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Synthesis of Pyrazolone Derivatives. XXXV.[1] Synthetic and Pharmacological Studies on Some (4*S*,7*R*)-4,7-Methano-1*H*-indazoles[2]

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Treatment of (1*R*,4*S*)-2-oxobornaneglyoxylic acid (**1**) with substituted hydrazines gave (4*S*,7*R*)-1-substituted-4,7-methano-1*H*-indazole-3-carboxylic acids (**2**). (4*S*,7*R*)-1-Phenyl-4,7-methanoindazole-3-ol (**8**) was synthesized by two independent synthetic routes. (4*S*,7*R*)-N-Substituted-4,7-methanoindazole-3-carboxamides (**4a, b**) were tested on an isolated nerve-muscle preparation of bullfrog. Compound **4b** caused marked contracture of the muscle.

Keywords——(4*S*,7*R*)-1-substituted-4,7-methanoindazoles; 2-oxobornaneglyoxylic acid; nucleophilic reaction; NMR of 4,7-methanoindazoles; nerve-muscle preparation of bullfrog; contracture of the muscle

Our continued interest in pyrazole derivatives possessing pharmacological activities prompted us to investigate the syntheses and pharmacological effects of condensed pyrazole ring compounds. As a part of our investigation, we previously prepared a number of benzocycloheptapyrazoles and studied their reactivities.[4] This report deals with the synthesis and pharmacology of optically active (4*S*,7*R*)-4,7-methanoindazoles (**2**, **4** and **8**) which contain *d*-camphor [(1*R*,4*S*)-bornane-2-one] and pyrazole moieties in their molecules. Camphor was formerly used intramuscularly as a reflex respiratory stimulant, and the systematic effects of camphor are known to be related primarily to stimulation of the central nervous system (CNS).[5] Although quite a few derivatives of 4,7-methanoindazoles have been reported in the past, there is no description in the literature of the pharmacological properties of these compounds.

In this paper we describe the synthesis of some (4*S*,7*R*)-1-substituted-4,7-methanoindazoles (**2** and **8**), and some pharmacological studies on (4*S*,7*R*)-4,7-methanoindazole-3-carboxamides (**4**), which are structually related to Niketamide (a well-known CNS stimulant).

Synthesis

The principal route for the preparation of optically active 4,7-methanoindazoles (**2**) is illustrated in Chart 1; (1*R*,4*S*)-2-oxobornaneglyoxylic acid (**1**) was condensed with nucleophilic reagents such as hydrazine and hydrazine derivatives to give (4*S*,7*R*)-1-substituted-4,7-methanoindazoles (**2**).

Compound **1** was prepared by the reaction of (1*R*,4*S*)-bornane-2-one with diethyl oxalate in the presence of sodium metal. Since the nuclear magnetic resonance (NMR) spectrum of **1** showed the bridgehead proton as a doublet at δ 3.11 attributable to coupling with the adjacent C-5 *exo* proton, compound **1** appears to take an enol form rather than a keto form,

1) Part XXXIV: T. Ueda, F. Kato, H. Sugiura, N. Oda, and I. Ito, *Ann. Rept. Pharm. Nagoya City Univ.*, **26**, 27 (1978).
2) A part of this work was presented at the 96th Annual Meeting of the Pharmaceutical Society of Japan, Nagoya, April 1976.
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4) I. Ito and S. Nagai, *Chem. Pharm. Bull.* (Tokyo), **22**, 2131, 2796 (1974).
5) L. Goodman and A. Gilman, "The Pharmacological Basis of Therapeutics," 5th ed., Macmillan Publishing Co., Inc., New York, 1975, p. 951.

