Dyes.—The dye condensations are listed in Table II. They were carried out as already detailed.[4] The yields of crude and of purified dyes are given and the volume of solvent required for recrystallization.

D1 formed red needles with a blue reflex, 2 and 3 being similar; 4 and 5 consisted of yellow-brown prisms, 6 reddish-brown needles, 7 yellow-orange tablets, 8 brownish-yellow crystals, 9 light-brown prisms; 10 consisted of amber needles; 11 formed minute orange-brown crystals with a green reflex, and 12, 13 and 15 all consisted of reddish-brown needles with a green reflex; 14 formed reddish-brown crystals.

The dyes were tested photographically by incorporation in a chloride emulsion. The maximum effect of D1 is at about 5175 Å., the effect extending to about 5500 Å. for the moderate exposure given. D2 and 3 both have maxima at 5250 Å., and D6 at 5350 Å. D4 and 5 both have maxima at 4775 Å. The order in which these dyes fall is the same, therefore, whether absorption or sensitizing maxima are considered with respect to increasing wave length, and the difference between corresponding absorption and sensitizing maxima varies from 425 to 525 Å.

In the 2′-pyridocyanine series the sensitizing maxima of D7 to 10 lie at 4700, 4750, 4750, and 4825 Å., respectively, and in the series D11 to 15 the corresponding figures are 5250, 5300, 5300, 4900 and 5400 Å., respectively.

Summary

1. Triethylamine has proved to be an excellent condensing agent for the preparation of the hitherto unknown thiazolo-2′-cyanines from quaternary salts of the 2-methylthiazoles and 2-iodoquinoline ethiodide. Three dyes of this series are described.

2. By using 2-iodopyridine ethiodide and 2-iodo-β-naphthoquinoline ethiodide there have likewise been prepared the corresponding thiazolo-2′-pyridocyanines and 5′,6′-benzo-thiazolo-2′-cyanines, respectively.

3. Bases of the 2-methyloxazole series have been used for the preparation of certain oxygen-containing dyes related to the above, and 2,4-dimethylselenazole has been synthesized and similarly applied to the formation of corresponding cyanine dyes.

4. Four dyes have been prepared in which there is a methyl substituent in the 4-position of the thiazole (or oxazole) nucleus. In every case the absorption maximum occurs at the same wave length as that of the related dye containing a 4-phenyl group. Further absorption relationships are discussed.

5. The new dyes are all photographic sensitizers and details of their action are given.

ROCHESTER, NEW YORK RECEIVED SEPTEMBER 5, 1935

[CONTRIBUTION FROM THE JOHN HARRISON LABORATORY OF CHEMISTRY OF THE UNIVERSITY OF PENNSYLVANIA]

A Study of Some Urea Derivatives in the Terpene Series

BY ROBERT L. BATEMAN AND ALLAN R. DAY

In connection with certain studies of urea and its derivatives, it was thought that the preparation and examination of some terpenyl ureas might be of interest. While certain of the terpenes and their derivatives are employed medicinally, little experimental work has been carried out with the purpose of modifying their properties by structural changes and little effort has been made to introduce terpene radicals into compounds of known physiological properties.

Menthyl and bornyl ureas and certain of their derivatives were chosen because of the known physiological properties of substituted ureas and because of the medicinal importance of menthol and camphor which were the starting materials. Menthol is known to possess mild antiseptic and anesthetic properties, while camphor acts as a depressant on the central nervous system and as a stimulant on the circulatory system. If these properties, in greater part, are inherent in the functional groups (hydroxyl and carbonyl, respectively) the introduction of the menthyl and bornyl radicals into urea would not be expected to produce marked effects, as the functional groups are absent. However, if their physiological properties depend in part on their cyclic structure, a definite modifying influence should be observed.

It will be noted that all but one of the derivatives prepared contain the simple menthyl or bornyl group. In order to determine the influence of the functional group, 2-keto-3-carbamidocamphane was prepared. This urea contains in its substituent not only the cyclic structure common to borneol and camphor, but also the functional group of camphor.

