tions and that at 2525 Å. for alkaline solutions.[7] Neutral and nearly neutral solutions were acidified with sulfuric acid and the absorption determined at 2505 Å. Concentration of residual 8-quinolinol in the chloroform phase was determined by difference in each case. The distribution coefficient was then evaluated as the ratio of the molar concentration of 8-quinolinol in the chloroform phase to the total molar concentration of all 8-quinolinol species in the aqueous phase. Substitution of concentrations for activities was permissible because of the low concentration levels employed.

Discussion

Variation in distribution coefficients with *p*H, as indicated in Table I, are easily understood in terms of the amphoteric character of 8-quinolinol. The basic and acidic properties of the compound are described by the equilibria

$$HOn + H^+ \rightleftharpoons HOn \cdot H^+ \quad (2)$$

$$HOn \rightleftharpoons H^+ + On^- \quad (3)$$

where HOn represents molecular 8-quinolinol. The basic and acidic dissociation constants have been determined[2,3-10] and permit evaluation of the concentrations of all three species at any *p*H. Since the only species existent in chloroform is the molecular one, it follows that essentially complete concentration of 8-quinolinol in the chloroform phase can be expected only over that *p*H range in which the quantity of the molecular species is maximum in the aqueous phase. As shown in Table I, *ca.* 99% of the 8-quinolinol in the latter phase is in the molecular form in the *p*H range 7.0–8.2, with more than 90% being molecular at as low a *p*H as 6.0. In this *p*H range, the average experimental distribution coefficient of 353 closely approximates that calculated for molecular 8-quinolinol.

TABLE I

DISTRIBUTION OF 8-QUINOLINOL BETWEEN CHLOROFORM AND WATER AT 25°

*p*H	Σc_{H_2O}[a] mole/liter, $\times 10^5$	c_{CHCl_3}[b] mole/liter, $\times 10^3$	c_{CHCl_3}/c_{H_2O}	Molecular HOn in aqueous layer, %
2.06	9.90	0.0575	0.58	0.12
2.65	4.28	0.0792	1.85	0.44
3.75	4.40	1.17	26.4	5.32
4.43	1.51	1.36	89.9	21.2
6.05	0.489	1.72	352	92
7.00	.351	1.21	350	99
7.05	.475	1.71	360	99
8.21	.489	1.72	352	98
9.24	.055	0.121	221	80.5
10.50	2.06	1.36	65.8	18.4
12.00	4.82	0.105	2.18	0.71

[a] Sum of concentrations of molecular, cationic and anionic species. [b] Concentration of molecular species.

On the other hand, in either more acidic or more alkaline aqueous solutions, only a small fraction of the 8-quinolinol present is in the molecular form. The experimentally determined distribution coefficients, as based upon the total 8-quinolinol concentration in the aqueous phase, decrease correspondingly. Thus, although the distribution coefficients given in Table I are really theoretical values for only the 6.0–8.2 *p*H range, they are of practical importance in determining optimum *p*H conditions for 8-quinolinol extractions.

(8) K. Stone and L. Friedman, THIS JOURNAL, **69**, 209 (1947).

(9) J. P. Phillips and L. L. Merritt, *ibid.*, **70**, 410 (1948).

(10) H. Irving, J. A. D. Ewart and J. T. Wilson, *J. Chem. Soc.*, 2672 (1949).

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Isolation of Methylchrysene from Petroleum

BY R. J. MOORE, R. E. THORPE AND C. L. MAHONEY

RECEIVED JANUARY 15, 1953

In the course of examining a Mid-continent medium petroleum distillate by silica gel chromatography, a white crystalline material has been isolated which is identified as 1-methylchrysene. After recrystallization from ethanol, the melting point was 253° (compared with 251° found by Brode and Pattersen[1]). The ultraviolet absorption spectrum was identical to that reported for synthetic 1-methylchrysene and the parent mass found with a high temperature mass spectrometer was 242, corresponding to $C_{19}H_{14}$. Excepting the *n*-paraffins, we believe that this is the highest molecular weight pure hydrocarbon thus far isolated from native petroleum.