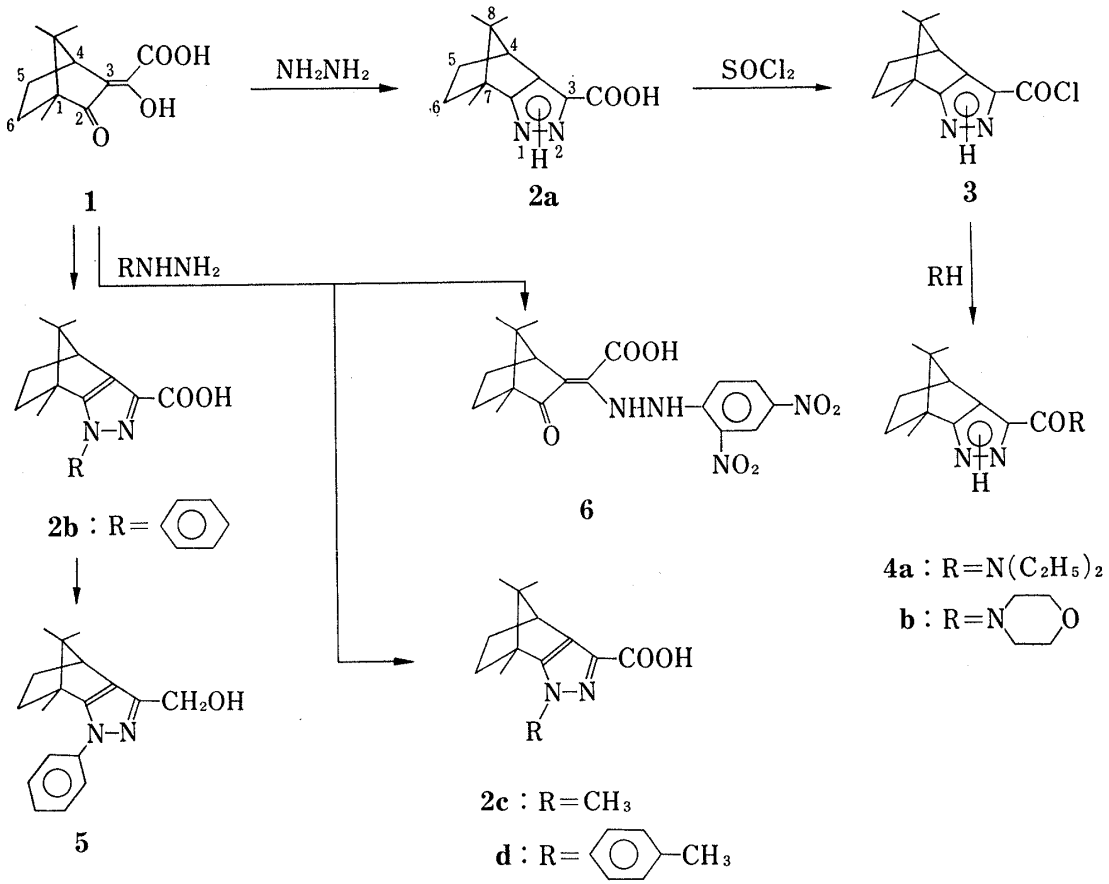


Chart 1

which might have one proton at the C-3 position, resulting in the appearance of the bridgehead proton as a doublet of doublets.

Condensation of **1** with hydrazine hydrate gave (4*S*,7*R*)-7,8,8-trimethyl-4,5,6,7-tetrahydro-4,7-methano-1*H*(2*H*)-indazole-3-carboxylic acid (**2a**) quantitatively. Treatment of **2a** with thionyl chloride yielded (4*S*,7*R*)-7,8,8-trimethyl-4,5,6,7-tetrahydro-4,7-methano-1*H*(2*H*)-indazole-3-carbonyl chloride (**3**). Compound **3** was reacted in a sealed tube with diethylamine and morpholine to give (4*S*,7*R*)-*N*,*N*-diethyl-7,8,8-trimethyl-4,5,6,7-tetrahydro-4,7-methano-1*H*(2*H*)-indazole-3-carboxamide (**4a**) and (4*S*,7*R*)-7,8,8-trimethyl-*N*-morpholino-4,5,6,7-tetrahydro-4,7-methano-1*H*(2*H*)-indazole-3-carboxamide (**4b**), which bear side chains structurally related to Niketamide.

