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Studies on the Morphine Alkaloids and Its Related Compounds. XVIII.[1] Syntheses of N-Substituted-morphinan Dihydronormethines and O-Alkylisoureas related to Morphinan, Norpethidine, or Phenethylamine

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Syntheses and pharmacological observations of the N-substituted-morphinan dihydronormethines and the O-alkyl-isoureas related to morphinan, norpethidine, or phenethylamine with interest to the basic center in the molecules were described.

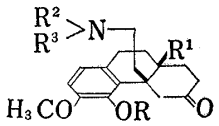
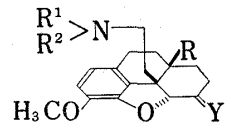
As the results of the studies on α- or β-morphimethines and its hydro-derivatives, it has been reported that the bond–cleavage between 9- and 17-positions in the morphinan-skeleton causes a marked decrease of the analgesic activity.[3] But on the 14-hydroxy-morphinan dihydromethines, which in the structure an intramolecular hydrogen bonding between the 14β-hydroxyl group and the nitrogen at 17-position was shown,[4] pharmacological observations has never been reported. In this paper, we wish to report syntheses of the N-substituted-morphinan dihydronormethines and its pharmacological observations considering with configurational relationship between 14β-hydroxyl group and the nitrogen of 17-position in these dihydronormethines. Syntheses and pharmacology of the O-alkyl-isoureas related to morphinan, norpethidine, or phenethylamine were also presented with interest on pharmacological effects of the basic character of this group with central nervous active amines such as morphinan, norpethidine, or phenethylamine.

14-Hydroxy-dihydrodeoxycodeine representing 6-deoxy-compounds, and 14-hydroxy-dihydrocodeinone, 14-hydroxy-dihydrothebainone 4-methyl ether and dihydrothebainone 4-methyl ether representing 6-oxo-compounds were chosen as the starting materials (I) because of their potent analgesic activities.[5] Dihydromethines derived from these parent alkaloids according to Hofmann's degradation followed by catalytic reduction were converted to the secondary amines by von Braun's degradation. And then the N-substituted-compounds (V) as shown in Table I were prepared by reaction of the secondary amines with phenethyl bromide expecting an increase of analgesic activity, and with allyl or propargyl bromide expecting an appearance of the morphine antagonism (Chart 1).

The some observations obtained in the course of syntheses are as follows: (1) It was observed that quaternization rate of the dihydromethines is higher than that of the parent alkaloids (I) because of the difference of steric atmophere on the N-atom of the both. Consequently, it took steps such as a gradual addition of the dihydromethines into cyanogen bromide in reverse and allylation or propargylation of the secondary amines in an aprotic solvent at low temperature to avoid forming quaternary salts. (2) On the N-cyano-6-deoxy-dihydromethines (II: Y=H_2) an acidic hydrolysis of N-cyano group to secondary amino group which was used ordinarily in treatment of the parent alkaloids readily proceeded to give the secondary

1) Part XVII: I. Seki, *Chem. Pharm. Bull.* (Tokyo), **18**, 671 (1970).
2) Location: *1-chome Hiromachi, Shinagawa-ku, Tokyo.*
3) O.J. Braenden, N.B. Eddy and H. Halbach, *Bull. of the W.H.O.*, **13**, 937 (1955); E. Mosetig, *J. Org. Chem.*, **5**, 401 (1940).
4) I. Seki, *Yakugaku Zasshi*, **85**, 359 (1965); *idem*, *Chem. Pharm. Bull.* (Tokyo), **14**, 453 (1966).
5) I. Seki, H. Takagi and S. Kobayashi, *Yakugaku Zasshi*, **84**, 280 (1964).

