The present correlation for the series of compounds listed in Table I does not include the q of the nitrogen atom because every compound in this series has the same $(C_2H_5)_2N(CH_2)_2^-$ group. Therefore, a constant q of the nitrogen is assumed. For other series of compounds with N-alkyl derivatives, the q of the nitrogen must be considered as variable, because heteroatoms are considered as active centers for binding with the receptors. However, the method does not take interatomic distance between heteroatoms into consideration at this moment.

The binding ability between the carbonyl group and the receptor depends on their coupling of vibrational states. Therefore, an alternate group with a stretching vibrational wave number around 1700 cm^{-1}, which has an electronic structure similar to that of the ester group (similar q_e), such as thiol esters, may also show the activities.

Finally, the toxicity effects, such as LD_{50}, must also be studied in order to establish an optimal equation which has positive as well as negative contributions. Generally, ED_{50} and LD_{50} have the same trend. Therefore, the effective drug must be the one for which several biological activities have been taken into consideration.

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Cycloalkanones. 3. Structure–Activity Relationships of Hypocholesterolemic Cyclooctanone Derivatives

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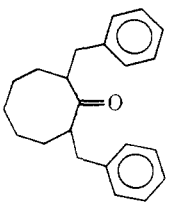
The structure–activity relationship (SAR) of a series of novel hypocholesterolemic agents related to 2,8-dibenzylcyclooctanone has been determined. Maximum lowering of cholesterol is obtained when an α,α'-dibenzyl-α,α'-disubstituted ketone system is present. Aromatic substitution has been studied in a successful attempt to eliminate the estrogenic side effect of the lead compound; 2,8-bis(4′-methylbenzyl)cyclooctanone retains some hypocholesterolemic activity and has little estrogenicity. The synthesis of 32 derivatives is described.

The hypocholesterolemic and antifertility activities of a series of dibenzylcycloalkanones have been previously reported.[1] The compounds reported here represent an extension of that work to determine the hypocholesterolemic and estrogenic activities of a series of derivatives of 2,8-dibenzylcyclooctanone (1). Four areas of the parent compound have been modified: the cyclooctane ring, the carbonyl function, the methylene side chain, and the aromatic nucleus.



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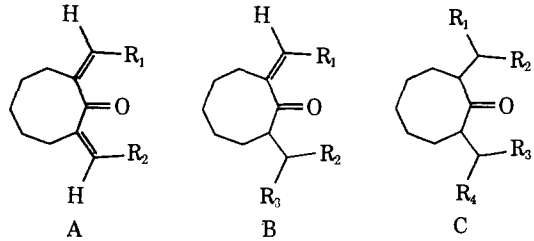
Experimental Section

Melting points were taken on a Mel-Temp apparatus and were corrected. Elemental analyses (Atlantic Microlab) indicated by element were correct within ±0.4%. Infrared and nmr spectra of all compounds were consistent with the assigned structure.

2,8-Bis(arylidene)cyclooctanones. General Procedure. A solution of 5 g (0.215 mol) of freshly cut Na in 125 ml of absolute EtOH was prepared in a 250-ml three-neck flask fitted with mechanical stirring and a Drierite protected reflux condenser. When the solution had cooled to room temperature, a mixture of 12.6 g (0.1 mol) of cyclooctanone and 0.2 mol of aldehyde was added in one portion. Absolute EtOH (5 ml) was used to rinse all of the mixture into the flask. An immediate rise in temperature was seen (usually ~10°). The mixture was allowed to stir several hours, the end being determined by successive tlc (silica G, benzene), since the bisylidene commonly moves ahead of all other materials. Reaction times were a few hours to several days at room temperature. At the conclusion of the reaction, the solid material was filtered and slurried with water to remove traces of base. Alternately, the gummy material was dissolved in benzene and extracted with water. After filtering or drying and solvent removal, the product was crystallized from 95% EtOH. Yields were typically 10–30% of the once crystallized product. More product remained in the liquor from the first filtration; however, the possible increase in yield did not justify the effort required to isolate more material. Table I lists the compounds prepared by this method.