Treatment of **1** with phenylhydrazine afforded (4*S*,7*R*)-7,8,8-trimethyl-1-phenyl-4,5,6,7-tetrahydro-4,7-methano-1*H*-indazole-3-carboxylic acid (**2b**) in 62% yield after purification by silica gel chromatography. Attempted reduction of the pyrazole ring in **2b** with lithium aluminum hydride gave (4*S*,7*R*)-7,8,8-trimethyl-1-phenyl-4,5,6,7-tetrahydro-4,7-methano-1*H*-indazole-3-methanol (**5**) as the only detectable product.

In an analogous manner, compound **1** was condensed with methylhydrazine and 4-methylphenylhydrazine to provide (4*S*,7*R*)-1,7,8,8-tetramethyl-4,5,6,7-tetrahydro-4,7-methano-1*H*-indazole-3-carboxylic acid (**2c**) and (4*S*,7*R*)-7,8,8-trimethyl-1-(4-methylphenyl)-4,5,6,7-tetrahydro-4,7-methano-1*H*-indazole-3-carboxylic acid (**2d**), respectively. The reaction of **1** with 2,4-dinitrophenylhydrazine, however, proceeded differently to provide (1*R*,4*S*)-3-carboxy-3-(2,4-dinitrophenylhydrazino)-2-oxobornane-3-ylidene (**6**) in 86% yield. In the infrared (IR) spectrum of **6**, the strong OH absorption band observed in the starting compound **1** had disappeared, but the absorptions of C=O and COOH remained unchanged.

The isolation of compound **6** showed that the enolized carbonyl group of **1** was more reactive towards nucleophilic reagents than the carbonyl group in the strained five-membered

ring. Consequently, the intermediate in (4*S*,7*R*)-4,7-methanoindazoles (**2b**—**d**) formation is clearly an ylidene such as **6**, which might be dehydrated, followed by the exclusive formation of N-1 substituted compounds (**2b**—**d**). In every case only one isomer was actually isolated, as determined by NMR examination and gas liquid chromatography (GLC). The view that all the substituents of **2b**—**d** are at the N-1 position was confirmed by the NMR spectrum. The N-1 substituent protons did not show downfield shifts, which might arise from deshielding effects by the adjacent carboxylic group if the substituents were located at the N-2 position.

A synthetic approach to (4*S*,7*R*)-4,7-methanoindazole-3-ol (**8**) was developed as outlined in Chart 2. Ethyl (1*R*,4*S*)-2-oxo-3-bornanecarboxylate (**7**) was reacted with phenylhydrazine