Table I

No.	R	R^1	R^2	R^3	mp°	Formula	Analysis (%) Calcd. C	H	N	Cl	Found C	H	N	Cl
														
1	H	H	Me[a]	Me	known compounds									
2	Me	H	Me	Me										
3	H	OH	Me	Me										
4	Me	OH	Me	Me										
5	Me	H	Me	H	138—139[c]	$C_{19}H_{28}O_3NCl \cdot 0.5H_2O$[c]	62.86	8.05	3.86	9.78	62.99	8.15	3.87	9.78
6	Me	H	Me	Ph[a]	60—65[b]	$C_{31}H_{41}O_9N \cdot 0.5H_2O$[b]	64.12	7.29	2.41	—	64.56	7.36	2.45	—
7	Me	OH	Me	Ph	110—120[b]	$C_{31}H_{41}O_{10}N \cdot 1.5H_2O$[b]	60.50	7.22	2.28	—	60.00	7.29	2.33	—
8	Me	H	Me	Al[a]	h.g.[b,d]	$C_{26}H_{37}O_9N \cdot H_2O$[b]	59.40	7.48	2.66	—	59.48	7.63	2.79	—
9	Me	H	Me	Pr[a]	89—92[b]	$C_{26}H_{35}O_9N \cdot 1.5H_2O$[b]	58.70	7.20	2.63	—	58.57	7.54	2.59	—
10	Me	H	H	Ph	h.g.[b]	$C_{30}H_{39}O_9N \cdot H_2O$[b]	62.60	7.19	2.43	—	62.68	7.39	2.02	—
11	Me	H	Ph	Ph	h.g.[b]	$C_{38}H_{47}O_9N \cdot 2H_2O$[b]	65.30	7.37	2.00	—	64.84	7.18	2.50	—
12	Me	H	Ph	Al	h.g.[b]	$C_{33}H_{43}O_9N \cdot H_2O$[b]	64.35	7.37	2.27	—	64.72	7.33	2.18	—
13	Me	H	Ph	Pr	h.g.[b]	$C_{33}H_{41}O_9N \cdot 1.5H_2O$[b]	63.70	7.12	2.24	—	63.70	7.10	2.46	—
14	Me	OH	Me	Al	h.g[c]	$C_{22}H_{32}O_4NCl$[c]	64.45	7.87	3.42	8.65	63.85	7.81	3.76	8.34
15	Me	OH	Me	Pr	h.g.[c]	$C_{22}H_{30}O_4NCl$[c]	64.77	7.41	3.43	8.69	64.72	7.46	3.30	8.52
16	Me	OH	Ph	Al	h.g.[b]	$C_{33}H_{43}O_{10}N \cdot 0.5H_2O$[b]	63.56	7.12	2.25	—	63.26	6.91	2.34	—
														
17	OH	Me	Me	Y=O	known compounds									
18	H	Me	Me	Y=O										
19	OH	Me	Ph	$Y=H_2$	80—85[b]	$C_{30}H_{39}O_9N \cdot 1.5H_2O$[b]	61.60	7.24	2.40	—	61.30	7.17	2.59	—
20	OH	Me	Ph	Y=O	80—90[b]	$C_{30}H_{37}O_{10}N \cdot 2H_2O$[b]	59.31	6.80	2.35	—	59.15	6.38	2.03	—

a) Me=methyl, Ph=phenethyl, Al=allyl, Pr=propargyl; *b*) bitartrate;
c) hydrochloride; *d*) h.g.=hygroscopic powder

amines in over 90% yield. But low yield (20—30%) of the secondary amines accompanied with a neutral amide-type compounds (30—40%) in the same reaction of the N-cyano-6-oxo-compounds (II: Y=O) was shown. Accordingly, for the preparation of N-nor-6-oxo-compounds the reductive decyanation of N-cyano-6-ethyleneketal compounds $\left(\text{II: Y}=\langle{}^{O}_{O}]\right)$ with lithium aluminum hydride followed by deketalization with acid was excellent.

In the 14-hydroxy-morphine alkaloids, although the O→N acetyl migration in the acidic hydrolysis of 14-acetoxy-N-cyano-normorphines was shown as side-reaction,[6] solvolysis of N-cyano-dihydronormethines (II: R=OAc) derived from 14-acetoxy-dihydromorphines has never been reported. For the examination of this problem, 14-hydrogen- or 14-acetoxy-N-cyanodihydromethines (II) were treated with methanol containing either bases or acids as catalyst at room temperature or in boiling with or without water. Among above attempts,