Table I. Derivatives of 2,8-Dibenzylcyclooctanone



A B C

Compd no.	Type	R_1	R_2	R_3	R_4	Mp, °C	Formula[a]
19	A	2′-ClC_6H_4	2′-ClC_6H_4			105–106	$C_{22}H_{20}Cl_2O$
20	C	2′-ClC_6H_4	H	2′-ClC_6H_4	H	89–90	$C_{22}H_{24}Cl_2O$
21	A	$C_{10}H_7$	$C_{10}H_7$			144–145	$C_{30}H_{26}O$
22	C	$C_{10}H_7$	H	$C_{10}H_7$	H	108–110	$C_{30}H_{30}O$
23	A	4′-ClC_6H_4	4′-ClC_6H_4			168–169	$C_{22}H_{20}Cl_2O$
24	A	2′-$CH_3C_6H_4$	2′-$CH_3C_6H_4$			68–70	$C_{24}H_{26}O$
25	C	2′-$CH_3C_6H_4$	H	2′-$CH_3C_6H_4$	H	86–88	$C_{24}H_{30}O$
26	A	2′-$CH_3OC_6H_4$	2′-$CH_3OC_6H_4$			135–138	$C_{24}H_{26}O_3$
27	C	2′-$CH_3OC_6H_4$	H	2′-$CH_3OC_6H_4$	H	92–94	$C_{24}H_{30}O_3$
28	A	2′,4′,6′-$(CH_3)_3C_6H_2$	2′,4′,6′-$(CH_3)_3C_6H_2$			130–131	$C_{28}H_{34}O$
29	C	2′,4′,6′-$(CH_3)_3C_6H_2$	H	2′,4′,6′-$(CH_3)_3C_6H_2$	H	94–95	$C_{28}H_{38}O$
30	B	4′-$CH_3OC_6H_4$	CH_3O	4′-$CH_3OC_6H_4$		141–142	$C_{25}H_{30}O_4$
31	C	4′-$CH_3OC_6H_4$	H	4′-$CH_3OC_6H_4$	CH_3O	89–90	$C_{25}H_{32}O_4$
33	A	4′-$CH_3C_6H_4$	4′-$CH_3C_6H_4$			Liquid	$C_{24}H_{27}O$
34	C	4′-$CH_3C_6H_4$	H	4′-$CH_3C_6H_4$	H	61–63	$C_{24}H_{30}O$

[a] All compounds analyzed within ±0.4% of theory.

2,8-Bis(cyclohexylmethylene)cyclooctanone (2). 2,8-Dibenzylcyclooctanone (5 g, 0.016 mol) was dissolved in 50 ml of absolute EtOH containing 2 g of 5% Rh/C and shaken on a Parr hydrogenator for 36 hr at 60°. The product was isolated by chromatography (silica gel 60–200 mesh, hexane–benzene 95:5 eluent) and recrystallized from MeOH to give 4 g (80%) of colorless needles, mp 61–62°. *Anal.* ($C_{22}H_{38}O$) C, H.

2-Carbethoxy-2-(β-phenylethyl)cyclooctanone (3). 2-Carbethoxycyclooctanone[2] (20 g, 0.1 mol) was dissolved in 50 ml of benzene and added slowly to 2.4 g (0.1 mol) of NaH in benzene. The reaction was stirred 1 hr after addition, 19 g (0.1 mol) of β-phenethyl bromide was added, and the reaction was refluxed 4 days. After cooling the mixture was poured into ice–HCl, extracted with three 100-ml portions of benzene, and dried, and solvent was removed. The oil was distilled to give 13 g (53%) of product [160–170° (0.05 mm)] and recovery of 4 g of 2-cathylcyclooctanone. *Anal.* ($C_{19}H_{26}O_3$) C, H.

3,7-Bis(phenylthio)cyclooctanone (4). 2,7-Cyclooctadienone[3] (5 g, 0.04 mol) was dissolved in 25 ml of EtOH containing 15 ml of benzenethiol and 600 mg of KOH and stirred overnight. The reaction was poured into water and extracted with two 100-ml portions of petroleum ether (bp 60–90°). Solvent removal gave 6 g of colorless oil which yielded 3.2 g (25%) of colorless needles, mp 77–80°, from 100 ml of MeOH. *Anal.* ($C_{20}H_{22}OS_2$) C, H, S.

2,8-Bis(diphenylmethyl)cyclooctanone (5). 2,8-Dibenzylidenecyclooctanone (5 g, 0.016 mol) was dissolved in 200 ml of dry Et_2O and HBr was bubbled into the solution for 0.5 hr. Ether was removed to give 5.5 g of white solid (mp 120–121° from EtOH) presumed to be the HBr adduct from the ir spectrum. The material was dissolved in 100 ml of dry benzene and 13 g of anhydrous $AlCl_3$ was added. After stirring 96 hr at room temperature the reaction was poured into water; the organic layer was separated, dried, and evaporated to give 4 g of product. Two crystallizations from EtOH gave 3.8 g (50%) of colorless needles, mp 201–203°. *Anal.* ($C_{34}H_{34}O$) C, H.