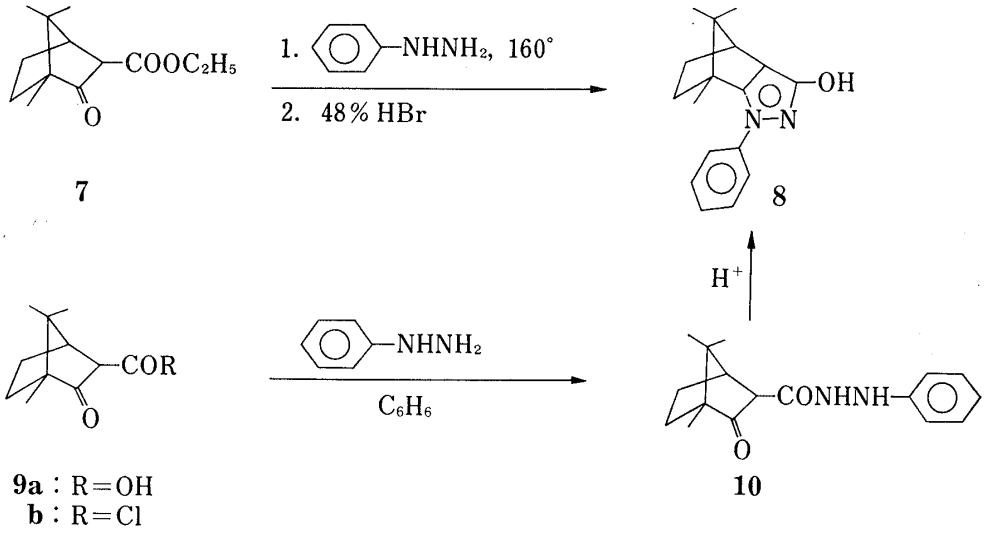


Chart 2

at 160°. The resulting oil, without purification, was heated with 48% hydrobromic acid to provide (4*S*,7*R*)-7,8,8-trimethyl-1-phenyl-4,5,6,7-tetrahydro-4,7-methano-1*H*-indazole-3-ol (**8**). Compound **8** was assigned as an enolic form rather than a keto form due to the absence of the characteristic amidocarbonyl absorption in IR spectrum and a positive color test with ferric chloride. The 1-phenyl substituted structure of **8** was confirmed by the appearance of a sharp singlet for the phenyl protons at δ 7.52. If the phenyl group was located at the N-2 position, one might expect the phenyl protons to give rise to a multiplet pattern because of the magnetic anisotropy of the adjacent hydroxy group.

In order to further confirm this structure, a different synthetic procedure was then attempted. The acid chloride (**9b**) prepared from (1*R*,4*S*)-2-oxo-3-bornanecarboxylic acid (**9a**) was reacted with phenylhydrazine in hot benzene to give (1*R*,4*S*)-3-(3-phenylcarbazoyl)-bornane-2-one (**10**) exclusively due to the higher nucleophilic reactivity of the β-nitrogen atom of phenylhydrazine. The NMR spectrum of compound **10** showed a doublet at δ 8.71 and a broad singlet at δ 5.78 attributable to two protons of the hydrazo group.

Ring closure was accomplished by heating **10** with a catalytic amount of sulfuric acid to yield colorless plates, mp 290—291°, identical with compound **8**.

Pharmacological Results and Discussion

The pharmacological effects of the newly synthesized compounds **4a** and **4b** were tested on isolated preparations of bullfrog. Peripheral actions of the compounds were examined on the isolated perfused heart and isolated nerve-muscle preparations, and central actions were tested on the isolated perfused spinal cord.

Methods

1) **Isolated perfused Heart of Bullfrog**——Isolated bullfrog (*Rana catesbeiana*) heart was perfused with Ringer's solution according to Yagi's method. The activity of the heart

was recorded on a smoked drum by an isotonic lever. The drugs tested were dissolved in Ringer's solution and applied to a venous reservoir (volume, 3 ml).

2) **Nerve-muscle Preparation of Bullfrog**——The nerve-muscle preparation (m. ext. dig. long. IV) of bullfrog was isolated and suspended in a 10 ml organ bath filled with Ringer's solution. The peroneal nerve branch was placed on a pair of Ag–AgCl stimulating electrodes and stimulated with an electronic stimulator (0.2 Hz, 0.1 msec, supramaximal; Nihonkohden MES-20). The twitch was recorded on a smoked drum by an isotonic lever. The drugs dissolved in Ringer's solution were applied to the organ bath.

3) **Isolated perfused Spinal Cord Preparation of Bullfrog**——Bullfrog spinal cord was isolated and perfused through the ventral spinal artery (Matsuura *et al.*, 1969; Kudo and Fukuda, 1972). The spontaneous discharges from the ventral root were detected by means of a pair of Ag–AgCl electrodes and the rate of spontaneous discharges was measured with an integrator (Kudo and Fukuda, 1972; Kudo *et al.*, 1975). The drugs dissolved in Ringer's solution were applied by perfusion through the ventral spinal artery.

Results

1) Effects on the isolated Heart of Bullfrog

After the application of compound **4a** (10^{-4} g/ml), a transient negative inotropic action followed by a slight positive inotropic action was noted. The heart rate was clearly reduced in all instances. Compound **4b** at the same concentration as **4a** showed almost same action on the isolated heart.

2) Effects on the Nerve-muscle Preparation of Bullfrog

Compounds **4a** and **4b** showed characteristic actions on the muscle. Compound **4a** at a concentration of 10^{-4}—10^{-3} g/ml augmented the twitch amplitude. At a higher concentration of 5×10^{-3} g/ml the twitch amplitude was markedly augmented and the resting tension of the muscle increased (contracture). This effect seemed to be similar to that induced by caffeine (10^{-3}—5×10^{-3} M), which also caused a marked contracture of the muscle. The twitches induced by electrical stimulations could be blocked by the application of *d*-tubocurarine chloride (*d*-Tc), while the contracture induced by the drug was not affected even after pretreatment with *d*-Tc (5×10^{-6} M). Compound **4b** caused the same effects as **4a** at lower concentration of 5×10^{-5}—10^{-3} g/ml.