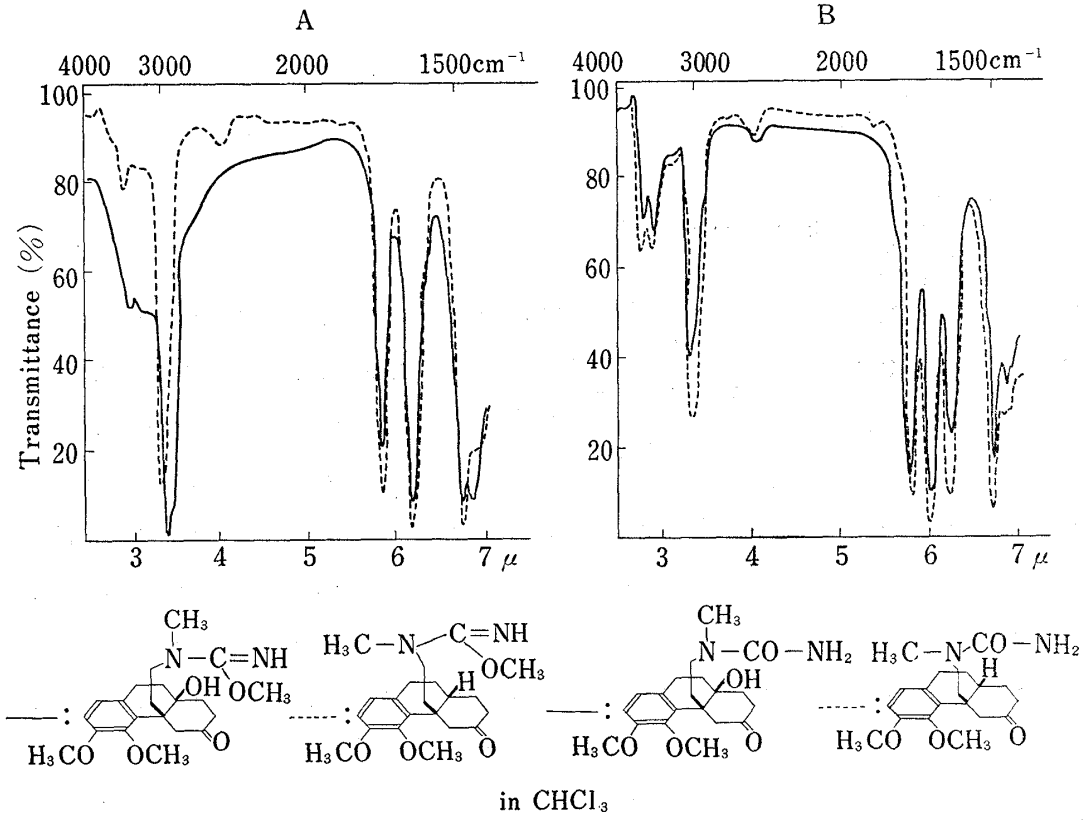


Fig. 1

the treatment with methanol containing sodium methoxide gave a basic substance as sole product. The results of elemental analysis and the observations of nuclear magnetic resonance (NMR) spectra of the product indicated addition of one methoxyl group to the starting materials (*e.g.* in the case of compounds No. 23 and 26 in Table II the singlet signal (3H) at 3.60 and 3.67 ppm were observed, respectively). And their infrared (IR) spectra shows a characteristic strong band at 6.15—6.18 μ as shown in Fig. 1—A.[7] Heating in diluted aqueous or ethanolic hydrochloric acid of the basic substances quantitatively gave the neutral substances which have observed a new band at 6.02 μ with disappearance of a band at 6.15—6.18 μ in the IR spectra as shown in Fig. 1—B and one of the singlet signals due to methoxyl group have disappered in the NMR spectra compared with those of the basic ones.

From these results, it was supposed that the basic substances are isourea-type compounds (III) which formed by introduction of one methoxyl group into the starting materials (II) and so these were hydrolyzed readily into urea-type compounds (IV) with acid as illustrated in Chart 1, and the elemental analysis mentioned above supported with this supposition.

6) A.C. Currie, G.T. Newbold and F.S. Spring, *J. Chem. Soc.*, **1961**, 4693.

7) In the IR spectra of O-alkyl-isoureas a presence of a strong band due to NH deformation at about 6.15 μ have been reported. *a*) J. Fabian, M. Legrand and P. Poirier, *Bull. Soc. Chim. France*, **1956**, 1499; A. Piasek and T. Urbanski, *Tetrahedron Letters*, **1962**, 723; *b*) S.E. Forman, C.A. Erickson and H. Adelman, *J. Org. Chem.*, **28**, 2653 (**1961**).