2,4-Dibenzyl-3-pentanone (6). 2,4-Dibenzylidene-3-pentanone[4] (5 g, 0.02 mol) was hydrogenated with 200 mg of 5% Pd/C in EtOAc. The colorless oil obtained was chromatographed on silica (70–325 mesh) with benzene eluent: yield, 2.9 g (57%). *Anal.* ($C_{19}H_{22}O$) C, H.

Diepoxydibenzylcyclooctanone (7). 2,8-Dibenzylidenecyclooctanone (14 g, 0.046 mol) was dissolved in 500 ml of gently boiling MeOH. H_2O_2 (15 ml, 50%) was added, followed by 600 mg of KOH dissolved in 20 ml of MeOH. The reaction was stirred at reflux until completely colorless (~0.75 hr). Water was added until clouding occurred. Upon cooling, product crystallized and recrystallization from 95% EtOH gave 15 g (97%) of colorless needles, mp 156–158°. *Anal.* ($C_{22}H_{22}O_3$) C, H.

2,8-Bis(α-benzylthiobenzyl)cyclooctanone (8). 2,8-Dibenzylidenecyclooctanone (3 g, 0.01 mol) was dissolved in 100 ml of EtOH containing 10 ml of α-toluenethiol and 100 mg of KOH. After stirring at room temperature 16 hr, the white solid obtained was filtered and recrystallized from *i*-PrOH to give 4 g (72%) of colorless needles, mp 114–115°. *Anal.* ($C_{36}H_{28}OS_2$) C, H, S.

2,8-Bis(α-phenylthiobenzyl)cyclooctanone (9) was prepared as for the benzylthio derivative using benzenethiol. A mixture of the mono and bis adduct is obtained unless the reaction is refluxed overnight: yield (bis) 2.5 g (48%), mp 150–151° from EtOH; (mono) 1.3 g (25%), mp 128–130° from EtOH. The bis adduct crystallized directly from the reaction and was separated by filtration. *Anal.* (mono, $C_{28}H_{28}OS$) C, H, S; (bis, $C_{34}H_{34}OS_2$) C, H, S.

2-Benzyl-8-(α-ethoxybenzyl)cyclooctanone (10). 2-Benzylidene-8-(α-ethoxybenzyl)cyclooctanone (9 g, 0.026 mol), isolated from a 24-hr reaction time preparation of 2,8-dibenzylidenecyclooctanone, was hydrogenated by the general procedure. The oil obtained was chromatographed on 60–200 mesh silica with benzene to give 3.5 g (38%) of pure oil. *Anal.* ($C_{24}H_{30}O_2$) C, H.

1,5-Diphenyl-3-pentanone (11) was prepared by hydrogenation of dibenzalacetone[5] and purified by distillation.[6] *Anal.* ($C_{17}H_{18}O$) C, H.

2,5-Dibenzylcyclopentanol (12) was isolated by chromatography from the hydrogenation of 2,5-dibenzylidenecyclopentanone,[7] mp 54–55° (lit.[8] 58°). *Anal.* ($C_{19}H_{22}O$) C, H.

2,6-Diphenyl-3,5-dimethyltetrahydro-4-pyrone (13) was prepared by a modification of the method of Japp and Maitland.[9] 3-Pentanone (86 g, 1 mol) and 212 g (2 mol) of freshly distilled benzaldehyde were dissolved in 600 ml of absolute EtOH and water was added until the solution was barely clouded. KOH (10 g) dissolved in 10 ml of water was added and the solution stirred at 60° for 2 hr. Five 40-g portions of KOH were added over the next 2 hr without additional heating and the reaction was stirred overnight. The pyrone was collected by filtration and recrystallized from ether to give 100 g (35%), mp 111–113°. *Anal.* ($C_{19}H_{20}O_2$) C, H.