3) Effects on the Isolated Perfused Spinal Cord of Bullfrog

Compounds **4a** and **4b** at a concentration of 10^{-4} g/ml showed only slight depressant actions on the spontaneous discharges from the ventral root of the isolated perfused spinal cord.

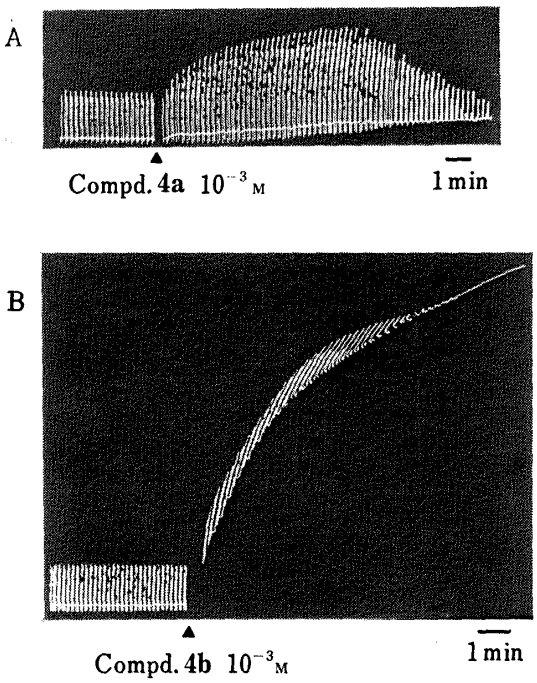


Fig. 1. Effects of Compound **4a** and **4b** on Isolated Neuromuscular Preparations (m. ext. dig. long IV) of Bullfrog

Muscle twitches were elicited by alternative direct and indirect stimulations. A: Effect of compound **4a** (10^{-3} M). B: Effect of compound **4b** (10^{-3} M).

Discussion

The effects of compounds **4a** and **4b** on the isolated heart and spinal cord of bullfrog were weak and indistinct. These drugs, however, showed marked stimulatory actions on the nerve-

muscle preparation. The contracture induced by these drugs seemed to have similar characteristics to that induced by caffeine. As the contracture induced by these drugs was not influenced by the administration of *d*-Tc, the drugs might affect the muscle contracture mechanisms. These drugs may therefore represent powerful pharmacological tools to investigate the mechanisms of muscle contraction.

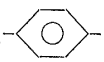
Experimental

All melting points were determined on a Yanagimoto melting point apparatus and are uncorrected. NMR spectra were recorded on a JEOL JNM-MH-100 spectrometer using tetramethylsilane as an internal standard with deuteriochloroform as a solvent unless otherwise indicated, and chemical shift (δ) are given in ppm relative to tetramethylsilane. Abbreviations are as follows: s, singlet; d, doublet; q, quartet; br, broad. Mass spectra were measured on a Hitachi M-52 mass spectrometer. Optical rotations were measured with a Yanagimoto OR-10 photo-magnetic direct reading polarimeter. IR spectra were measured with an IRA-2 unit (Nihon Bunko Spectroscopic Co.) and recorded as Nujol mulls unless otherwise indicated.

(1*R*,4*S*)-2-Oxobornaneglyoxylic Acid (1)——From the reaction of 50 g (0.276 mol) of (1*R*,4*S*)-bornane-2-one, 85.2 g (0.6 mol) of diethyl oxalate, and 12.7 g (0.276 mol) of powdered sodium in 1000 ml of toluene according to the procedure[6] described for the synthesis of *dl*-2-oxobornaneglyoxylic acid, 20 g (32.3%) of **1** was obtained as colorless plates, mp 84.5—86.5°. *Anal.* Calcd. for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.32; H, 7.08. IR ν_{max} cm^{-1}: 3320 (OH), 1733 (CO), 1677 (COOH). NMR δ: 3.11 (1H, d, J=4 Hz, C(4)–H), 7.57 (1H, br s, OH). MS *m/e*: 224 (M^+). $[\alpha]_D^{23}$ +6.2° (c=0.324, EtOH).

