m.p. 79–80°, undepressed by admixture of an authentic sample; infrared spectrum in chloroform superimposable on that of the authentic sample.

B. With Autoclaved *C. globosum* or its Fermentation Filtrates.—*C. globosum* was grown in two 250 ml. Erlenmeyer flasks containing 50 ml. of the medium. After 72 hr. at 27° on a rotary shaker, one flask was autoclaved for 20 min. at 1.05 kg./cm.^{2} and 120°; the other flask was filtered under sterile conditions to remove the mycelia. Coprostan-5β-ol-3-one (10 mg.) in 0.3 ml. of dimethylformamide was then added to each of the autoclaved flasks and the flask containing only the filtrate. The flasks were again placed on the rotary shaker. Chloroform extracts of samples taken at 24, 48 and 72 hr. after steroid addition were chromatographed by the thin layer silica gel plate method,[23] using chloroform as the mobile phase. After spraying with 2,4-dinitrophenylhydrazine (0.4% in 2 *N* HCl) each of the mixtures showed a spot corresponding in mobility to that of Δ^4-cholestenone.

(23) H. K. Mangold and D. C. Malius, *J. Am. Oil. Chem. Soc.*, **37**, 383 (1960).

New Benzomorphan Analgetics

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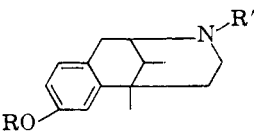
The analgetic phenazocine (I)[1] shows a partial separation of analgesia and addiction liability in both monkeys[2] and humans.[3] Certain other benzomorphans with aralkyl or alkyl groups on the nitrogen seem to extend this separation of effects in animals[4] and some of these aralkyl derivatives are reported in this communication. The compounds prepared and a partial report of their test data are summarized in Table I, with reference to the formula



(1) E. L. May and N. B. Eddy, *J. Org. Chem.*, **24**, 294 (1959).

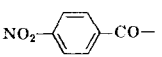
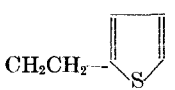
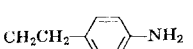
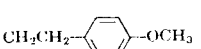
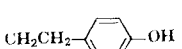
(2) G. A. Deneau, D. A. McCarthy and M. H. Seevers, Addendum 1 of Minutes, 20th Meeting of Committee on Drug Addiction and Narcotics, p. 13, Jan. 10–11, 1959, Washington, D. C.

(3) H. F. Fraser and H. Isbell, Minutes of 20th Meeting of Committee on Drug Addiction and Narcotics, Addendum 3, p. 1, Jan. 10–11, 1959, Washington, D. C.

(4) Except for phenazocine, these compounds have not been tested in man.

TABLE I

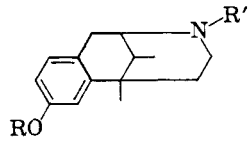
PHARMACOLOGICAL ACTIVITIES OF SUBSTITUTED BENZMORPHINE

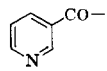
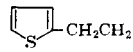
No.	R	R′	ED_{50} Analgesia, mg./kg.	Monkey addiction liability	Ratio Suppressant dose / Analgetic ED_{50} (mouse)
I	H	$CH_2CH_2C_6H_5$	0.11 rat 0.25 mouse	17 mg. = 3 mg. morphine[a]	68
II	CH_3CO—	$CH_2CH_2C_6H_5$	0.14 rat 0.19 mouse	Partial suppression[b] at 32 mg./kg.	>172
III		$CH_2CH_2C_6H_5$	0.4 mouse	Nearly complete suppression[c] at 32 mg./kg.	>80
IV		$CH_2CH_2C_6H_5$	0.17 mouse 0.3 rat	Complete suppression[d] at 100 mg./kg., except neuromuscular signs.	~600
V	H	$CH_2CH_2CH_2C_6H_5$	13.5 mouse	No suppression up to 30 mg./kg.[b]	Incomplete
VI	H		0.055 mouse 0.06 rat	Slight suppression at 2 mg./kg.[b] Higher doses were stimulating.	>40
VII	H		0.074 rat 0.11 mouse	0.5 mg. ≅ 3 mg. morphine[b] sympathetic signs not suppressed well	>4.5
VIII	H		0.3 rat 0.32 mouse	Nearly complete suppression at 16 mg./kg. 24 mg./kg. produced convulsions[c] as did 32 mg./kg.	>100
IX	H		0.2 rat		
X	CH_3	$CH_2CH_2C_6H_5$	42.9 mouse	No suppression[d] at 12 mg./kg.	Incomplete
XI	H	H	None at 100		