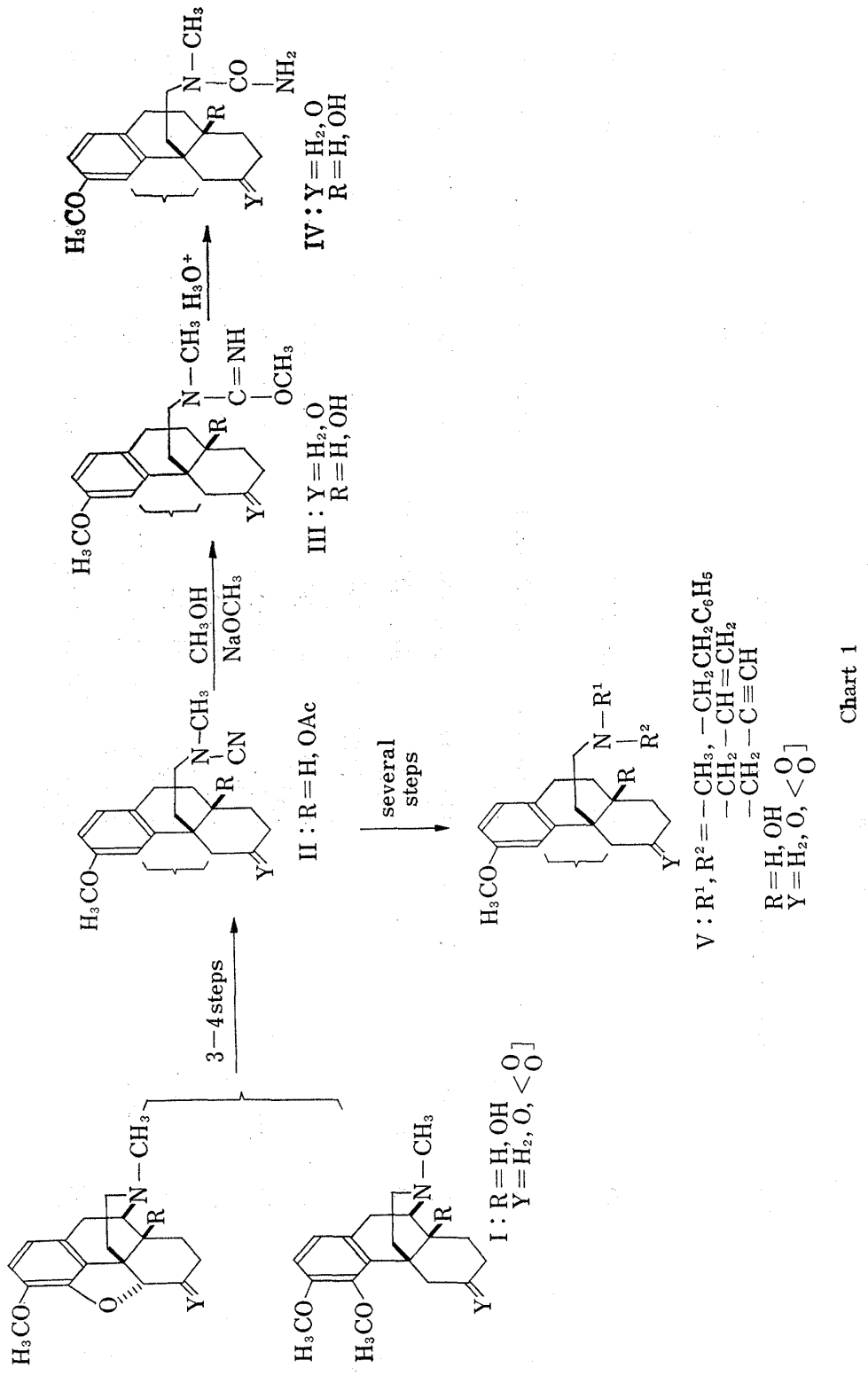
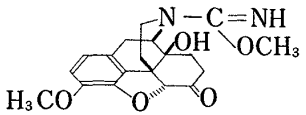
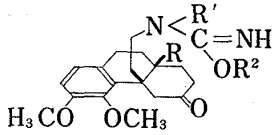
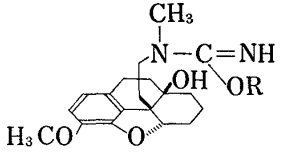
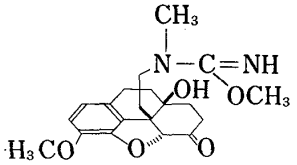