(4*S*,7*R*)-7,8,8-Trimethyl-4,5,6,7-tetrahydro-4,7-methano-1*H*(2*H*)-indazole-3-carboxylic Acid (2a)——A mixture of 1 g of **1** and 0.36 g of 80% hydrazine hydrate methanol solution in 10 ml of methanol was refluxed for 2 hr. After cooling, the crystals precipitated were filtered off. Analytical and physical data are summarized in Table I. Gas chromatography was carried out on a JEOL JGC 1100 gas liquid chromatograph using a stainless steel column (3 mm × 2 m) packed with 3% Apiezone Grease L on 80—100 mesh Chromosorb-W with N_2 carrier gas at 220°. Detector, FID. N_2, 1.6 kg/cm²; H_2, 0.5 kg/cm²; air, 2 kg/cm²; t_R=2.9.

Table I. (4*S*, 7*R*)-1-Substituted-7,8,8-trimethyl-4,5,6,7-tetrahydro-4,7-methano-1*H*-indazole-3-carboxylic Acids (2)

Compd. No.	R	mp (°C) (Rec. solv.) and appearance	$[\alpha]_D^{25}$ in EtOH (C)	Yield (%)	MS *m/e* (M^+)	Formula	Analysis (%) Calcd (Found) C	H	N	NMR
2a[a]	H	268—270 (EtOAc) Colorless plates	+78.3° (0.24)	80	220	$C_{12}H_{16}N_2O_2$	65.43 (65.36	7.32 7.51	12.72 12.74)	3.06 (1H, d, J= 4 Hz, C(4)–H)
2b		201—203 (EtOAc–MeOH) Colorless prisms	+60.7° (0.382)	62	296	$C_{18}H_{20}N_2O_2$	72.94 (72.73	6.80 6.75	9.45 9.65)	7.44 (5H, s, phenyl protons) 10.22 (1H, s, CO_2H)
2c	CH_3	192—194 (EtOAc–petro.ether) Colorless prisms	+66.1° (0.33)	62	234	$C_{13}H_{18}N_2O_2$	66.64 (66.61	7.74 7.71	11.96 11.87)	3.96 (3H, s, N–CH_3) 11.42 (1H, s, CO_2H)
2d	CH_3- 	222—224 (EtOAc) Pale yellow needles	+60.2° (0.332)	57	310	$C_{19}H_{22}N_2O_2$	73.52 (73.42	7.14 7.05	9.03 8.96)	2.42 (3H, s, CH_3)

a) IR ν_{max} cm^{-1}: 3260 (NH), 1695 (CO_2H).

6) P. Chorley and A. Lapworth, *J. Chem. Soc.*, **117**, 728 (1920).

(4*S*,7*R*)-7,8,8-Trimethyl-1-phenyl-4,5,6,7-tetrahydro-4,7-methano-1*H*-indazole-3-carboxylic Acid (2b)——A solution of 0.5 g of **1** and 0.24 g of phenylhydrazine in 5 ml of EtOH was refluxed for 1 hr then evaporated down. The residual oil was chromatographed on silica gel. Elution with $CHCl_3$ afforded a powder. Analytical and physical data are summarized in Table I.

(4*S*,7*R*)-1,7,8,8-Tetramethyl-4,5,6,7-tetrahydro-4,7-methano-1*H*-indazole-3-carboxylic Acid (2c)——A solution of 1 g of **1** and 0.2 g of methylhydrazine in 10 ml of EtOH was refluxed for 2 hr and worked up as described for the preparation of **2b**. Analytical and physical data are summarized in Table I.

(4*S*,7*R*)-7,8,8-Trimethyl-1-(4-methylphenyl)-4,5,6,7-tetrahydro-4,7-methanol-1*H*-indazole-3-carboxylic Acid (2d)——A solution of 0.5 g of **1** and 0.26 g of 4-methylphenylhydrazine hydrochloride in 10 ml of EtOH was refluxed for 2 hr then evaporated down. The residue was washed with $NaHCO_3$ solution and extracted with $CHCl_3$. Removal of the solvent gave an oil which was triturated with ether to give a powder. Analytical and physical data are summarized in Table I.

