last years of his life he collected his lecture notes into a series of six books, entitled *Lectures on Theoretical Physics*. The successive volumes cover mechanics, the mechanics of deformable media, electrodynamics, optics, thermodynamics and statistics, and partial differential equations of physics. All these volumes except the one on thermodynamics and statistics have appeared in English translation as well as in German; he had nearly completed the manuscript for this volume at the time of his death. Like his earlier books, these works are characterized by extraordinary clarity of expression and argument.

Sommerfeld received many honorary degrees and awards, and was honorary member of many scientific academies. Two years ago the American Association of Physics Teachers presented to him the Oersted Medal, in recognition of his outstanding contributions as a teacher of physics. Additional recognition of Sommerfeld's contributions as an investigator and a teacher was given by his students in four memorial volumes: the book *Probleme der modernen Physik*, celebrating his sixtieth birthday, the December 1938 issue of *Physical Review*, celebrating his seventieth birthday, the book *Cosmic Radiation*, fifteen lectures edited by Heisenberg and given in honor of Sommerfeld's seventy-fifth birthday, and the August–November 1948 issue of the *Zeitschrift für Naturforschung*, honoring his eightieth birthday. The hazard of a mechanized world has prevented his students from celebrating during his lifetime still further anniversaries of the birth of this great man, who retained his extraordinary mental vigor and acuity up to the end.

Technical Papers

A New Class of Hypnotics: Unsaturated Carbinols

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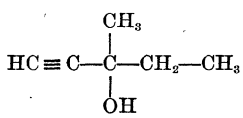
Recent pharmacological investigation (*1*) has shown that certain ethinyl tertiary carbinols (*2*) exhibit significant hypnotic activity in several species (mice, rats, guinea pigs, rabbits, cats, dogs, and monkeys). Hypnotic effects followed oral as well as parenteral administration of the compounds. Earlier investigators have described the induction of generalized central nervous system depression in experimental animals with tertiary carbinols (*3*). The only tertiary carbinol to attain clinical use as a hypnotic is amylene hydrate, a saturated compound (*4, 5*). In our studies, the simple unsaturated aliphatic carbinols were found to possess high activity, desirable duration of action, and low toxicity. Of the latter group, 3-methyl-pentyne-ol-3,[1] was considered worthy of extensive pharmacodynamic, biochemical, and clinical study. Its structural formula is



Barbiturate potentiation in the mouse (*6*) and direct hypnotic activity in dogs were used to evaluate quantitatively the oral hypnotic efficacy of the test compounds. The hypnotic effect was characterized by the appearance of a distinct and sequential reaction pattern—sedation, loss of righting reflex, and sleep. An interesting parallel in relative hypnotic activity for 3-methyl-pentyne-ol-3 and other hypnotics was found in experimental animals and in man (Table 1). (The value of 100 has been arbitrarily assigned to pentobarbital sodium.)

TABLE 1

ORAL ACTIVITY OF 3-METHYL-PENTYNE-OL-3 AND OTHER HYPNOTICS IN EXPERIMENTAL ANIMALS AND IN MAN

Drug	Human dose (mg/70 kg)	Relative activity		
		Man	Dog	Mouse
3-Methyl-pentyne-ol-3	250	40.0	20.0	71.9
Amylene hydrate	1500	6.7	10.0	20.0
Paraldehyde	5000	2.0	4.3	4.6
Phenobarbital	100	100.0	50.0	100.0
Pentobarbital sodium	100	100.0	100.0	100.0
Presidon	300	33.3	20.0	33.3

3-Methyl-pentyne-ol-3 is distinguished by a high selectivity of action. When measured in rats at the maximal tolerated dose, according to a modified Wolff-Hardy procedure (*7, 8*), it was not analgesic (*1*). The absence of analgesic effect was confirmed in mice and dogs. No anesthesia was observed when the compound was administered intravenously to dogs in sublethal amounts. This absence of anesthetic properties was observed in mice and rats also (*1*). When tested according to the *in vitro* Magnus-Dale technique, 3-methyl-pentyne-ol-3 was found not to possess antispasmodic action. Furthermore, in marked contrast to barbiturates and other hypnotics, 3-methyl-pentyne-ol-3, even in large doses, did not depress respiration. Caffeine given parenterally caused rapid recovery from the deep hypnotic state induced by overdoses.

[1] Dormison, trade-mark of Schering Corporation, Bloomfield, N. J.

No undesirable aftereffects have been observed in animals given overdoses of the drug.

