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Syntheses of N-(2-Hexahydropyrimidinoethyl)propionanilides[1]

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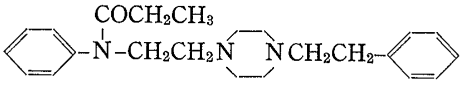
N-(2-Hexahydropyrimidinoethyl)anilines (**6a**—**f**) were prepared by the condensation of N-(β-bromoethyl)aniline hydrobromide and hexahydropyrimidines. They were further converted to N-(2-hexahydropyrimidinoethyl)propionanilides by N-propionylation.

The analgesic activities of the twelve compounds thus obtained were examined by subcutaneous administration to mice.

Among the propionanilides, the N-isopropyl- and N-benzylhexahydropyrimidine derivatives (**7c**, **e**) possessed *ca.* 1/3 and 1/6 of the analgesic effect of pentazocine, respectively, and **7e** showed a lower toxicity. On the other hand, the N-phenethyl derivative (**7f**) was inactive.

Keywords——syntheses of analgesics; N-(2-hexahydropyrimidinoethyl)propionanilides; N-(β-bromoethyl)aniline hydrobromide; hexahydropyrimidines; N-propionylation

In the previous paper[3] we reported the syntheses and analgesic activities of N-(2-piperazinoethyl)propionanilides and showed that N-[2-(4-phenethylpiperazino)ethyl]propionanilide (**1**) and N-[2-(3-methyl-4-phenethylpiperazino)ethyl]propionanilide (**2**) possessed *ca.* 1/2 of the analgesic effect of pentazocine.



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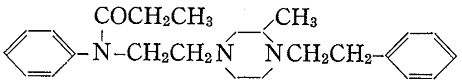

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In general, potent analgesics tend to have potent undesirable side effects, including toxicity. Therefore, a new compound with weak side effects is of interest, even if it has a weak analgesic activity. Some work has been done on the synthesis of the hexahydropyrimidine analog of phenampromid, N-(1-methyl-2-piperidinoethyl)propionanilide.[4] Further, the *tert*-amino group of phenampromid is known to play an important role in the pharmacological effects.[5] Thus, the two nitrogen atoms of hexahydropyrimidines might also result in important pharmacological effects of these compounds. In this paper, the syntheses and analgesic activities of N-(2-hexahydropyrimidinoethyl)propionanilides (**7a**—**f**) are reported.

According to the previously outlined procedures,[6a] 1-ethyl- (**4b**), 1-benzyl- (**4e**). 1-phenethyl- (**4f**) and 1-cyclohexyl-hexahydropyrimidine (**4g**) were prepared by ring closures of the corresponding trimethylenediamines (**3b**,[7a] **3e**,[7b] **3f**,[7c] **3g**[7b]) with formaldehyde as shown in Chart 1.

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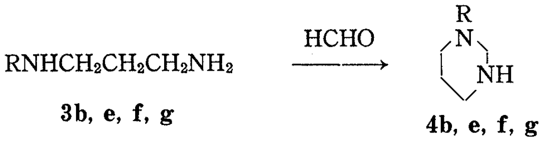