(4*S*,7*R*)-7,8,8-Trimethyl-4,5,6,7-tetrahydro-4,7-methano-1*H*(2*H*)-indazole-3-carbonyl Chlordie (3)——A mixture of 3 g of **2a** and 3 ml of thionyl chloride in 30 ml of dry $CHCl_3$ was refluxed for 3 hr then evaporated to dryness. The residual oil was allowed to stand to yield a pale yellow powder, which was used for subsequent reaction without purification. IR ν_{max} cm^{-1}: 1792 (COCl). NMR δ: 3.34 (1H, d, J=4 Hz, C(4)–H), 9.88 (1H, br s, NH).

(4*S*,7*R*)-*N*,*N*-Diethyl-7,8,8-trimethyl-4,5,6,7-tetrahydro-4,7-methano-1*H*(2*H*)-indazole-3-carboxamide (4a)——A solution of 1.2 g of **3** and 1 g of diethylamine in 10 ml of dry benzene was heated in a sealed tube at 100° for 18 hr. After removal of the solvent by evaporation, the residue was dissolved in $CHCl_3$ and chromatographed on silica gel. Elution with $CHCl_3$ gave crystals. Analytical and physical data are summarized in Table II.

(4*S*,7*R*)-7,8,8-Trimethyl-*N*-morpholino-4,5,6,7-tetrahydro-4,7-methano-1*H*(2*H*)-indazole-3-carboxamide (4b)——A solution of 1.2 g of **3** and 1 g of morpholine in 10 ml of dry benzene was heated at reflux for 20 hr then evaporated down under reduced pressure. The residue was triturated with ether to give a powder. Analytical and physical data are summarized in Table II.

Table II. (4*S*,7*R*)-3-N-Substituted-7,8,8-trimethyl-4,5,6,7-tetrahydro-4,7-methano-1*H*(2*H*)-indazole-3-carboxamides (4)

Compd. No.	R	mp (°C) (Rec. solv.) and appearance	$[\alpha]_D^{22}$ (c, Solv.)	Yield (%)	Formula	Analysis (%) Calcd (Found) C	H	N	NMR
4a	$N(C_2H_5)_2$	123—125 (n-hexane) Colorless prisms	+72.2° (0.18, MeOH)	52	$C_{16}H_{25}N_3O$	69.78 (69.53	9.15 9.15	15.26 14.99)	3.59 (4H, q, J=6.8 Hz, $2\times C\underline{H}_2CH_3$) 10.68 (1H, br s, NH)
4b		199—201 (isopropyl ether–acetone) Colorless plates	+62.3° (0.17, EtOH)	56	$C_{16}H_{23}N_3O_2$	66.41 (66.21	8.01 7.88	14.52 14.30)	3.77 (8H, s, morpholine) 10.44 (1H, br s, NH)

(4*S*,7*R*)-7,8,8-Trimethyl-1-phenyl-4,5,6,7-tetrahydro-4,7-methano-1*H*-indazole-3-methanol (5)——A mixture of 3 g of **2b** and 0.3 g of $LiAlH_4$ in 10 ml of THF was stirred at reflux for 5 hr. After treatment with 10% acetic acid, the mixture was extracted with $CHCl_3$. Removal of the solvent gave solids which were recrystallized from ether to yield colorless prisms, mp 136—138°. Yield 0.22 g (77%). *Anal.* Calcd. for $C_{18}H_{22}N_2O$: C, 76.57; H, 7.85; N, 9.92. Found: C, 76.29; H, 7.77; N, 9.68. NMR δ: 3.12 (1H, br s, OH), 4.70 (2H, s, CH_2), 7.44 (5H, s, phenyl protons). $[\alpha]_D^{23}$ +29.3° (c=0.41, EtOH).