(1) W. R. Brode and J. W. Pattersen, THIS JOURNAL, **63**, 3252 (1941).

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Carbazic Acid Esters as Carbonyl Reagents

BY NORMAN RABJOHN AND H. D. BARNSTORFF[1]

RECEIVED JANUARY 5, 1953

The common derivatives of aldehydes and ketones such as phenylhydrazones, substituted phenylhydrazones, oximes and semicarbazones, as well as a rather large number of lesser known condensation products, are described extensively in the literature and textbooks for qualitative organic analysis. However, it appears that little use[2] has been made of the esters of carbazic acid as carbonyl reagents. These materials are stable, crystalline solids which can be synthesized readily from hydrazine and an organic carbonate.

The present work describes the preparation of a number of carbonyl derivatives of methyl and ethyl carbazates which have not been reported previously. The data obtained for a series of carbomethoxyhydrazones are given in Table I. The properties of the carboethoxyhydrazones are listed in Table II.

Formaldehyde, benzalacetophenone and benzil gave mixtures of products with both methyl and

(1) From a thesis submitted by Henry D. Barnstorff to the Graduate School of the University of Missouri, 1949, in partial fulfillment of the requirements for the degree of Master of Arts.

(2) A relatively few derivatives are recorded in the following leading references: K. v. Auwers and Th. Breyhan, *J. prakt. Chem.*, **143**, 259 (1935); H. J. Backer and W. Meyer, *Rec. trav. chim.*, **45**, 82 (1926); H. DeGraff, Diss. Leiden (1930), *C. A.*, **24**, 5723 (1930); O. Diels and P. Fritzsche, *Ber.*, **44**, 3018 (1911); D. N. Majumdar and P. C. Guha, *J. Indian Chem. Soc.*, **10**, 685 (1933); and R. B. Woodward, T. P. Kohman and G. C. Harris, THIS JOURNAL, **63**, 120 (1941).

TABLE I

CARBOMETHOXYHYDRAZONES, $RCH(R)=NNHCO_2CH_3$

Carbonyl compd.	Corrected m.p., °C.	Formula	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
o-Chlorobenzaldehyde	149–150	$C_9H_9O_2N_2Cl$	50.83	50.93	4.27	4.32
m-Chlorobenzaldehyde	120–121	$C_9H_9O_2N_2Cl$	50.83	50.64	4.27	4.53
Cinnamaldehyde	171–172	$C_{11}H_{12}O_2N_2$	64.69	64.43	5.92	5.89
p-Dimethylaminobenzaldehyde	167–168	$C_{11}H_{15}O_2N_3$	59.71	59.68	6.83	6.75
2-Ethylhexaldehyde	82–83	$C_{10}H_{20}O_2N_2$	59.97	59.77	10.07	10.17
Furfural	142–143	$C_7H_8O_3N_2$	50.00	50.02	4.80	4.70
p-Hydroxybenzaldehyde	193–194	$C_9H_{10}O_3N_2$	55.66	55.75	5.19	5.14
Isobutyraldehyde	98–99	$C_6H_{12}O_2N_2$	49.98	49.77	8.39	8.45
o-Methoxybenzaldehyde	154–155	$C_{10}H_{12}O_3N_2$	57.68	57.67	5.81	5.85
m-Nitrobenzaldehyde	202–203	$C_9H_9O_4N_3$	48.43	48.17	4.06	4.31
Salicylaldehyde	165–166	$C_9H_{10}O_3N_2$	55.66	55.78	5.19	5.25
o-Tolualdehyde	127–128	$C_{10}H_{12}O_2N_2$	62.48	62.32	6.29	6.58
m-Tolualdehyde	113–114	$C_{10}H_{12}O_2N_2$	62.48	62.73	6.29	6.50
p-Tolualdehyde	154–155	$C_{10}H_{12}O_2N_2$	62.48	62.72	6.29	6.21
Vanillin	185–186	$C_{10}H_{12}O_4N_2$	53.57	53.34	5.39	5.54
Acetophenone	127–128	$C_{10}H_{12}O_2N_2$	62.48	62.42	6.29	6.60
Benzophenone	120–121	$C_{16}H_{14}O_2N_2$	70.85	70.66	5.55	5.64
p-Bromoacetophenone	147–148	$C_{10}H_{11}O_2N_2Br$	44.30	44.45	4.09	4.28
Cyclopentanone	78–79	$C_7H_{12}O_2N_2$	53.83	53.59	7.74	7.92
Desoxybenzoin	126–127	$C_{16}H_{16}O_2N_2$	71.62	71.58	6.01	5.97
Dibenzyl ketone	146–147	$C_{17}H_{18}O_2N_2$	72.32	72.23	6.43	6.52
Diethyl ketone	65–66	$C_7H_{14}O_2N_2$	53.14	52.99	8.92	9.17
Fluorenone	167–168	$C_{15}H_{12}O_2N_2$	71.41	71.43	4.80	4.91
o-Hydroxyacetophenone	172–173	$C_{10}H_{12}O_3N_2$	57.68	57.48	5.81	6.00
Isophorone	174–175	$C_{11}H_{18}O_2N_2$	62.83	62.56	8.63	8.87
Methyl *n*-amyl ketone	69–70	$C_9H_{18}O_2N_2$	58.03	57.83	9.74	9.91
Methyl *n*-propyl ketone	76–77	$C_7H_{14}O_2N_2$	53.14	52.95	8.92	9.17
Methyl *p*-tolyl ketone	139–140	$C_{11}H_{14}O_2N_2$	64.06	63.85	6.84	6.82
Pinacolone	67–68	$C_8H_{16}O_2N_2$	55.79	55.49	9.36	9.52
Propiophenone	161–162	$C_{11}H_{14}O_2N_2$	64.06	63.98	6.84	6.98