3b, e, f, g

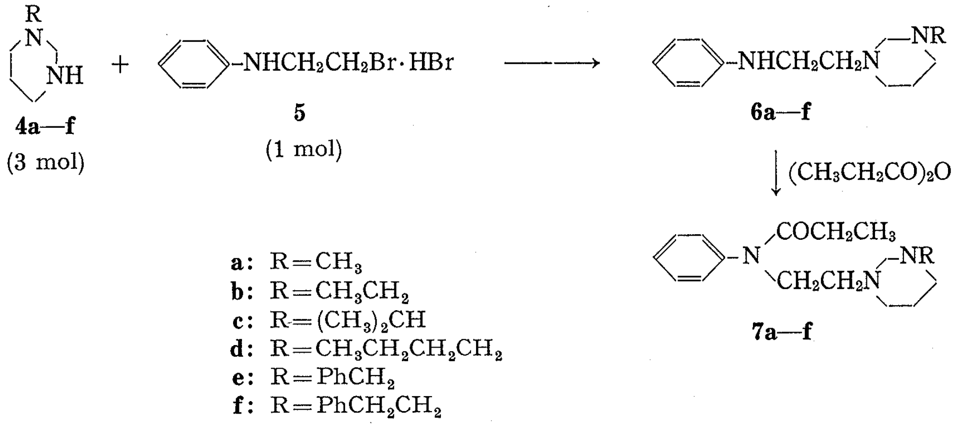
4b, e, f, g

b: $R=CH_3CH_2$
e: $R=PhCH_2$
f: $R=PhCH_2CH_2$
g: $R=c\text{-}C_6H_{11}$

Chart 1

Similarly, 1-methyl- (**4a**),[6b] 1-isopropyl- (**4c**)[6c] and 1-*n*-butyl-hexahydropyrimidine (**4d**)[6a] were used as starting materials for the following syntheses.

Analogously to the synthesis of the similar piperazine derivatives,[3] N-(2-hexahydropyrimidinoethyl)anilines (**6a**—**f**) were prepared by the condensation of the above obtained hexahydropyrimidines (**4a**—**f**) with N-(β-bromoethyl)aniline hydrobromide (**5**) (mole ratio 3: 1) as shown in Chart 2. The recovery of excess hexahydropyrimidines ranged from 70 to 90%. However, the condensation of **4a**—**f** and **5** (mole ratio 1: 1) in alcohol or absolute benzene in the presence of potassium carbonate, sodium carbonate or precipitated calcium carbonate failed to give **6a**—**f**. Under these conditions, high-boiling unknown products were formed.



4a—**f**
(3 mol)

5
(1 mol)

6a—**f**

$(CH_3CH_2CO)_2O$

7a—**f**

a: $R=CH_3$
b: $R=CH_3CH_2$
c: $R=(CH_3)_2CH$
d: $R=CH_3CH_2CH_2CH_2$
e: $R=PhCH_2$
f: $R=PhCH_2CH_2$

Chart 2

N-Propionylation of **6a**—**f** was not as smooth as in the case of piperazine analogs.[3] Namely, neither N-propionylation by propionic anhydride without a solvent, nor the reaction of propionyl chloride (mole ratio 1: 1) in absolute benzene in the presence of potassium carbonate or sodium carbonate gave the desired propionanilides (**7a**—**f**). Finally, they were obtained in unsatisfactory yields (21—24%) by the reaction of propionic anhydride (mole ratio 1: 1) in absolute benzene.

Pharmacological Results

The twelve oxalates (**6**, **7a**—**f**) described above were examined by subcutaneous administration to mice for analgesic activity in terms of the inhibition of writhing induced by acetic acid[8] in comparison with pentazocine. These compounds were also tested for acute toxicity in mice (*s.c.*). These pharmacological results are listed in Table I.

The conclusions can be summarized as follows.

(1) Among the twelve oxalates, four oxalates (**6c**, **6e**, **7c**, **7e**) exhibited over 44% inhibition at 30 mg/kg *s.c.*

(2) The N-isopropylhexahydropyrimidine derivative (**7c**) possessed *ca.* 1/3 of the analgesic effect of pentazocine.

(3) N-Propionylation increased the analgesic activity, except for **7b** and **7d**.

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Table I. Analgesic Activity

Compd. No.	Route[a)]	mg/kg	Inhibition (%) of writhing	Toxicity mg/kg (*s.c.*)
6a	*s.c.*	30	31	300 Sedation, mydriasis
6b	*s.c.*	30	40	300 Sedation, mydriasis
6c	*s.c.*	30	47	300 Convulsion, sedation, mydriasis
6d	*s.c.*	30	37	100 Sedation, mydriasis
6e	*s.c.*	30	44	300 Sedation, mydriasis
6f	*s.c.*	30	0	300 Sedation, mydriasis, trembling
7a	*s.c.*	30	32	100 Sedation
7b	*s.c.*	30	0	100 Sedation
7c	*s.c.*	10	17	30 Sedation, mydriasis
	s.c.	30	97	
7d	*s.c.*	30	0	300 Sedation
7e	*s.c.*	30	47	300 Normality
7f	*s.c.*	30	0	30 Sedation
Pentazocine	*s.c.*	5	32	150 Convulsion, mydriasis, trembling
	s.c.	10	81	

a) subcutaneous administration.