2,8-Dibenzylcyclooctanol (14). A solution of 2 g of $LiAlH_4$ in 100 ml of Et_2O was prepared and a solution of 6.5 g of $AlCl_3$ in 100 ml of Et_2O was added slowly. 2,8-Dibenzylcyclooctanone (12 g, 0.04 mol) was dissolved in 200 ml of Et_2O, 8 g of $AlCl_3$ was added, and the complex was added dropwise over 2 hr to the refluxing $LiAlH_4$–$AlCl_3$ complex solution. After 24 hr at reflux 25 ml of EtOAc was added, followed by enough saturated aqueous sodium sulfate to hydrolyze intermediate salts. The solution was dried by adding anhydrous sodium sulfate and filtered, and the oil obtained after solvent removal was chromatographed on 300 g of silica gel (benzene). Recovery was 7 g (58%) of colorless oil

Table II. % of Control of Serum Cholesterol and Body Weight after Administration of 10 mg/kg of Test Compound (N = 8)

Compd, orally	Serum cholesterol, no. of days dosed 4th	10th	16th	Body wt (% of control on day 16)
Control (1% CMC)	100 ± 16	100 ± 10	100 ± 13	
1	48 ± 13[a]	50 ± 12[a]	42 ± 18[a]	75[a]
2	93 ± 10	90 ± 8	76 ± 9	100
6	56 ± 23[b]	51 ± 12[a]	54 ± 14[a]	65[a]
11	98 ± 8	89 ± 9	81 ± 13[c]	100
12	95 ± 12	87 ± 12	83 ± 9[b]	100
14	93 ± 7	82 ± 14[b]	83 ± 9[a]	99
17	98 ± 13	106 ± 15	113 ± 15	100
18	89 ± 17	91 ± 9	73 ± 6[a]	100
20	98 ± 27	73 ± 18[b]	78 ± 15[b]	100
21	71 ± 13[a]	100 ± 18	78 ± 10[a]	100
22	91 ± 13	72 ± 12[b]	80 ± 5[a]	100
25	77 ± 19[c]	82 ± 7[b]	56 ± 14[b]	100
27	99 ± 15	78 ± 3[a]	67 ± 25[b]	100
29	64 ± 13[b]	89 ± 13	93 ± 10	100
31	77 ± 27	114 ± 13	83 ± 8[c]	100
32	77 ± 23	80 ± 13	83 ± 20[b]	100
34	83 ± 19	79 ± 10[a]	79 ± 9[b]	95

[a] p = 0.001. [b] p = 0.010. [c] p = 0.025.

which slowly solidified to needles, mp 47–50°. *Anal.* ($C_{22}H_{20}O$) C, H.

2,5-Dibenzylidene-*trans*-3,4-dimethylcyclopentanone (15). A solution of 8.9 g of NaOH was prepared in 89 ml of water and 71 ml of EtOH was added. While stirring vigorously, 10 g of *trans*-3,4-dimethylcyclopentanone (0.09 mol) and 19 g of benzaldehyde (0.18 mol) were added. After 30 min the solid was filtered and washed with water. Recrystallization from EtOAc gave 23 g (65%) of yellow prisms, mp 112–115°. *Anal.* ($C_{21}H_{20}O$) C, H.

1,3-Dibenzylcyclooctane (16). A suspension of 2 g of $LiAlH_4$ in 100 ml of ether was treated dropwise with a solution of 6.5 g of aluminum chloride in ether. After the addition, a solution of 12 g of 2,8-dibenzylidenecyclooctanone (0.04 mol) and 8 g of aluminum chloride in 200 ml of ether was added slowly, and the reaction was refluxed 24 hr. Work-up as in the cyclooctanol preparation gave 7.7 g of oil which was hydrogenated directly and purified by chromatography (silica, hexane–benzene 9:1) to give 3.1 g (27%) of product. *Anal.* ($C_{22}H_{28}$) C, H.

2-Benzoylcyclooctanone (17) was prepared by the method of Hauser,[10] mp 59–61° (lit. 59–61°).

2-Benzylcyclooctanone (18) was synthesized by refluxing 26 g of cyclooctanonepyrrolidineenamine and 20 g of benzyl chloride in 125 ml of dioxane for 28 hr. The dioxane was removed by flash evaporation, and the oil was taken up in 400 ml of ether and washed with 5% aqueous HCl and water. After drying and solvent removal the oil was distilled [bp 120–130° (0.3 mm)] [lit.[11] 115–120° (0.2 mm)] to give 10.3 g of product. *Anal.* ($C_{12}H_{20}O$) C, H.