TABLE II

CARBOETHOXYHYDRAZONES, $RCH(R)=NNHCO_2C_2H_5$

Carbonyl compd.	Corrected m.p., °C.	Formula	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
o-Chlorobenzaldehyde	99–100	$C_{10}H_{11}O_2N_2Cl$	52.98	53.05	4.89	4.94
m-Chlorobenzaldehyde	98–99	$C_{10}H_{11}O_2N_2Cl$	52.98	52.90	4.89	5.03
p-Dimethylaminobenzaldehyde	154–155	$C_{12}H_{17}O_2N_3$	61.25	61.15	7.28	7.44
2-Ethylhexaldehyde	53–54	$C_{11}H_{22}O_2N_2$	61.65	61.34	10.35	10.46
p-Hydroxybenzaldehyde	217–218	$C_{10}H_{12}O_3N_2$	57.68	57.54	5.81	5.94
Isobutyraldehyde	68–69	$C_7H_{14}O_2N_2$	53.14	52.89	8.92	9.14
o-Methoxybenzaldehyde	120–121	$C_{11}H_{14}O_3N_2$	59.45	59.18	6.35	6.28
m-Nitrobenzaldehyde	165–166	$C_{10}H_{11}O_4N_3$	50.63	50.84	4.67	4.94
o-Tolualdehyde	124–125	$C_{11}H_{14}O_2N_2$	64.06	64.25	6.84	7.09
m-Tolualdehyde	102–103	$C_{11}H_{14}O_2N_2$	64.06	64.05	6.84	6.85
Benzalacetone	156–157	$C_{13}H_{16}O_2N_2$	67.22	67.31	6.94	7.15
Benzophenone	112–113	$C_{16}H_{16}O_2N_2$	71.62	71.45	6.01	6.04
p-Bromoacetophenone	150–151	$C_{11}H_{13}O_2N_2Br$	46.33	46.16	4.59	4.51
Cyclopentanone	103–104	$C_8H_{14}O_2N_2$	56.45	56.21	8.29	8.44
Desoxybenzoin	104–105	$C_{17}H_{18}O_2N_2$	72.32	72.04	6.43	6.51
Dibenzyl ketone	98–99	$C_{18}H_{20}O_2N_2$	72.95	73.10	6.80	6.84
Fluorenone	126–127	$C_{16}H_{14}O_2N_2$	72.16	72.45	5.30	5.33
o-Hydroxyacetophenone	134–135	$C_{11}H_{14}O_3N_2$	59.45	59.32	6.35	6.32
Isophorone	128–129	$C_{12}H_{20}O_2N_2$	64.25	64.00	8.99	9.28
Methyl *p*-tolyl ketone	110–111	$C_{12}H_{16}O_2N_2$	65.43	65.66	7.32	7.31
Pinacolone	84–85	$C_9H_{18}O_2N_2$	58.03	58.04	9.74	9.97
Propiophenone	144–145	$C_{12}H_{16}O_2N_2$	65.43	65.30	7.32	7.45

