

TABLE I

UREAS DERIVED FROM N-MONOSUBSTITUTED PIPERAZINES R-N  N-CONHR'

Compound no.	R	R'	M.p., °C.	Empirical formula	Analyses, %			
					Carbon		Hydrogen	
				Calcd.	Found	Calcd.	Found	
I	C ₆ H ₅ CH ₂	Et	226-228	C ₂₄ H ₂₁ N ₃ O·HCl	59.2	59.1	7.8	7.7
II	Me	C ₆ H ₅ ^a	134 208-210	C ₁₂ H ₁₇ N ₃ S C ₁₂ H ₁₇ N ₃ S·HCl	61.2 53.0	60.9 53.1	7.3 6.7	7.0 6.8
III	<i>n</i> -C ₈ H ₁₇	H	236-237 ^e dec.	C ₁₃ H ₂₇ N ₃ O·HCl	56.2	56.1	10.2	10.0
IV	<i>n</i> -C ₁₁ H ₂₃	H ^b	231-233 ^e dec.	C ₁₆ H ₃₃ N ₃ O·HCl	60.1	60.0	10.7	10.3
V	<i>n</i> -C ₁₆ H ₃₃	H ^c	222-225 ^e dec.	C ₂₁ H ₄₃ N ₃ O·HCl	64.6	65.1	11.4	11.6
VI	<i>p</i> -BrC ₆ H ₄ CH ₂	H ^d	238-241 ^e dec.	C ₁₂ H ₁₆ BrN ₃ O·HCl	43.1	43.2	5.1	5.0
VII	3,4-Cl ₂ C ₆ H ₃ CH ₂	H	245.5-246.5 dec.	C ₁₂ H ₁₅ Cl ₂ N ₃ O·HCl	44.5	44.6	5.0	4.8
VIII	Ph ₂ CH	H	203-204	C ₁₈ H ₂₁ N ₃ O·HCl	65.1	65.5	6.7	6.5
IX	α-C ₁₀ H ₇ CH ₂	H	203	C ₁₆ H ₁₉ N ₃ O·HCl	62.8	62.9	6.6	6.5

^a Thiourea. ^b The base, crystallized from ether-hexane mixture, melts at 96°. ^c The base crystallizes from hexane in small platelets and melts at 99.5-100.5°. ^d The base crystallizes in needles from 40% ethanol, m.p. 177-179.5°. ^e Platelets.

Experimental

All the ureas were prepared by conventional methods. Compound I was obtained by the reaction of benzylpiperazine¹ with ethyl isocyanate; compound II from methylpiperazine² and phenyl isothiocyanate. The other ureas were formed by the reaction of the appropriate bases with nitrourea. Compounds VIII and IX were crystallized from ethanol-ether mixture, the hydrochloride of II from aqueous ethanol and the other compounds of Table I from absolute ethanol.

Intermediates.—N-Octyl-, -undecyl- and -cetyl-piperazines³ and N-benzhydrylpiperazine⁴ are known.

N-(*p*-Bromobenzyl)-N'-carbethoxypiperazine.—Carbethoxypiperazine⁵ was allowed to react with *p*-bromobenzyl bromide in alcohol in the presence of sodium carbonate. After standing several hours with occasional shaking, water was added to dissolve the inorganic material and the solution was partitioned between ether and water. The ethereal layer was then extracted with dilute hydrochloric acid and the extract was evaporated *in vacuo*. The residual hydrochloride was recrystallized from ethanol-ether mixture, m.p. 223° dec.

Anal. Calcd. for C₁₄H₁₉BrN₂O₂·HCl: C, 46.2; H, 5.5. Found: C, 46.6; H, 5.6.

N-(*p*-Bromobenzyl)-piperazine.—The above carbamate was refluxed 20 hours in 6 *N* hydrochloric acid and the solution was evaporated *in vacuo*. The residual solid, which was unmelted at 290°, was recrystallized from a little water.

Anal. Calcd. for C₁₁H₁₅BrN₂·2HCl: C, 40.3; H, 5.2. Found: C, 39.9; H, 5.1.