(4) The N-phenethylhexahydropyrimidine derivative (**7f**) was inactive, whereas the N-phenethylpiperazine derivatives (**1**) and (**2**) possessed *ca.* 1/2 of the analgesic effect of pentazocine.

(5) Among these compounds, the N-benzylhexahydropyrimidine derivative (**7e**) showed low toxicity, and no mice died even after the subcutaneous administration of 300 mg/kg.

Experimental

All melting and boiling points are uncorrected. IR spectra were recorded on a Hitachi 215 spectrometer or a Hitachi 260-10 spectrometer and ^{1}H-NMR spectra on a Varian A-60 spectrometer or a JEOL JNM-PMX 60 spectrometer operating at 60 MHz in $CDCl_3$ solution with tetramethylsilane or in D_2O solution with sodium 3-(trimethylsilyl)-propionate-d_4 as an internal standard. Mass spectra were determined with a JEOL JMS-01SG-2 mass spectrometer.

Hexahydropyrimidines——1-Ethylhexahydropyrimidine (**4b**): A solution of N-ethyltrimethylenediamine (10 g) in H_2O (19 ml) was neutralized with c-HCl and N-ethyltrimethylenediamine (9 g) was added. An aqueous solution of 37% formaldehyde (15 g) was added dropwise over a period of 30 min. The reaction mixture was stirred for 1 hr at room temperature and then NaOH pellets (37.2 g) were added. The precipitate was removed by filtration and the filtrate was concentrated to dryness *in vacuo*. The oily residue was distilled under reduced pressure to give **4b** (13.6 g, 64.0% yield) as a colorless liquid, bp 65° (25 mmHg). IR ν_{max}^{Film} cm^{-1}: 3225 (NH), 2900 (CH_2). NMR ($CDCl_3$) δ: 1.07 (3H, t, $J=7$ Hz, $NCH_2\underline{CH_3}$), 1.61 (2H, m, $NCH_2\underline{CH_2}CH_2N$), 2.32 (1H, s, NH), 3.38 (2H, s, NCH_2N). MS *m/e*: 113 (M^+-H). Oxalate: mp 197° (MeOH–H_2O). *Anal.* Calcd for $C_6H_{14}N_2 \cdot 2C_2H_2O_4 \cdot 3/2H_2O$: C, 37.38; H, 6.54; N, 8.72. Found: C, 37.36; H, 6.65; N, 8.82.

1-Benzylhexahydropyrimidine (**4e**): N-Benzyltrimethylenediamine (21 g) was converted into **4e** (12 g, 53.2% yield) by the method described above (c.f. **4b**): Colorless liquid, bp 108—110° (5 mmHg). IR ν_{max}^{Film} cm^{-1}: 3200 (NH), 2900 (CH_2). NMR ($CDCl_3$) δ: 1.82 (1H, s, NH), 3.40 (2H, s, NCH_2N), 7.28 (5H, s, $NCH_2\underline{Ph}$). MS *m/e*: 175 (M^+-H). Oxalate: mp 215° (MeOH–H_2O). *Anal.* Calcd for $C_{11}H_{16}N_2 \cdot 2C_2H_2O_4 \cdot H_2O$: C, 48.13; H, 5.88; N, 7.49. Found: C, 48.18; H, 6.01; N, 7.76.