Chart 1

Consequently, it can be concluded that in the presented condition the base catalyzed addition of methanol to N-cyano group as reported in some literatures[8] proceeded to afford the O-methyl-isoureas having morphinan dihydronormethine skeleton as shown in Table II.

8) R.H. Mckee, *Am. Chem. J.*, **42**, 1 (1909); *Chem. Abstr.*, **3**, 2444 (1909); F.H.S. Curd, D.G. Davey and D.N. Richardson, *J. Chem. Soc.*, **1949**, 1732; in 7*b*); *cf.* also F.C. Schaefer and G.A. Peters, *J. Org. Chem.*, **26**, 412 (1961); R. Robinson, *J. Chem. Soc.*, **1963**, 2417.

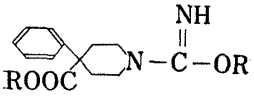
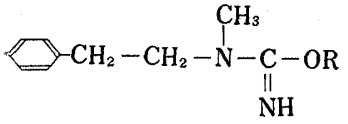
Table II

Structure	No.	Functional group	mp°	Formula	Analysis (%) Calcd. C	H	N	Found C	H	N
	21	—	glassy solid	$C_{19}H_{22}O_5N_2$	63.67	6.19	7.82	63.95	6.34	7.98
	22	—	amorphous powder[b]	$C_{34}H_{46}O_{12}N_2 \cdot 0.5H_2O$[b]	59.72	6.93	4.10	59.43	6.70	3.90
	23 R=OH; R^1=Me[a]; R^2=Me		145—147 (ether)	$C_{21}H_{30}O_5N_2$	64.41	7.84	7.09	64.59	7.74	7.17
	24 H	Ph[a] Me	amorphous powder[b]	$C_{32}H_{42}O_{10}N_2 \cdot 0.5H_2O$[b]	61.60	6.95	4.50	61.35	6.75	4.64
	25 H	Me Me	amorphous powder[b]	$C_{25}H_{36}O_{10}N_2$[b]	57.24	6.92	5.34	56.76	7.11	5.15
	26 R=Me		117—123 (ether)	$C_{20}H_{28}O_4N_2$	66.64	7.83	7.77	66.65	7.91	7.72
	27 Et[a]		glassy solid	$C_{21}H_{30}O_4N_2$	67.35	8.08	7.48	67.84	7.91	7.50
	28 *n*-Pr[a]		glassy solid	$C_{22}H_{32}O_4N_2$	68.01	8.30	7.21	68.20	7.87	7.38
	29 *n*-Bu[a]		amorphous powder[b]	$C_{27}H_{40}O_{10}N_2$[b]	58.68	7.30	5.07	58.47	7.09	5.13
	30 *n*-Am[a]		amorphous powder[b]	$C_{28}H_{42}O_{10}N_2 \cdot H_2O$[b]	57.52	7.59	4.79	57.53	7.02	5.02
	35	—	glassy solid	$C_{20}H_{26}O_5N_2$	64.15	7.00	7.48	63.70	7.14	6.91

a) Me=methyl; Ph=phenethyl; Et=ethyl; Pr=propyl; Bu=butyl; Am=amyl
b) bitatrate

By the application of above mentioned reaction the various O-alkyl-isoureas as shown in Table II were synthesized with pharmacological interest due to the fact that these compounds have a strong basic center in the similar position to the 17-position of morphinan-skeleton which contributes greatly to an appearance of the analgesic action. Also, the O-alkyl-isoureas having phenethylamine- or norpethidine-skeleton as shown in Table III were prepared from the corresponding cyanamides by the above reaction with interest to the basic character of these. The order on the stability of the isoureas against acidic media is as follows: 6-deoxy-morphinans=6-deoxy-morphinan dihydromethines=phenethylamines>6-oxo-morphinans>6-oxo-morphinan dihydromethines=norpethidines. And in the 6-deoxy-compounds it was recovered quantitatively from its bitartrate even after heating a t80° for 10 hours or standing for 120 hours at room temperature in the water.