ethyl carbazates. Low melting solids or oils resulted from the condensation of methyl carbazate with *n*-butyraldehyde, methyl ethyl ketone, mesityl oxide and cyclohexanone. Similar results were obtained with ethyl carbazate and *n*-butyraldehyde, methyl ethyl ketone, methyl *n*-propyl ketone, diethyl ketone, mesityl oxide, methyl *n*-amyl ketone and cyclohexanone.

Experimental

Methyl and Ethyl Carbazates.—These esters were prepared in about 90% yields from 85% hydrazine hydrate and dimethyl and diethyl carbonates, respectively, by the procedure of Diels.[3]

Preparation of the Carbomethoxy- and Carboethoxyhydrazones.—Approximately 1 g. of the aldehyde or ketone was dissolved in 3–4 ml. of alcohol and sufficient water was added to cause a faint turbidity. This was removed by means of a few drops of alcohol, and then 3 drops of acetic acid and 1 g. of the carbazate were added. The mixture was shaken and allowed to stand for a few minutes. If crystallization did not result, the reaction mixture was heated to reflux for one hour and cooled. The precipitate was removed by filtration, weighed and crystallized. In those cases where a solid was not obtained readily, the reaction was carried out without the addition of water, and after refluxing for one hour, the solvent was evaporated and the residue recrystallized.

In practically all of the condensations, the yields of the derivatives were high. The products were purified by recrystallization from dilute alcohol or a mixture of benzene and petroleum ether.

(3) O. Diels, *Ber.*, **47**, 2183 (1914).

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Streptohydrazid

BY FRANK C. PENNINGTON, PETER A. GUERCIO AND I. A. SOLOMONS

RECEIVED JANUARY 19, 1953

Previous investigators[1] have demonstrated the condensation of streptomycin with a wide variety of amino compounds. Since isoniazid and streptomycin are both used in the chemotherapy of tuberculosis and have been proposed for combined therapy,[2] it was of interest to prepare and characterize an analogous condensation product, Streptohydrazid.[3]

The condensation of streptomycin with isoniazid was found to occur readily, and it was possible to isolate Streptohydrazid sulfate and hydrochloride as white crystalline products. Whereas isoniazid exhibits an absorption maximum in water at 262 mμ (ε 4,360), Streptohydrazid absorbs at 260 mμ (ε 14,700). The latter value was obtained in the presence of a large molar excess of streptomycin to prevent hydrolysis. It was found that by utilizing the difference in absorption at 260 mμ the extent of reaction could be estimated. It was also observed that in concentrated aqueous solutions Streptohydrazid hydrolyzes very little, but in very dilute solution it dissociates into its component parts.

In tuberculosis protection studies in animals Streptohydrazid has been found at least as effective as combined therapy utilizing streptomycin and isoniazid.[2]

Streptomyclideneisonicotinylhydrazine Trihydrochloride.—A mixture of 30 g. of streptomycin hydrochloride and 6 g. of isoniazid in 300 ml. of absolute methanol was boiled under reflux for 15 minutes. The solution was allowed to stand several days in a refrigerator, and large crystals slowly formed. The supernatant solution was decanted and the product filtered, washed with cold methanol and dried; yield 19.0 g. (54%), decomposes *ca.* 200°.

The infrared spectrum exhibits broad strong absorption at 1650 cm.$^{-1}$ and at longer wave lengths is very similar to isoniazid. Weak absorption is evident near 1350, 1300, 1210, 1140, 1110, 1060 and 1010 cm.$^{-1}$.