N-(3,4-Dichlorobenzyl)-piperazine.—3,4-Dichlorobenzic acid was reduced to 3,4-dichlorobenzyl alcohol⁶ by lithium aluminum hydride. The alcohol was converted (at least partially) to the chloride by the method of Norris⁷ and the latter was added in benzene solution to carbethoxypiperazine in alcohol in the presence of sodium carbonate. The working up, which was similar to that of the *p*-bromobenzyl analog, afforded a product that crystallized in leaflets, melted at 212-213° and was not quite pure as judged by analysis. After hydrolysis with 6 *N* hydrochloric acid, N-(3,4-dichlorobenzyl)-piperazine dihydrochloride, m.p. 257° dec., was obtained. It was crystallized from ethanol-ethyl acetate mixture.

Anal. Calcd. for C₁₁H₁₄Cl₂N₂·2HCl: C, 41.5; H, 5.1. Found: C, 41.5; H, 5.3.

N-(α-Naphthylmethyl)-piperazine.—The reaction of α-chloromethylnaphthalene with piperazine in 95% ethanol is

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(3) R. Baltzly, *THIS JOURNAL*, **76**, 1164 (1954).

(4) K. E. Hamlin, A. W. Weston, F. E. Fischer and R. J. Michaels, Jr., *ibid.*, **74**, 2731 (1949).

(5) J. S. Moore, M. Boyle and V. M. Thorn, *J. Chem. Soc.*, 39 (1929).

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(7) J. F. Norris and J. T. Blake, *THIS JOURNAL*, **50**, 1808 (1928).

rather unsatisfactory, presumably due to extensive solvolysis. The base was isolated as the fraction insoluble in water and soluble in dilute acid. It boils at 178° at 1 mm. pressure. The dihydrochloride melts at 273°.

Anal. Calcd. for C₁₅H₁₈N₂·2HCl: C, 60.2; H, 6.7. Found: C, 60.1; H, 6.6.

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Polarography of Phenyl 2-Thienyl and 2,2'-Dithienyl Ketones

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The effect of aromatic groups in ketones in promoting double-wave formation upon polarographic reduction of the carbonyl group has been pointed out in recent publications.^{1,2} Heterocyclic groups, such as thienyl, would be expected from both steric and resonance considerations to impart greater stability than a phenyl group to the dimer assumed to form in basic solution.³ Thus phenyl 2-thienyl ketone would be expected to form double waves in basic media more readily than benzophenone. Likewise 2,2'-dithienyl ketone should produce double waves more readily than phenyl 2-thienyl ketone.

These two ketones have been prepared and their polarography studied in buffered ethanol-water media over the pH range of 1 to 13. The above expectations were found to be true, as shown in Table I.

Phenyl 2-thienyl ketone shows normal behavior in acid media, giving two waves of about equal height at pH 3.2 and 4.1.⁴ The second wave is masked by discharge of hydrogen at pH 1.0. The two waves are merged at pH 5.1 into one wave of full height. The half-wave potential of this single wave becomes progressively more negative as the pH is increased. The larger increase at pH 8.1 is usually noted on change to a borate buffer. At pH 10.1 a small second wave is present. This wave increases in height at the expense of the first wave as

(1) R. A. Day, Jr., S. R. Milliken and W. D. Shults, *THIS JOURNAL*, **74**, 2741 (1952).

(2) R. A. Day, Jr., and R. E. Biggers, *ibid.*, **75**, 738 (1953).

(3) M. Ashworth, *Collection Czechoslov. Chem. Commun.*, **13**, 229 (1948).

(4) All pH values herein are of the aqueous buffer.

the pH is further increased up to 13.0. In 0.1 M sodium hydroxide the first wave is only about 13% higher than the second.

TABLE I
 $E_{1/2}$ vs. THE SATURATED CALOMEL ELECTRODE (ALL $E_{1/2}$ VALUES ARE NEGATIVE)