Table III

Structure	No.	Functional group	mp°; bp°/mmHg	Formula	Analysis (%) Calcd. C	H	N	Found C	H	N
	31	R=Me[a]	78.5—79.5 (ether)	$C_{16}H_{22}O_3N_2$	65.32	7.35	10.07	65.19	7.30	10.14
	32	Et	amorphous powder[b]	$C_{21}H_{30}O_9N_2$[b]	55.50	6.65	6.16	56.06	6.72	6.16
	33	*n*-Pr	amorphous powder[b]	$C_{23}H_{34}O_9N_2$[b]	57.25	7.10	5.81	57.22	7.25	5.52
	34	*n*-Bu	amorphous powder[b]	$C_{25}H_{38}O_9N_2$[b]	58.81	7.50	5.49	59.24	7.57	5.65
	36	R=Me[c]	133/4	$C_{11}H_{16}ON_2$	68.72	8.39	14.57	68.88	8.43	14.08
	37	Et	135—7/4	$C_{12}H_{18}ON_2$	69.87	8.80	13.58	70.09	8.89	13.74
	38	*n*-Pr	147—9/5	$C_{13}H_{20}ON_2$	70.87	9.15	12.72	71.11	9.15	12.76
	39	*i*-Pr	134—6/4	$C_{13}H_{20}ON_2$	70.87	9.15	12.72	70.48	9.40	12.74
	40	*n*-Bu	154—6/4	$C_{14}H_{22}ON_2$	71.75	9.46	11.96	72.22	9.45	12.00
	41	*n*-Am	164—5/4	$C_{15}H_{24}ON_2$	72.54	9.74	11.28	73.06	9.76	11.11

a) Me=methyl; Et=ethyl; Pr=propyl; Bu=butyl; Am=amyl *b*) bitartrate
c) bitatrate: mp 117—118°, *Anal.* Calcd. for $C_{15}H_{22}O_7N_2$: C, 52.62; H, 6.48; N, 8.18. Found: C, 52.60; H, 6.43; N, 8.12.

Table IV

Compound No.[a]	Analgesia ED_{50} mg/kg (in mice)	Tail-up	Respiratory depression
2	24 (10 —57.6)[b]	—	weak
3	>30	—	very weak
6	>30	—	very weak
7	2.6 (1.33— 5.07)	+	strong
19	>30	—	very weak
20	17.5 (9.7 —33.1)	—	weak
Morphine	7.4 (5.6 — 9.8)	+	strong

a) administered as hydrochlorides in water
b) Parenthesized values shows 95% confidence limit.

Pharmacology

Analgesic action (measured by Haffner's pressure stimulation method,[9] in mice, *i.p.*), respiratory depression (measured in cats, *i.v.*), and acute toxicity (measured in mice, *i.v.* or

9) F. Haffner, *Deut. Med. Wochschr.*, **18**, 731 (1929).

i.p.) of the compounds listed in Table I were very weak except the compounds as shown in Table IV which shown marked analgesic activity. However, antitussive action (measured by Takagi's method[10] in guinea pigs, *s.c.*) was not observed in all compounds.

In the O-alkyl-isoureas derived from morphinan dihydromethines no pharmacological activities were shown. O-Alkyl-isoureas having phenethylamine-skeleton lacked analgesic activity, but antitussive action in No. 38 (at 30 mg/kg), and local anaesthetic action (measured by Chance and Lobstein's corneal reflex test[11] in guinea pigs) in No. 41 (at in 1.0% concentration) were observed. Although one having norpethidine-skeleton had very weak analgesic activity, no antitussive activity was shown. And in No. 33 and 34 local anaesthetic action were observed at 0.5—1.0% concentration. Acute toxicity of O-alkyl-isoureas having phenethylamine- or norpethidine-skeleton were stronger than that of one having morphinan dihydromethine-skeleton.