1-Phenethylhexahydropyrimidine (**4f**): N-Phenethyltrimethylenediamine (18 g) was converted into **4f** (11 g, 57.2% yield) by the method described above (c.f. **4b**): Colorless liquid, bp 139—141° (5 mmHg). IR ν_{max}^{Film} cm^{-1}: 3200 (NH), 2910 (CH_2), 700 (benzene nucleus). NMR ($CDCl_3$) δ: 1.93 (1H, s, NH), 3.43 (2H, s, NCH_2N), 7.21 (5H, s, $NCH_2CH_2\underline{Ph}$). MS *m/e*: 189 (M^+-H). Oxalate: mp 211° (MeOH–H_2O). *Anal.* Calcd for $C_{12}H_{18}N_2 \cdot 2C_2H_2O_4 \cdot 1/2H_2O$: C, 50.66; H, 6.07; N, 7.39. Found: C, 50.24; H, 6.37; N, 7.79.

1-Cyclohexylhexahydropyrimidine (**4g**): N-Cyclohexyltrimethylenediamine (18 g) was converted into **4g** (11 g, 56.7% yield) by the method described above (c.f. **4b**): Colorless liquid, bp 100° (5 mmHg). IR ν_{max}^{Film} cm^{-1}: 3200 (NH), 2875 (CH_2). NMR ($CDCl_3$) δ: 1.82 (1H, s, NH), 3.55 (2H, s, NCH_2N). MS *m/e*: 167 (M^+-H). Oxalate: mp 217° (MeOH–H_2O). *Anal.* Calcd for $C_{10}H_{20}N_2 \cdot 2C_2H_2O_4 \cdot H_2O$: C, 45.90; H, 7.10; N, 7.65. Found: C, 45.44; H, 7.31; N, 7.95.

N-(2-Hexahydropyrimidinoethyl)anilines——N-[2-(3-Methylhexahydropyrimidino)ethyl]aniline (**6a**): A mixture of 1-methylhexahydropyrimidine (32 g), N-(β-bromoethyl)aniline hydrobromide (30 g) and EtOH (300 ml) was refluxed for 4 hr. The mixture was concentrated to dryness *in vacuo* and the residue was dissolved in H_2O (40 ml). The solution was made alkaline with 15% aqueous NaOH solution and extracted with $CHCl_3$. The $CHCl_3$ extract was dried over $MgSO_4$ and concentrated *in vacuo*. The oily residue was distilled under reduced pressure to give a first fraction, 1-methylhexahydropyrimidine (15 g, recovery 70.3% yield): bp 39° (47 mmHg); and a second, **6a** (19.2 g, 82.1% yield) as a colorless liquid: bp 117° (0.07 mmHg). IR $\nu_{\max}^{\text{Film}}$ cm^{-1}: 1598 (benzene nucleus). NMR ($CDCl_3$) δ: 2.21 (3H, s, NCH_3), 3.07 (2H, s, NCH_2N), 4.42 (1H, broad s, NH). MS *m/e*: 219 (M^+). Oxalate: mp 208° (EtOH–H_2O). *Anal.* Calcd for $C_{13}H_{21}N_3 \cdot 2C_2H_2O_4 \cdot H_2O$: C, 48.92; H, 6.48; N, 10.07. Found: C, 48.49; H, 6.19; N, 9.94.

N-[2-(3-Ethylhexahydropyrimidino)ethyl]aniline (**6b**): A mixture of 1-ethylhexahydropyrimidine (**4b**) (3.65 g), N-(β-bromoethyl)aniline hydrobromide (**5**) (3 g) and EtOH (30 ml) was refluxed for 4 hr. The mixture was treated in the manner described above (c.f. **6a**) to give **4b** (1.989 g, recovery 81.7% yield) and **6b** (1.832 g, 73.6% yield). **6b**: Colorless liquid, bp 140° (0.4 mmHg). IR $\nu_{\max}^{\text{Film}}$ cm^{-1}: 1600 (benzene nucleus). NMR ($CDCl_3$) δ: 1.08 (3H, t, $J=7$ Hz, $NCH_2\underline{CH_3}$), 3.14 (2H, s, NCH_2N), 4.38 (1H, broad s, NH). MS *m/e*: 233 (M^+). Oxalate: mp 218—219° (MeOH–H_2O). *Anal.* Calcd for $C_{14}H_{23}N_3 \cdot 2C_2H_2O_4 \cdot 3/2H_2O$: C, 49.09; H, 6.82; N, 9.54. Found: C, 49.18; H, 6.69; N, 9.61.