pH (aq.)	pH (alc.)	$E_{1/2}$	$E_{21/2}$	$E_{121/3}^a$	$E_{31/2}$	Curr., μ a. 1st wave	2nd wave
Phenyl 2-Thienyl Ketone ^b							
1.0	1.4	0.80	0.60	..
2.4	2.8	.8958	..
3.2	3.8	.97	1.2150	0.64
4.1	4.6	1.01	1.2064	.66
5.1	5.7	1.16	..	1.23	..
6.0	6.6	1.18	..	1.38	..
7.0	7.5	1.18	..	1.27	..
8.1	8.8	1.29	..	1.18	..
9.1	9.8	1.30	..	1.27	..
10.1	10.6	1.32	1.79	1.14	.20
11.0	11.6	1.33	1.69	0.86	.30
12.0	12.1	1.36	1.77	.75	.44
13.0	13.0	1.36	1.68	.68	.52
2,2'-Dithienyl Ketone ^b							
1.0	1.4	0.75	0.73	..
2.4	2.8	.85	1.1876	0.92
3.2	3.8	.90	1.2178	.73
4.1	4.6	.94	1.2180	.80
5.1	5.7	1.00	1.2174	.68
6.0	6.6	1.03	1.2069	.74
7.0	7.5	1.06	1.2168	.73
7.7	8.3	1.10	1.2380	.80
8.1	8.8	1.16	1.3264	.70
9.1	9.8	1.25	1.79	1.24	.24
10.1	10.6	1.26	1.71	1.00	.42
11.0	11.6	1.26	1.65	1.04	.44
12.0	12.1	1.28	1.71	.68	.64
13.0	13.0	1.28	1.63	.84	.60

^a Indicates $E_{1/2}$ of wave formed by merging waves 1 and 2. ^b Concentration of each ketone 0.000250 M .

The behavior of 2,2'-dithienyl ketone is strikingly similar to that of the ketone fluorenone in its tendency to form double waves.¹ At pH 1.0 the second wave is masked by discharge of hydrogen, but at pH 2.4 both acid waves are observed. These two waves are not merged until the pH is increased to 9.1. In this solution another small wave is present. As the pH is further increased this second wave increases in height at the expense of the first and in 0.1 M sodium hydroxide the waves are about equal in height. In other words two waves are observed over the entire pH range as with fluorenone. The waves are not as sharply separated as those of fluorenone in the pH range 6 to 8 but are easily recognized.

Both calcium and tetramethylammonium ions in basic media tend to shift the half-wave potential of the second wave to more positive values. In a calcium hydroxide-calcium chloride buffer of pH 12.0 and in 0.01 M tetramethylammonium hydroxide the two waves of both ketones are merged. This is in accord with the effect of these cations found by Ashworth.³

Experimental

The current-voltage curves were determined with a Leeds and Northrup Electro-Chemograph Type E. The instru-

ment was normally operated at a damping of 3, the half-wave potentials being corrected for lag at this damping. The electrolysis cell, buffer solutions and experimental procedure were the same as previously described.¹

A single capillary of Corning Marine barometer tubing was used. Its characteristics were: drop-time 6.0 sec., $m = 1.291$ mg./sec., determined in 25% ethanol, citrate-phosphate buffer of pH 5.5 with an open circuit. Half-wave potentials were corrected for IR drop when this amounted to as much as 0.01 v.

All cell solutions were 25% by volume of 95% ethanol. The concentration of ketone was 0.00025 M in all cases. All electrolyses were carried out in a constant temperature bath at $25.0 \pm 0.1^\circ$. A Beckman model H-2 pH meter with a glass electrode was used for pH measurements.

Phenyl 2-thienyl ketone was prepared according to directions in "Organic Syntheses."⁵ After several recrystallizations from petroleum ether the melting point was $54-55^\circ$ (uncor.). The directions of Blicke and Zienty⁶ were used for the preparation of thiophene-2-carboxylic acid. The acid was treated with thionyl chloride to form 2-thienoyl chloride. The latter compound was treated with thiophene-2-magnesium bromide to form 2,2'-dithienyl ketone. After two recrystallizations from ethanol the ketone had a melting point of $86-88^\circ$ (uncor.). The melting point reported in the literature is $87-88^\circ$.⁷

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Aromatic Compound and Complex Formation¹

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In recent years, considerable attention has been given to the stability and absorption spectra of aromatic complexes and one popular classification of them has grouped them into so-called σ - and π -complexes. The nature of the π -complexes is not well understood yet. For instance, the contributions to their stability from such effects as polarization, resonance, van der Waals forces, and acid-base interactions have not been clearly defined. It has been said that the relative stability of π -complexes of the alkylbenzenes is due primarily to polarization.³ According to one prominent school of thought,⁴ molecular addition compounds (MAC's) arise through a polarization of one molecule by a second and then the two moieties are held together by dipole-induced dipole forces. Hence, it was thought that a knowledge of the relative tendencies of benzene derivatives to form MAC's⁵ might shed some light upon the importance of po-

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