Experimental[12]

General Method for Preparation of N-Substituted-morphinan Dihydronormethines——In a draft chamber, a solution of dihydromethines or 14-acetoxy-dihydromethines derived from the parent alkaloids according to Hofmann's degradation followed by catalytic reduction[13] in $CHCl_3$ was added gradually into 35% (by weight) BrCN–$CHCl_3$ solution (105 mole%) under refluxing within 2 hours, and then the mixture was refluxed for 2 hours. After a removal of $CHCl_3$ with distillation *in vacuo*, the residue was dissolved in $CHCl_3$ and the $CHCl_3$ solution was washed with 5% AcOH and with then water. The $CHCl_3$ solution was dried over Na_2SO_4, and evaporated to dryness *in vacuo*. The residue was chromatographed on active Al_2O_3 (Merck "nach Brockmann," 10 times). The benzene eluate was collected to give N-cyano-compound.

14-Acetoxy-dihydro-deoxycodeine Dihydromethine——mp 115—117° (*n*-hexane–ether). *Anal.* Calcd. for $C_{21}H_{29}O_4N$: C, 70.17; H, 8.13; N, 3.90. Found: C, 69.81; H, 8.16; N, 3.84.

14-Acetoxy-dihydro-deoxycodeine N-Cyano-dihydro-normethine (II)——mp 144.5—145.5° (EtOH). Yield 71.5%. *Anal.* Calcd. for $C_{21}H_{26}O_4N_2$: C, 68.09; H, 7.07; N, 7.56. Found: C, 67.46; H, 7.09; N, 7.31.

14-Acetoxy-dihydro-codeinone N-Cyano-dihydro-normethine——mp 175—177° (EtOH). Yield 54.3%. *Anal.* Calcd. for $C_{21}H_{24}O_5N_2$: C, 65.61; H, 6.29; N, 7.29. Found: C, 65.23; H, 6.55; N, 7.10.

Dihydro-thebainone 4-Methyl Ether N-Cyano-dihydro-normethine (Ib)——Glassy solid. Yield 80%. *Anal.* Calcd. for $C_{26}H_{29}O_{10}N_5$ (picrate): C, 54.64; H, 5.11; N, 12.25. Found: C, 54.47; H, 5.27; N, 12.28.

The de-cyanation was carried out as follows: 1) with 10% HCl. A mixture of N-cyano-compound (1 part) and 10% HCl (30 parts) was refluxed for 7—10 hours. After cooling, the pale yellowish solution was made alkaline with NH_4OH and extracted with benzene. The benzene solution was extracted with 10% AcOH. The AcOH solution was washed with benzene, made alkaline with NH_4OH, and extracted with benzene. The benzene solution was washed with water, dried over Na_2SO_4, and evaporated to dryness *in vacuo* to give the secondary amines. Yield: in the case of 6-deoxy-compound, 80—90%; in the case of 6-oxo-compound, 20—30%.

2) with $LiAlH_4$. A mixture of 14-acetoxy-dihydro-thebainone 4-methyl ether dihydromethine (18.4 g), ethylene glycol (106 ml), *p*-$TsOH \cdot H_2O$ (16.3 g), and benzene (480 ml) was refluxed for 7 hours under removal of water with azeotropic distillation. After cooling, the mixture was washed with 10% Na_2CO_3 (80 ml × 3) and then with water (240 ml × 3), dried over Na_2SO_4, and evaporated to dryness to give the ketal.

In a draft chamber, a solution of the ketal (13.6 g) in $CHCl_3$ (175 ml) was added gradually into 35% (by weight) BrCN–$CHCl_3$ (10.0 g) under refluxing within 2 hours, and then the mixture was refluxed for 2.5 hours. After removal of $CHCl_3$ with distillation *in vacuo*, the residue was dissolved in $CHCl_3$ (70 ml). The $CHCl_3$ solution was washed with 5% AcOH and then with water, dried over Na_2SO_4, and evaporated to dryness *in vacuo* to give the N-cyano-compound.