N-[2-(3-Isopropylhexahydropyrimidino)ethyl]aniline (**6c**): A mixture of 1-isopropylhexahydropyrimidine (**4c**) (15.5 g), **5** (11.3 g) and EtOH (110 ml) was refluxed for 4 hr. The mixture was treated in the manner described above (c.f. **6a**) to give **4c** (7.75 g, recovery 75.0% yield) and **6c** (8.7 g, 87.6% yield). **6c**: Colorless liquid, bp 154° (1 mmHg). IR $\nu_{\max}^{\text{Film}}$ cm^{-1}: 1600 (benzene nucleus). NMR ($CDCl_3$) δ: 1.04 (6H, d, $J=7$ Hz, $NCH(\underline{CH_3})_2$), 3.23 (2H, s, NCH_2N), 4.35 (1H, broad s, NH). MS *m/e*: 247 (M^+). Oxalate: mp 228—229° (MeOH–H_2O). *Anal.* Calcd for $C_{15}H_{25}N_3 \cdot 2C_2H_2O_4 \cdot 1/2H_2O$: C, 52.30; H, 6.88; N, 9.63. Found: C, 52.03; H, 7.09; N, 9.88.

N-[2-(3-*n*-Butylhexahydropyrimidino)ethyl]aniline (**6d**): A mixture of 1-*n*-butylhexahydropyrimidine (**4d**) (3 g), **5** (2 g) and EtOH (20 ml) was refluxed for 4 hr. The mixture was treated in the manner described above (c.f. **6a**) to give **4d** (0.804 g, recovery 80.4% yield) and **6d** (1.208 g, 65.0% yield). **6d**: Colorless liquid, bp 143° (0.3 mmHg). IR $\nu_{\max}^{\text{Film}}$ cm^{-1}: 1598 (benzene nucleus). NMR ($CDCl_3$) δ: 0.90 (3H, This triplet signal was poorly defined. CH_3), 3.15 (2H, s, NCH_2N), 4.30 (1H, broad s, NH). MS *m/e*: 261 (M^+). Oxalate: mp 223° (H_2O). *Anal.* Calcd for $C_{16}H_{27}N_3 \cdot 2C_2H_2O_4 \cdot H_2O$: C, 52.29; H, 7.19; N, 9.15. Found: C, 52.25; H, 7.45; N, 9.35.

N-[2-(3-Benzylhexahydropyrimidino)ethyl]aniline (**6e**): A mixture of 1-benzylhexahydropyrimidine (**4e**) (3.76 g), **5** (2 g) and EtOH (20 ml) was refluxed for 4 hr. The mixture was treated in the manner described above (c.f. **6a**) to give **4e** (1.955 g, recovery 78.0% yield) and **6e** (1.21 g, 57.6% yield). **6e**: Colorless liquid, bp 189° (0.8 mmHg). IR $\nu_{\max}^{\text{Film}}$ cm^{-1}: 1597 (benzene nucleus). NMR ($CDCl_3$) δ: 3.20 (2H, s, NCH_2N), 4.25 (1H, broad s, NH), 7.30 (5H, s, $NCH_2\underline{Ph}$). MS *m/e*: 295 (M^+). Oxalate: mp 228—228.5° (dioxane–H_2O). *Anal.* Calcd for $C_{19}H_{25}N_3 \cdot 2C_2H_2O_4 \cdot 1/2H_2O$: C, 57.02; H, 6.20; N, 8.68. Found: C, 56.82; H, 6.24; N, 8.90.