[a] See Reference 3. [b] G. A. Deneau and M. H. Seevers, Addendum 1 of Minutes of 21st Meeting of Committee on Drug Addiction and Narcotics, Jan. 11–12, 1960, Philadelphia, Penna. [c] G. A. Deneau and M. H. Seevers, Addendum 1 of Minutes of 23rd Meeting of Committee on Drug Addiction and Narcotics, Jan. 16–17, 1961, New York, N. Y. [d] Private communication from G. A. Deneau and M. H. Seevers.

TABLE II

SYNTHESIS OF SUBSTITUTED BENZOMORPHANS



No.	R	R'	Yield, %	M. p., °C.
II[a]	CH_3CO—	$C_6H_5CH_2CH_2$—	94	240–244
III[b]	*p*-$NO_2C_6H_4CO$—	$C_6H_5CH_2CH_2$—	53	281–282
IV[b]		C_6H_5—CH_2CH_2—	95	103–104
V[d]	H	$C_6H_5(CH_2)_3$—	60	135–137
VI[c]	H		34	151–152 Picrate: 180–181
VII[g]	H	*p*-$NH_2C_6H_4CH_2CH_2$—	20	186–187
VIII[d]	H	*p*-$CH_3OC_6H_4CH_2CH_2$—	43	246–247
IX[e]	H	*p*-$HOC_6H_4CH_2CH_2$—	60	186–189
X[f]	CH_3	$C_6H_5COCH_2$—	13	225–227

No.	Molecular Formula	Calculated, % C	H	N	Found, % C	H	N
II[a]	$C_{24}H_{29}NO_2 \cdot HBr$	64.86	6.80	3.15	64.42	6.94, 6.87	3.39
III[b]	$C_{29}H_{30}N_2O_4 \cdot HCl$	68.69	6.16	5.53	68.67	6.38	5.86, 5.52
IV[b]	$C_{28}H_{30}N_2O_2$	78.84	7.09	6.57	78.74	7.26	6.64, 6.60
V[d]	$C_{23}H_{29}NO \cdot HCl$	74.27	8.13	3.77	73.85, 73.92	8.21, 8.20	3.80
VI[c]	$C_{26}H_{28}N_4O_8S$	56.10	5.07	S, 5.76	56.18, 56.31	5.47, 5.51	S, 5.74
VII[g]	$C_{22}H_{28}N_2O$	78.53	8.39	8.33	78.76	8.15	8.43, 8.70
VIII[d]	$C_{23}H_{29}NO_2 \cdot HBr$	63.88	6.99		63.73, 63.59	6.96, 7.10	
IX[e]	$C_{22}H_{27}NO_2 \cdot HBr$	63.16	6.75	3.35	62.93	6.88	3.66, 3.85
X[f]	$C_{23}H_{27}NO_2 \cdot HCl$	71.58	7.31		71.15, 71.05	7.51, 7.68	

[a] Prepared by reaction of XI with acetic anhydride. [b] Prepared by reaction with the acyl halide in pyridine. [c] Prepared by reaction with the appropriate alkyl halide. [d] Prepared by reaction with acyl halide followed by $LiAlH_4$ reduction. [e] Prepared by HBr demethylation of VIII. [f] Prepared by treating XI with diazomethane and then phenacyl bromide. [g] Prepared by reaction of IX with *p*-nitrophenethyl bromide and then reduction with palladium on carbon.