The terpenylureas were obtained in satisfactory

TABLE I

MENTHYL AND BORNYLUREA AND DERIVATIVES

Substance	Form	M. p., °C., corr.	$[\alpha]^{25}D$ in 95% alcohol	Nitrogen, %[a] Calcd.	Found
Menthylurea	Prisms	140.2–140.6	−80.0	14.14	13.96
sym-Acetylmenthylurea	Needles	118 –119	−83.3	11.66	11.63
Chloral addn. product ($RNHCONHCHOHCCl_3$)	Needles	146.2–147.2	−49.1	8.10	8.08
sym-Bromoacetylmenthylurea	Plates	111.8–112.3	−66.9	8.78	8.80
sym-Cinnamoylmenthylurea	Leaflets	144.3–145.1	−67.9	8.54	8.51
syn-*p*-Nitrobenzoylmenthylurea	Needles	158.7–159.2	insol.	12.09	11.75
sym-*p*-Aminobenzoylmenthylurea	Needles	208–210 (dec.)	−72.3	13.25	13.11
Bornylurea	Needles	165.7–166.3	+ 5.83	14.28	14.21
sym-Acetylbornylurea	Needles	129 –129.5	+23.5	11.76	11.70
Chloral addn. product	Cryst. powder	180 (dec.)	+ 7.3	8.15	8.07
sym-Bromoacetylbornylurea	Tabular prisms	136.1–136.5	+16.3	8.83	8.75
sym-Cinnamoyl bornylurea	Needles	220.2–220.8	insol.	8.59	8.54
sym-*p*-Nitrobenzoylbornylurea	Needles	230 (dec.)	insol.	12.17	11.93
sym-*p*-Aminobenzoylbornylurea	Needles	233 (dec.)	+15.6	13.83	12.90
2-Keto-3-carbamidocamphane ($C_{11}H_{18}N_2O_2 \cdot {}^1/_2H_2O$)	Cryst. powder	177.8–178.4	+18.3	12.78	12.68

[a] Average values.

yields by the interaction of nitrourea and terpenylamine

$$RNH_2 + H_2NCONHNO_2 = RNHCONH_2 + N_2O + H_2O$$

A number of acyl derivatives as well as the chloral addition products of the above ureas were also prepared for the purpose of modifying the physiological properties of the terpenylureas.

Experimental

l-Menthylurea.[1]—To 20 g. of *l*-menthylamine hydrochloride[2] and 20 g. of nitrourea[3] in 600 cc. of water was slowly added with stirring a slight excess of sodium bicarbonate and after twelve hours the colorless reaction product was recrystallized from dilute alcohol; yield 78%.

A similar procedure was followed in the preparation of *d*-bornylurea[4,5,6] and a yield of 90% was obtained.

The menthyl as well as the bornylurea was acylated directly with acetic anhydride and in benzene solution with bromoacetyl bromide, cinnamoyl chloride and *p*-nitrobenzoyl chloride. The yields were almost the theoretical except in the case of bromoacetylmenthylurea. In the latter case it dropped to 20%. In general the crude products were readily purified by recrystallization from alcohol. *d*-Cinnamoylbornylurea was recrystallized from acetone and *d*-*p*-nitrobenzoylurea from a mixture of glacial acetic acid (2 parts) and acetone (8 parts).

Chloral Addition Products of *l*-Menthyl and *d*-Bornylurea.—Five grams of chloral was slowly added to 5 g. of the urea with stirring and the mixture allowed to stand for one hour in the absence of moisture. The excess chloral was removed with a little ligroin and the crude product recrystallized from alcohol. The compounds were quite stable and did not hydrolyze readily in the presence of water; yields, 80–86%.

1-*p*-Aminobenzoylmenthylurea and *d*-*p*-Aminobenzoylbornylurea.—Seven grams of the corresponding nitro compound was partially dissolved in 60 cc. of hot alcohol and 60 cc. of 6 *M* ammonium sulfide added. After two hours' refluxing on a water-bath, the solution was diluted with water and the crude product recrystallized from alcohol; yield, about 90%. The corresponding hydrochlorides were prepared by saturating an ether solution of the free base with dry hydrogen chloride. They were obtained as colorless powders and were quite insoluble in the common solvents.

***d*-2-Keto-3-carbamidocamphane.**—This compound was prepared by the reduction of the stable (*syn*) form of isonitrosocamphor[7] with zinc dust and acetic acid to the corresponding amine[8] and the latter then converted to the corresponding urea by the nitrourea method. The crude product was recrystallized from hot water; yield, 75–80%, based on the hydrochloride used. Its analysis indicated the probable presence of water of hydration which could not be removed by drying in vacuum or by heating below its decomposition point. Its *p*-nitrobenzoyl derivative analyzed correctly for $C_{18}H_{21}N_3O_5$. Calcd.: N, 11.70. Found: N, 11.63.[9]

The physical constants and analytical data for the various compounds prepared are given in Table I.

Pharmacological Tests

Some preliminary tests on six of these derivatives have been carried out by Dr. Carl F. Schmidt of The Pharmacology Department of the Uni-

(1) O. Wallach, *Ann.*, **300**, 279 (1898). Wallach obtained a 30% yield by the acti n of potassium cyanate on menthylamine hydrochloride, m. p. 134–136°.

(2) E. Beckmann, *ibid.*, **250**, 325 (1889).

(3) T. L. Davis and K. C. Blanchard, THIS JOURNAL, **51**, 1794 (1929).

(4) M. O. Forster, *J. Chem. Soc.*, **73**, 390 (1898).

(5) R. Leuchart and Bach, *Ber.*, **20**, 104 (1887).