N-[2-(3-Phenethylhexahydropyrimidino)ethyl]aniline (**6f**): A mixture of 1-phenethylhexahydropyrimidine (**4f**) (4.06 g), **5** (2 g) and EtOH (20 ml) was refluxed for 4 hr. The mixture was treated in the manner described above (c.f. **6a**) to give **4f** (2.37 g, recovery 87.6% yield) and **6f** (1.283 g, 58.3% yield). **6f**: Colorless liquid, bp 177° (0.4 mmHg). IR $\nu_{\max}^{\text{Film}}$ cm^{-1}: 1599 (benzene nucleus). NMR ($CDCl_3$) δ: 3.21 (2H, s, NCH_2N), 4.01 (1H, broad s, NH), 7.21 (5H, s, $NCH_2CH_2\underline{Ph}$). MS *m/e*: 309 (M^+). Oxalate: mp 204—205° (dioxane–H_2O). *Anal.* Calcd for $C_{20}H_{27}N_3 \cdot 2C_2H_2O_4 \cdot 1/2H_2O$: C, 57.83; H, 6.43; N, 8.43. Found: C, 57.61; H, 6.50; N, 8.36.

N-(2-Hexahydropyrimidinoethyl)propionanilides——N-[2-(3-Methylhexahydropyrimidino)ethyl]propionanilide (**7a**): A mixture of **6a** (5 g), propionic anhydride (3 g) and absolute benzene (40 ml) was refluxed for 3 hr. The mixture was concentrated to dryness *in vacuo*, then the residue was made acidic with 20% aqueous HCl solution and washed with Et_2O. The acidic aqueous solution was made alkaline with 15% aqueous NaOH solution and extracted with Et_2O. The Et_2O extract was dried over $MgSO_4$ and concentrated to dryness. The oily residue was distilled under reduced pressure to give crude **7a** (3.5 g), bp 164° (0.7 mmHg). Crude **7a** (3.5 g) was subjected to silica gel column chromatography with MeOH–$CHCl_3$ (1 : 10) to afford a pale yellow oil **7a** (2.4 g): IR $\nu_{\max}^{\text{Film}}$ cm^{-1}: 1643 (C=O). NMR ($CDCl_3$) δ: 1.02 (3H, t, $J=7$ Hz, $NCOCH_2\underline{CH_3}$), 2.20 (3H, s, NCH_3), 3.09 (2H, s, NCH_2N), 3.86 (2H, t, $J=8$ Hz, $PhN\underline{CH_2}$).

A solution saturated with oxalic acid (anhydrous) in absolute Et_2O was added dropwise to a mixture of the oil (2.4 g) and absolute Et_2O (30 ml). The resulting finely dispersed crystals were collected by filtration. The crystals were washed with absolute Et_2O, dried and recrystallized from MeOH–H_2O to give **7a** oxalate (2.3 g, 22.9% yield) as a colorless powder, mp 187° (MeOH–H_2O). MS *m/e*: 275 (M^+). *Anal.* Calcd for $C_{16}H_{25}N_3O \cdot 2C_2H_2O_4 \cdot 1/2H_2O$: C, 51.72; H, 6.47; N, 9.05. Found: C, 51.51; H, 6.55; N, 9.31.

N-[2-(3-Ethylhexahydropyrimidino)ethyl]propionanilide (**7b**): A mixture of **6b** (1.5 g), propionic anhydride (0.84 g) and absolute benzene (12 ml) was refluxed for 3 hr. The mixture was treated in the manner described above (c.f. **7a**) without distillation under reduced pressure to give **7b** oxalate (0.659 g, 21.4% yield) as a colorless powder, mp 190—191° (MeOH–H_2O). IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 1640 (C=O). NMR (D_2O) δ: 0.99 (3H, t, $J=7$ Hz, $NCOCH_2\underline{CH_3}$), 1.33 (3H, t, $J=7$ Hz, $NCH_2\underline{CH_3}$). MS *m/e*: 289 (M^+). *Anal.* Calcd for $C_{17}H_{27}N_3O \cdot 2C_2H_2O_4 \cdot 1/2H_2O$: C, 52.72; H, 6.69; N, 8.79. Found: C, 52.53; H, 6.73; N, 9.02.