Several members of the class were tested for acute toxicity in rodents and dogs by oral and parenteral routes. Among these, 3-methyl-pentyne-ol-3 was notably low in toxicity. The acute oral LD_{50} for mice, rats, and guinea pigs, ranged from 600 to 900 mg/kg. The animals died in a state of coma. A few active compounds with low acute toxicity were tested for chronic toxicity in mice, rats, and dogs. 3-Methyl-pentyne-ol-3 at 200–300 mg/kg/day (approximately 70 times the recommended human dose) did not produce any gross or micropathological changes. Blood sugar levels, hemoglobin values, and erythrocyte, white blood cell, and differential counts were normal. Dogs that had received chronically 3-methyl-pentyne-ol-3 *per os* showed normal renal function (phenolsulfonphthalein test).

In metabolic studies on 3-methyl-pentyne-ol-3, the acetylenic hydrogen was used to identify and estimate the compound through the formation of the silver acetylide and the microdetermination of silver (*9*). Following the oral administration of 3-methyl-pentyne-ol-3 (200 mg/kg) to adult dogs, 0.5–4.6% of the total dose was excreted in the urine during the first 24 hr; thereafter, only traces could be detected. In preliminary trials, no drug was detected in the urine obtained from three human subjects during a 60-hr period after a single oral dose of 100 mg. It was estimated that no more than 8% of the total dose could have been present in any 4-hr specimen. Following intravenous administration to dogs (200 mg/kg), it was found that the blood contained during the first 10 min 20% of the total dose; no drug could be detected in the blood at 2 hr. Analyses of rat tissues (brain, spleen, kidney, adipose, muscle, and liver) taken while the animals were still under the hypnotic action of 3-methyl-pentyne-ol-3 (800 mg/kg), revealed that adipose, muscle, and liver tissues together contained approximately 20% of the total dose. No unchanged compound was found in any of the organs or tissues when the effects of the drug were no longer manifest. *In vitro* experiments in which 3-methyl-pentyne-ol-3 was added to whole blood from dogs and rats indicated that there was no breakdown of the compound; i.e., the acetylenic hydrogen was still present. However, slices of kidney or liver, and to a lesser degree slices of brain, changed this molecule in such a way as to render it nonreactive with the silver reagent (*9*).

In a clinical study in 134 subjects, the majority of whom previously required barbiturates for sleep, 3-methyl-pentyne-ol-3 was found to be highly active, without toxic effect, and free from undesirable side actions (*10*). The effective oral dose in adults was 200–300 mg. Sleep was brought about in the majority of patients in less than ½ hr. The patients who received 3-methyl-pentyne-ol-3 experienced restful sleep and had no "hangover" upon awakening. A number of patients have been given daily doses of the compound for more than 6 months without any untoward effects. Complete blood counts, urinalyses, blood sugar, blood urea nitrogen, creatinine, total serum protein, albumin, globulin, phosphorous, alkaline phosphotase, total cholesterol, free and combined cholesterol, and in addition, the icterus index, Van den Bergh, thymol turbidity, or cephalin flocculation values were determined, before and after medication with 3-methyl-pentyne-ol-3. These clinical laboratory tests indicated that there were no pathological changes attributable to the drug.

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The Life Span of the Red Blood Cell in Chronic Leukemia and Polycythemia[1,2]

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The anemia associated with leukemia and neoplastic diseases is still not completely understood; infiltration of the bone marrow in some cases, with crowding out of the erythropoietic tissue, has been postulated as a significant factor in the pathogenesis of the anemia. However, Huff and co-workers (*1*) have shown with radioactive iron that in some patients with leukemia the rate of production of red blood cells was greater than the 0.8% per day that would be anticipated if the cells lived a normal life span of approximately 120 days (*2*). These same workers showed that in polycythemia vera the rate of production of red cells was much greater than 0.8% per day. These findings may be explained by postulating a decrease in the life span of the red blood cells in these diseases. Using N^{15}-labeled glycine, which Shemin and Rittenberg (*2*) demonstrated to be a specific precursor of the porphyrin of hemoglobin, London *et al.* (*3*) found a normal life span of the red blood cell in a single case of polycythemia vera.

Since C^{14}-labeled glycine has been shown to be satisfactory for the labeling of rat hemoglobin (*4, 5*) and for the determination of the life span of the red blood

[1] This study was supported in part by the Atomic Energy Commission and the U. S. Public Health Service.

[2] Presented before the American Federation for Clinical Research, Atlantic City, N. J., May 1, 1951.