(1*R*,4*S*)-3-Carboxy-3-(2,4-dinitrophenylhydrazino)-2-oxobornane-3-ylidene (6)——A solution of 0.5 g of **1** and 0.46 g of 2,4-dinitrophenylhydrazine in 10 ml of EtOH was refluxed for 16 hr then evaporated down. The residual crystals were recrystallized from EtOAc–petroleum ether to give yellow prisms, mp 220—221° (foaming). Yield 0.78 g (86%). *Anal.* Calcd. for $C_{18}H_{20}N_4O_7$: C, 53.46; H, 4.99; N, 13.86. Found: C, 53.22; H, 5.05; N, 13.66. IR ν_{max} cm^{-1}: 1750 (C=O), 1690 (COOH). NMR ($CDCl_3$–CD_3OD) δ: 3.90 (1H, d, J=4 Hz, C(4)–H). $[\alpha]_D^{23}$ +350° (c=0.2, EtOH).

(4*S*,7*R*)-7,8,8-Trimethyl-1-phenyl-4,5,6,7-tetrahydro-4,7-methano-1*H*-indazole-3-ol (8)——a) A mixture of 2 g of **7** and 0.96 g of phenylhydrazine was stirred at 160° for 4 hr. A mixture of 25 ml of AcOH and 1 ml of 48% HBr was added to the residual oil, and the mixture was refluxed for 2 hr. The residue obtained

after removal of AcOH was washed with $NaHCO_3$ solution and extracted with $CHCl_3$. Removal of $CHCl_3$ gave solids which were recrystallized from MeOH to afford colorless prisms, mp 290—291°. Yield 0.12 g (5%). *Anal.* Calcd. for $C_{17}H_{20}N_2O$: C, 76.09; H, 7.51; N, 10.44. Found: C, 76.33; H, 7.32; N, 10.45. NMR (CF_3CO_2D–$CDCl_3$) δ: 7.52 (5H, s, phenyl protons). MS *m/e*: 268 (M^+), 253 (M^+-CH_3). $[\alpha]_D^{23}$ +28.4° (c=0.31, $CHCl_3$).

b) A solution of 0.37 g of $SOCl_2$ in 10 ml of dry benzene was added dropwise to a solution of 0.5 g of (1*R*,4*S*)-2-oxobornane-3-carboxylic acid (**9a**) in 10 ml of dry benzene. The mixture was allowed to stand at 0° for 1 hr and then refluxed for 1 hr. Removal of the solvent gave crude (1*R*,4*S*)-2-oxobornane-3-carbonyl chloride (**9b**) as pale yellow crystals. A mixture of **9b** and 2 equivalents of phenylhydrazine in 15 ml of dry benzene was stirred at reflux for 5 hr and phenylhydrazine hydrochloride (0.2 g) was filtered off. The filtrate was evaporated down and the resulting oil was chromatographed on silica gel. Elution with $CHCl_3$ gave crystals which were recrystallized from EtOAc to afford (1*R*,4*S*)-3-(3-phenylcarbazoyl)bornane-2-one (**10**) as colorless plates, mp 135—136°. Yield 0.52 g (71%). *Anal.* Calcd. for $C_{17}H_{22}N_2O_2$: C, 71.30; H, 7.74; N, 9.78. Found: C, 71.47; H, 7.66; N, 9.69. IR ν_{max} cm^{-1}: 3240 (NH), 1724 (CO), 1653 (CONH). NMR δ: 5.78 (1H, br s, $C_6H_5\underline{NH}$), 8.71 (1H, br s, CONH). MS *m/e*: 286 (M^+), 179 ($M^+-C_6H_5NHNH$). $[\alpha]_D^{23}$+60° (c=0.25, EtOH). A solution of 0.1 g of **10** and 5 ml of EtOH containing a few drops of H_2SO_4 was refluxed for 1 hr. After cooling, the solution was poured into ice-water. The precipitates were filtered off, washed with water and dried. Recrystallization from AcOH gave colorless prisms, mp 290—291°. Yield 0.086 g (92%). *Anal.* Calcd. for $C_{17}H_{20}N_2O$: C, 76.09; H, 7.51; N, 10.44. Found: C, 76.13; H, 7.67; N, 10.44. The IR spectrum was identical with that of **8** prepared by method a).

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