2-(α,4-Dimethoxybenzyl)-8-(4-methoxybenzylidene)cyclooctanone (31). General Method for α-Methoxy Derivatives. A solution of 5 g of Na in 100 ml of MeOH was prepared, and 12.6 g (0.1 mol) of cyclooctanone and 27.2 g (0.2 mol) of freshly distilled *p*-methoxybenzaldehyde were added. The reduction was stirred at room temperature for 6 days; the product was filtered, washed with water, and recrystallized from EtOH: yield 10 g (26%); mp 140.5–142°.

2,8-Bis(4-methoxybenzyl)cyclooctanone (32). Hydrogenated **31** (17 g, 0.05 mol) was melted and heated to 195°. $KHSO_4$ (0.5 g) was added and the reaction was stirred under a steady stream of nitrogen for 1 hr at 195–205° while MeOH was eliminated. After cooling, the reaction was dissolved in $CHCl_3$ and washed with H_2O to remove inorganics and dried, and $CHCl_3$ was removed. The dark yellow oil (17 g, crude) had an appropriate ir spectrum. Hydrogenation in EtOAc according to our standard procedure was followed by chromatography on silica ($CHCl_3$–C_6H_6, 60:40) to isolate 5 g (26%) of the product which was recrystallized from MeOH, mp 64–66°. *Anal.* ($C_{24}H_{30}O_3$) C, H.

Hydrogenation. General Procedure. 2,8-Bis(arylidene)cyclooctanone (10 g) was dissolved (or suspended) in 100 ml of dry EtOAc containing 1 g of 5% Pd/C catalysts. The suspension was hydrogenated on a Parr apparatus, generally overnight, although uptake of the theoretical amount of hydrogen usually occurred within 4 hr. Initial pressure in the hydrogenator was between 30 and 50 psig. After hydrogenation the catalyst was removed by filtration and solvent was flash evaporated; the oil remaining was recrystallized from MeOH or EtOH.

Biological Studies. Animals and Diet. Male Sprague–Dawley rats (Zivic-Miller, Allison Park, Pa.) were fed Purina rodent lab chow with water *ad libitum* for the duration of the experiment. Initial weight of the rats used was approximately 140 g.

Administration of Drugs. Each test compound was suspended in 1% carboxymethylcellulose–H_2O and homogenized. Doses (10 mg/kg) were calculated on weekly weights of the rats. All drugs were administered to the animals by an oral intubation needle (0.2 cc) daily at 11:00 A.M.

Serum Cholesterol, Animal Weight, and Autopsy and Estrogenic Activity. These methods have been outlined previously.[1] LD_{50} were determined by the Litchfield and Wilcoxon method.[12]

Results

Those compounds which demonstrated activity in lowering serum cholesterol are presented in Table II. 2,4-Dibenzyl-3-pentanone (**6**) was the most active of the modified compounds studied, reducing serum cholesterol by 50% when administered orally. Several compounds listed in Table II caused a moderate reduction (25%) of serum cholesterol.

Control animals given 1% CMC showed a percentage increase in body weight of 156 ± 2% after 16 days. Animals receiving **6** showed only 104 ± 5% increase in body weight after 16 days. The weight of vesicular glands and vas deferens plus epididymus expressed as percentage of body weight at autopsy after 16 days of treatment with **6, 25, 27, 32,** or **34** was significantly reduced (Table III).

Active compounds tested for estrogenic activity (Table IV) showed approximately half the activity, *i.e.*, increase in uterine weight in ovariectomized immature females, at 10 mg/kg as ethinylestradiol at 10 μg/kg. Compound **6** has an LD_{50} of 2.66 g/kg; all other active compounds were nontoxic at soluble dose levels.

Discussion

Examination of the SAR data in Table II suggests that the minimum requirement for hypocholesterolemic activi-

Table III. % Total Body Weight 24 hr after 16 Doses of Drug at 10 mg/kg

	Liver	Testes	Vesicular glands	Vas deferens and epididymis
Control	3.92 ± 0.40	1.12 ± 0.16	0.32 ± 0.10	0.44 ± 0.11
1	4.55 ± 1.28	0.91 ± 0.14	0.06 ± 0.02[a]	0.25 ± 0.09[c]
6	4.95 ± 0.28[a]	0.84 ± 0.21[c]	0.06 ± 0.02[a]	0.25 ± 0.09[c]
25	4.19 ± 0.41	1.13 ± 0.10	0.12 ± 0.06[a]	0.31 ± 0.10[c]
27	4.16 ± 0.45	1.10 ± 0.07	0.21 ± 0.11	0.34 ± 0.05
32	4.11 ± 0.33	1.16 ± 0.13	0.18 ± 0.04[b]	0.24 ± 0.04[a]
34	4.46 ± 0.11[b]	1.06 ± 0.02	0.13 ± 0.01[a]	0.25 ± 0.09[c]