Anal. Calcd. for $C_{27}H_{47}N_{10}O_{12}Cl_3$: C, 40.03; H, 5.85; N, 17.29; Cl, 13.13. Found: C, 39.94; H, 5.90; N, 17.23; Cl, 13.18.

Streptomycylideneisonicotinylhydrazine Sesquisulfate.—Streptomycin trihydrochloride calcium chloride double salt (50 g.) assaying about 660 mcg. per mg., was dissolved in 160 ml. of water containing 8.5 g. of isoniazid. Over a period of 0.5 hour, 85 ml. of methanolic triethylamine sulfate solution (1.98 *M* in $SO_4^=$, *p*H 5) was introduced with stirring, followed by the addition of 255 ml. of methanol during the succeeding hour. The precipitated $CaSO_4$ was collected and washed with a mixture of one part methanolic triethylamine sulfate solution, two parts of water, and three parts of methanol.

Methanol (about 100 ml.) was added until a haze persisted and the mixture was then allowed to crystallize. Methanol (2000 ml.) was added dropwise with stirring and the white crystalline product was collected, washed with methanol, and dried *in vacuo;* yield 36.0 g. (75%), decomposes *ca.* 230°.

Anal. Calcd. for $C_{27}H_{44}N_{10}O_{12}\cdot 3/2H_2SO_4$: C, 38.25; H, 5.59; N, 16.52; S, 5.67. Found: C, 38.04; H, 5.74; N, 16.22; S, 5.63.

Streptohydrazid trihydrochloride and sesquisulfate are extremely soluble in water. The former is partially soluble in methanol, whereas the latter is insoluble. Both salts are insoluble in less polar solvents.

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Hypotensive Agents. III.[1] Dialkylaminoalkyl Pyrrolidine Derivatives[2a,b]

BY LEONARD M. RICE, CHARLES H. GROGAN AND E. EMMET REID[3]

RECEIVED DECEMBER 19, 1952

In the course of a continuing study of potential hypotensive compounds we investigated the reduction of various N-dialkylaminoalkyl succinimides. The various substituted succinimides were obtained in good yields by the reaction of equimolecular amounts of the appropriate dialkylaminoalkylamine with succinic anhydride. After the exothermic reaction had subsided, the resulting mixture was heated at 160–170° for two hours to complete the reaction. Ohki[4] had prepared this type of imide and studied its electrolytic reduction. He isolated the corresponding pyrrolidone by this means.

The reduction of N-phenylsuccinimide to yield N-phenylpyrrolidine with lithium aluminum hydride has been reported by Spitzmueller.[5] Wojcik and Atkins[6] obtained N-amylpyrrolidine by reduction of amylsuccinimide by means of copper chromite catalyst in excellent yields. In our past experi-

(1) W. A. Winsten, C. I. Jarowski, F. X. Murphy and W. A. Lazier, THIS JOURNAL, **72**, 3969 (1950).

(2) G. L. Hobby and T. F. Lenert, "The Action of Isoniazid and Streptomycin Alone and in Combination," Annual Meeting Public Health Association, Cleveland, Ohio, October 24, 1952.

(3) Chas. Pfizer and Co., Inc., trade name for streptomyclideneisonicotinylhydrazine.

(1) For the first paper in this series see L. M. Rice, A. Popovici, M. Rubin, C. F. Geschickter and E. E. Reid, THIS JOURNAL, **74**, 3025 (1952).

(2) (a) Supported (in part) by a research grant from the Geschickter Fund for Medical Research, Inc. (b) Presented at the Meeting of the American Chemical Society at Atlantic City, N. J., Sept., 1952.

(3) Professor Emeritus, Johns Hopkins University, Baltimore, Md.

(4) Sadao Ohki, *J. Pharm. Soc. Japan*, **70**, 92 (1950).

(5) Weldon G. Brown, "Organic Reactions," Vol. VI, John Wiley and Sons, Inc., New York, N. Y., 1951, p. 492.

(6) B. Wojcik and H. Adkins, THIS JOURNAL, **56**, 2419 (1934).