A solution of N-cyano-compound (13.8 g) in dried tetrahydrofuran (138 ml) was added rapidly under refluxing and stirring into a solution of $LiAlH_4$ (11.1 g) in dried tetrahydrofuran (138 ml), and the mixture was refluxedfor 3 hours under stirring. After ice-cooling, the mixture of $CHCl_3$ and water was added carefully at 0—5° for a decomposition of excess of $LiAlH_4$. The mixture was filtered, and the residue was washed with $CHCl_3$. The filtrate and washings was combined, and poured into water (3720 ml). After a separation of $CHCl_3$ layer, water layer was extracted with $CHCl_3$. The $CHCl_3$ layers were combined,

10) K. Takagi, H. Fukuda and K. Yano, *Yakugaku Zasshi*, **80**, 1497 (1960).
11) M.R.A. Chance and H. Lobstein, *J. Pharmacol. Exptl. Therap.*, **82**, 203 (1944).
12) All melting points were uncorrected. The NMR spectra were measured by a Varian A-60 at 60 Mc in $CDCl_3$ and used Me_4Si as internal standard.
13) *e.g.*, C. Schöpf, *Ann.*, **452**, 249 (1927).

and extracted with 10% AcOH. The AcOH solution was made alkaline with NH_4OH, and extracted with benzene. The benzene solution was washed with water, dried over Na_2SO_4, and evaporated to dryness *in vacuo* to give 14-hydroxy-dihydro-thebainone 4-methyl ether dihydro-normethine 6-ethylene glycol ketal (10.2 g).

This ketal was converted to corresponding 6-oxo-compound by heating with 10% HCl.

14-Hydroxy-dihydro-deoxycodeine Dihydro-normethine——mp 180—181° (*n*-hexane). Yield 77.3% (with $LiAlH_4$). *Anal.* Calcd. for $C_{18}H_{25}O_3N$: C, 71.25; H, 8.31; N, 4.62. Found: C, 70.84; H, 8.40; N, 4.67.

3,4-Dimethoxy-6-oxo-13β-(β-phenethylaminoethyl)-octahydrophenanthrene Bitartrate——Amorphous powder. *Anal.* Calcd. for $C_{30}H_{39}O_9N \cdot H_2O$: C, 62.60; H, 7.19; N, 2.43. Found: C, 62.68; H, 7.39; N, 2.02.

Dihydro-thebainone 4-Methyl Ether Dihydro-normethine Hydrochloride——Silky needles. mp 138—139° (EtOH). Yield 51.2%. *Anal.* Calcd. for $C_{19}H_{28}O_3NCl \cdot 0.5H_2O$: C, 62.86; H, 8.05; N, 3.86; Cl, 9.78. Found: C, 62.79; H, 8.15; N, 3.87; Cl, 9.78.

The secondary amines obtained as mentioned above was converted to the tertiary amines as shown in Table I by the reaction with phenethyl, allyl, or propargyl bromide (each 105 mole%) under a presence of K_2CO_3 (200 mole%). The reaction was carried out at room temperature for 5—7 hours in benzene in the case of allyl or propargyl bromide, and in boiling *n*-butanol for 20 hours in the case of phenethyl bromide.

General Method for Preparation of O-Alkyl-isoureas——N-Cyano-compound (0.01 mole) was added to the solution of Na (0.014 mole) in ab. alcohol (30 ml) and the solution was refluxed for 2 hours. Pale yellowish solution was evaporated to dryness *in vacuo* and the residue was extracted with benzene. The benzene solution was washed with water, and then extracted 10% AcOH. The AcOH solution was made alkaline with NH_4OH and extracted with benzene. The benzene solution was washed with water, dried over Na_2SO_4, and evaporated to dryness *in vacuo* to give O-alkyl-isoureas as shown in Table II.

N-Cyano-norpethidine was obtained by the reaction of norpethidine (18.4 g) with 35% (by weight) $BrCN$–$CHCl_3$ (11.9 g; 50 mole%) in 75.4% yield. bp 202—205° (4 mmHg). *Anal.* Calcd. for $C_{15}H_{18}O_2N_2$: C, 69.74; H, 7.02; N, 10.88. Found: C, 69.70; H, 7.01; N, 10.89.

Methyl-β-phenethyl-cyanamide was prepared from phenethylamine *via* N,N-dimethyl-phenethylamine according to the literature.[14,15] Overall yield 46.7%. bp 149—151° (6 mmHg); 157—159° (9 mmHg) [lit.[15] bp 164—165° (10 mmHg)].

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14) *Org. Synth.*, Coll. Vol. **III**, 723.
15) J. von Braun, *Chem. Ber.*, **43**, 3209 (1910).