238 ($C_6H_6$) | 40 | $C_{21}H_{10}Br_2F_3NO$ |
| 80 | 2,3-$Cl_2$, 6-$CF_3$ | 251-254 ($C_6H_6$) | 69 | $C_{21}H_{10}Cl_2F_3NO$ |
| 81 | 2,3-$Br_2$, 6-$CF_3$ | 248-250 ($C_6H_6$) | 16 | $C_{21}H_{10}Br_2F_3NO$ |
| 82 | 2,4-$Cl_2$, 6-$CF_3$ | 211-212 (aq $Me_2CO$) | 67 | $C_{21}H_{10}Cl_2F_3NO$ |
| 83 | 2,4-$Br_2$, 6-$CF_3$ | *e* | | $C_{21}H_{10}Br_2F_3NO$ |
| 84 | 3,4-$Cl_2$, 6-$CF_3$[f] | 176-177 (EtOH) | 45 | $C_{21}H_{10}Cl_2F_3NO$ |
| 85 | 6-Cl, 2,4-$(CF_3)_2$ | 188 (EtOH-$C_6H_6$) | 51 | $C_{22}H_{10}ClF_6NO$ |
| 86 | 7-Cl, 2,4-$(CF_3)_2$ | 187 ($C_6H_6$) | 26 | $C_{22}H_{10}ClF_6NO$ |
| 87 | 2,4,6-$(CF_3)_3$ | 134 (hexane) | 36 | $C_{23}H_{10}F_9NO$ |
| 88 | 5,7-$Cl_2$, 3-$CF_3$ | 174-177 ($H_2O$ wash) | 59 | $C_{21}H_{10}Cl_2F_3NO$[g] |
| 89 | 6,7-$Cl_2$, 6-$CF_3$ | 265-268 | 76 | $C_{21}H_{10}Cl_2F_3NO$[g] |
| 90 | 6,7-$Cl_2$, 2,4-$(CF_3)_2$ | 223-227 | 33 | $C_{22}H_9Cl_2F_6NO$[g] |

[a]All compds were analyzed for C, H, N except 65 which was analyzed for C, H, Cl. [b]The crude reac prod deposited 66 from EtOH. Concn of the filt provided 67. These compds were used without analyses. [c]Pyridylation of the Et ester of 43 was more effective than pyridylation of 43 itself; mp of the ester, 217-218° (EtOH). *Anal.* ($C_{19}H_{15}F_3O_4S$) C, H. 74 was used without analysis. [d]Obtd by oxidizing 72 (Experimental Section). [e]Attempted synthesis of this compd (83) *via* pyridylation of 52 in THF gave only the 4-debrominated compd (68). [f]We are grateful to Dr. Richard E. Strube of the Walter Reed Army Institute of Research for providing the starting material 3,4-dichloro-6-trifluoromethylphenanthrene-9-carboxylic acid. [g]Used without crystn.

fluoromethyl)benzoic acid (52 g, 0.2 mole) (Pierce Chemical Co.) and $SOCl_2$ (118 g, 1 mole) was heated at reflux for 2 hr. Excess $SOCl_2$ was removed under reduced pressure, the residual acid chloride was dissolved in diglyme (200 ml) and the soln was cooled to −70°. A soln of LiAl(*tert*-OBu)$_3$H (48.3 g, 0.19 mole) in diglyme (200 ml) was added dropwise during 1 hr. The reaction was allowed to warm to room temp and poured into 10% HCl (1.4 l.). Vac distn of the resulting oil gave 32.5 g (72%) of the aldehyde, bp 47-48° (0.2 mm), which was analyzed as the oxime; mp 86-87° (hexane). *Anal.* ($C_9H_5F_6NO$) C, H, N.

2-Pyridyl 3-Carboxy-6-trifluoromethyl-9-phenanthryl Ketone (73). Routine treatment of 72 (Table IX) with $CrO_3$-$H_2SO_4$ gave 58% of 2-pyridyl 3-formyl-6-trifluoromethyl-9-phenanthryl ketone; mp 195-196° (EtOH). *Anal.* ($C_{22}H_{12}F_3NO_2$) C, H, N. Oxidn of this aldehyde with $KMnO_4$ in aqueous $Me_2CO$ (2 hr, 25°) afforded 60% of 73.

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