(6) M. O. Forster and H. M. Atwell, *J. Chem. Soc.*, **85**, 1188 (1904). Leuchart and Bach first obtained this urea by the action of potassium cyanate on *d*-bornylamine hydrochloride, m. p. 164°. Later Forster and Atwell prepared it by the same method and reported a melting point of 175°.

(7) M. O. Forster, *J. Chem. Soc.*, **83**, 514 (1903); **85**, 905 (1904).

(8) Claisen and Manasse, *Ann.*, **274**, 79 (1893).

(9) Rupe [*Ber.*, **27**, 584 (1894); **28**, 778 (1895)] obtained this urea by the action of potassium cyanate on *d*-3-aminocamphor hydrochloride and reported its melting point as 169°.

versity of Pennsylvania School of Medicine. The compounds were dissolved in ethylene glycol and injected intraperitoneally in white rats.

Menthyl urea in dosage of 220 mg. per kg. caused profound unconsciousness with the abolition of all reflexes. The narcosis appeared at the end of fifteen minutes and was undiminished seven hours after injection. At the end of twenty-two hours the animal had recovered completely and appeared normal. In dosage of 63 mg. per kg. there was definite drowsiness without visible muscular incoördination. The animal was easily aroused at all times and seemed normal when aroused. At twenty hours it was quite normal.

The low solubility of bromoacetylbornylurea and *p*-aminobenzoylmenthylurea made adequate testing impracticable. They had no demonstrable narcotic effects in the dosage used. Larger amounts of the solutions caused ethylene glycol poisoning.

Chloral menthylurea was clearly the most potent. It was the most toxic, slowest acting and most persistent of those tested.

Bornylurea and 2-keto-3-carbamidocamphane acted slowly and weakly with considerable muscular incoördination and the latter seemed to be intensely irritant locally.

Summary

1. *l*-Menthylurea, *d*-bornylurea and 2-keto-3-carbamidocamphane have been prepared by the nitrourea method.

2. The following new derivatives of *l*-menthylurea and *d*-bornylurea have been prepared: acetyl, bromoacetyl, chloral addition product, *p*-nitrobenzoyl and *p*-aminobenzoyl.

3. Preliminary tests on the narcotic effects of some of these ureas indicated that menthylurea was the most promising and may have some value. It acted rapidly without evident after-effects.

PHILADELPHIA, PENNA. RECEIVED AUGUST 19, 1935

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

Esters of the Aldehydrol Form of Sugars

BY M. L. WOLFROM

Diacetates of aliphatic aldehydes, $RCH(OAc)_2$, have long been known but have been little studied. Some of the earliest work was carried out by Geuther,[1] who prepared these derivatives by heating aliphatic aldehydes with acetic anhydride at relatively high temperatures (180°). Later work[2] showed that the reaction was greatly accelerated by zinc chloride or sodium acetate. Aceto-halogen compounds of aliphatic aldehydes, RCHOAc·X, have also been prepared.[3] From the standpoint of organic structural theory, compounds of this type may be considered as esters of the aldehydrol, $RCH(OH)_2$, irrespective of whether the aldehydrol is an intermediate in their formation.

In the sugar series, the first representative of this type of compound was the crystalline triacetate of gycolaldehyde prepared by H. O. L. Fischer and Dangschat[4] by treating vinyl acetate dibromide with potassium acetate and also directly from the sugar by heating with acetic anhydride. Micheel and co-workers[5] have reported the synthesis of the *d*- and *d,l*- forms of *aldehydo*-galactose heptaacetate as incidental to their important synthetic experiments in the transformation of hexoses into inositols.

Aldehydo-galactose pentaacetate readily forms crystalline carbonyl addition compounds with alcohols and water, the reaction product with the latter being a true aldehydrol.[6] This addition takes place readily at room temperature. We have now found that acetyl halide addition compounds of *aldehydo*-galactose pentaacetate can be readily formed. The resulting compounds are the open chain analogs of the cyclic sugar acetohalogen derivatives and may be named, for example, *aldehydo*-1-chloro-*d*-galactose hexaacetate. In the work herein reported the chloride, bromide and iodide are described. Their rota-

(1) A. Geuther, *Ann.*, **106**, 249 (1858).

(2) G. Kauffmann, *Ber.*, **16**, 683 (1883); M. Descudé, *Compt. rend.*, **133**, 371 (1901).

(3) A. Wurtz, *Ann. chim. phys.*, [3] **49**, 58 (1857); V. Meyer and L. Dulk, *Ann.*, **171**, 65 (1874).

(4) H. O. L. Fischer and Gerda Dangschat, *Ber.*, **62**, 862 (1929).

(5) F. Micheel, H. Ruhkopf and F. Suckfüll, *ibid.*, **68**, 1523 (1935).

(6) M. L. Wolfrom, THIS JOURNAL, **52**, 2464 (1930); *ibid.*, **53**, 2275 (1931); M. L. Wolfrom and W. M. Morgan, *ibid.*, **54**, 3390 (1932).