N-[2-(3-Isopropylhexahydropyrimidino)ethyl]propionanilide (**7c**): A mixture of **6c** (1.5 g), proiponic anhydride (0.79 g) and absolute benzene (12 ml) was refluxed for 3 hr. The mixture was treated in the manner described above (c.f. **7a**) without distillation under reduced pressure to give **7c** oxalate (0.630 g, 21.1% yield) as a colorless powder, mp 195° (MeOH–H_2O). MS *m/e*: 303 (M^+). *Anal.* Calcd for $C_{18}H_{29}N_3O \cdot 2C_2H_2O_4 \cdot 1/2H_2O$: C, 53.66; H, 6.91; N, 8.54. Found: C, 53.40; H, 6.99; N, 8.77. Free base: IR $\nu_{\max}^{\text{Film}}$ cm^{-1}: 1620 (C=O). NMR ($CDCl_3$) δ: 1.14 (9H, t, $J=7$ Hz, $NCOCH_2\underline{CH_3}$ and $NCH(\underline{CH_3})_2$ were overlapping.), 4.01 (2H, s, NCH_2N).

N-[2-(3-*n*-Butylhexahydropyrimidino)ethyl]propionanilide (**7d**): A mixture of **6d** (1.7 g), propionic anhydride (0.85 g) and absolute benzene (14 ml) was refluxed for 3 hr. The mixture was treated in the manner described above (c.f. **7a**) without distillation under reduced pressure to give **7d** oxalate (0.696 g, 21.1% yield) as a colorless powder, mp 217—218° (H_2O). IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 1625 (C=O). NMR (D_2O) δ: Exact values could not be determined because of broadening or overlapping. MS *m/e*: 317 (M^+). *Anal.* Calcd for $C_{19}H_{31}N_3O \cdot 2C_2H_2O_4 \cdot 1/2H_2O$: C, 54.55; H, 7.11; N, 8.30. Found: C, 54.52; H, 7.46; N, 8.47.

N-[2-(3-Benzylhexahydropyrimidino)ethyl]propionanilide (**7e**): A mixture of **6e** (0.5 g), propionic anhydride (0.22 g) and absolute benzene (4 ml) was refluxed for 3 hr. The mixture was treated in the manner described above (c.f. **7a**) without distillation under reduced pressure to give **7e** oxalate (0.225 g, 24.6% yield) as a colorless powder, mp 201—202° (MeOH–H_2O). IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 1640 (C=O). NMR (D_2O) δ: Exact values could not be determined because of broadening or overlapping. MS *m/e*: 351 (M^+). *Anal.* Calcd for $C_{22}H_{29}N_3O \cdot 2C_2H_2O_4 \cdot 1/2H_2O$: C, 57.78; H, 6.29; N, 7.78. Found: C, 57.73; H, 6.49; N, 8.08.

N-[2-(3-Phenethylhexahydropyrimidino)ethyl]propionanilide (**7f**): A mixture of **6f** (1.0 g), propionic anhydride (0.42 g) and absolute benzene (8 ml) was refluxed for 3 hr. The mixture was treated in the manner described above (c.f. **7a**) without distillation under reduced pressure to give **7f** oxalate (0.433 g, 23.8% yield) as a colorless powder, mp 178—180° (MeOH–H_2O). IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 1640 (C=O). NMR (D_2O) δ: 1.46 (3H, t, $J=7$ Hz, $NCOCH_2\underline{CH_3}$). MS *m/e*: 365 (M^+). *Anal.* Calcd for $C_{23}H_{31}N_3O \cdot 2C_2H_2O_4 \cdot H_2O$: C, 57.55; H, 6.57; N, 7.46. Found: C, 57.50; H, 6.57; N, 7.68.

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