[a] p = 0.001. [b] p = 0.010. [c] p = 0.025.

ty in this series of compounds is the bis(β-phenethyl) ketone system. Previous studies have shown that the ketone alone is inactive, and data are presented here showing that monosubstituted compounds are either inactive (17) or less active (18) than the symmetrically substituted ketone. The activity of the basic structure may be modulated by substitution of the α or β carbons, aromatic substitution, or modification of the ketone moiety.

Highest activity is seen when some substitution is present only at both α carbons (*e.g.*, 1 and 6). Removal of α substituents (11) or introduction of a more rigid framework as has been previously reported[1] (*e.g.*, 2,6-dibenzylcyclohexanone) leads to loss of activity. This pattern of high activity being associated with moderate steric hindrance at the α carbon suggests that there is a correlation between conformation and activity, and studies are underway to examine this relationship in more detail.

Reduction (*e.g.*, 2) or substitution of the aromatic ring lowers both hypocholesterolemic and estrogenic activity but at different rates. Since the estrogenic effect may be unrelated to the hypocholesterolemic activity and is an undesirable side effect of the hypocholesterolemia, an attempt was made to exploit this pattern.

Compounds **22**, **25**, **27**, **29**, **32**, and **34** show this differential effect of substitution upon the two biological activities. Of particular interest is compound **34**, which has a much lower estrogenic activity but retains some hypocholesterolemic effect. This raises the possibility that the estrogenic activity is due to a metabolite of 2,8-dibenzylcyclooctanone whose bioactivation is blocked by para substitution. Accordingly, the 4-chloro, 4-fluoro, and 4-hydroxy analogs are of some interest. Preliminary synthetic efforts have shown that the usual procedures are not successful because of the higher solubility of the bisylidenes and consequent difficulties in isolation. Some success has been achieved with an alternate route, which will be the subject of a later communication.

The addition of any group to the benzylic carbon (**5**, **8**, **9**, **10**, **31**) lowers activity, as does restricting rotation about the α–β bond (**7**, **21**). This is in congruence with our earlier finding that the intermediate ylidenes are devoid of activity.[1]

The carbonyl moiety may be reduced (14) or removed (16). Hypocholesterolemic activity drops upon reduction to the alcohol and is lost entirely when the carbonyl carbon is completely saturated. It is possible that carbonyl derivatives (*e.g.*, oximes) or related moieties such as the ester function would show activity. Synthetic difficulties have so far precluded the preparation of such analogs.

Table IV. Estrogenic Activity in Ovariectomized Sprague–Dawley Rat

	N	% control uterine wt	*P*
Control (1% CMC)	21	100 ± 23	
1	13	260 ± 22	0.001
6	8	148 ± 17	0.005
25	8	131 ± 20	0.050
27	8	143 ± 26	0.025
29	8	74 ± 6	n.s.
34	8	72 ± 16	n.s.
Ethinylestradiol (10 μg/kg)	13	259 ± 9	0.001

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A Hansch Analysis of the Anabolic Activities of Some Nandrolone Esters

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The anabolic activities in the rat of the butyrate to undecanoate normal fatty acid esters of nandrolone have been determined. Two peaks of activity were observed in plots of organ weight against time, for each ester, and assigned to release into the blood from the site of injection and from body fat, respectively. Anabolic activities were measured as increase in weight of levator ani over control weight, multiplied by duration of response. Solubilities in water and in ethyl oleate have been determined and distribution coefficients calculated. A binomial relationship was obtained between log anabolic activity and log ethyl oleate–water distribution coefficient. Similar equations were derived from the results of other authors.

The androgenic activity of testosterone can be enhanced and prolonged by esterification[1] and the times of maximum effect of the lower fatty acid esters, in the rat, are logarithmically related to the logarithms of their distribution coefficients.[2] Nandrolone decanoate (17β-decanoxyest-4-en-3-one) (Table I) has been shown pharmacologically to have a prolonged anabolic effect.[3] It is compared here with other nandrolone esters to determine if its enhanced biological activity is due to a favorable oil–water distribution coefficient.

Methods

Preparation of Esters. Nandrolone and nandrolone decanoate were gifts from Organon Laboratories, Ltd. The remaining esters