

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF RICHMOND]

N-Aryl-N'-alkyloxamides for the Identification of Primary Alkyl Amines<sup>1</sup>BY A. G. RICHARDSON,<sup>2a</sup> J. STANTON PIERCE<sup>2b</sup> AND E. EMMET REID

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Several aryl oxamate esters have been investigated as reagents for the identification of aliphatic amines. They react readily and selectively with primary aliphatic amines to give oxamides,  $\text{ArNHCOCONHR}$ . From 6 reagents and 20 amines, 107 derivatives have been prepared and characterized. These reagents have the great advantage over acid chlorides and aryl isocyanates of being indifferent to water and alcohols. They are selective for primary amines.

The purpose of this investigation was to find convenient and reliable reagents for the identification of aliphatic amines. The reagents studied are the ethyl N-aryloxamates,  $\text{ArNHCOCOOEt}$ , in which Ar is phenyl<sup>3</sup> (I), *p*-tolyl<sup>4</sup> (II), *p*-xenyl (III), *p*-chlorophenyl<sup>5</sup> (IV), *p*-bromophenyl<sup>6</sup> (V) or *p*-iodophenyl<sup>7</sup> (VI).

It is desirable to have several reagents since melting points of derivatives of two amines with a particular reagent may be close together, as in the case with butyl- and isobutylamine with reagent III. Both of these melt at 222° while those with reagent I melt at 152 and 176°, respectively. Reagents III and IV are useful for the normal amines up to octadecyl while I and II fail above decyl. For positive identification it may be desirable to prepare several derivatives.

These reagents have the great advantage over acid chlorides and aryl isocyanates in that they are insensitive to water and alcohols. In addition, they are selective. Primary amines may be isolated from mixtures with secondary amines and the amines which have substituents on the  $\alpha$ -carbon can be distinguished from normal ones.

Wallach<sup>8</sup> prepared N-phenyl-N'-methyloxamide and N-phenyl-N'-ethyloxamide from ethyl N-phenyloxamate and the corresponding amines. More recently de Vries<sup>9</sup> used ethyl N-cyclohexyloxamate with a number of primary amines. The cyclohexyl compounds melt about 20° higher than the corresponding phenyl, here recorded. De Vries used reagent (I) with cyclohexylamine. Reagent I is known to react with primary aromatic amines and can be used for their identification.<sup>10</sup>

At room temperatures in alcohol solution these reagents react promptly with normal primary amines and also with isobutylamine and isoamylamine. Five primary amines studied, in which there was a methyl group on the  $\alpha$ -carbon, varied considerably in reactivity. Isopropylamine reacted in 3 to 5 minutes with I, II and III, required 45 minutes with V, 120 minutes with VI and did not react with IV on standing overnight. The other amines with

$\alpha$ -methyl groups reacted with I in 5 to 10 minutes, with II in 20 to 30 minutes, with III in 60 to 150 minutes and did not react at all with IV, V and VI, on standing overnight. There is somewhat the same relation between the esterification velocities of the primary and secondary butyl alcohols. Secondary amines show no reactivity with any of these reagents. This makes it easy to obtain derivatives from primary amines in the presence of secondary.

Reagents I to VI dissolve in 100 ml. of 95% ethanol to the extent of 25, 24, 1.1, 0.7, 0.6 and 0.8 g., respectively. In all cases the reagent,  $\text{ArNHCOCOOC}_2\text{H}_5$ , is more soluble in alcohol than the oxamide,  $\text{ArNHCOCONHR}$ , formed in the identification of the amine. Thus, the oxamides precipitate from the solution when the primary amine is added to an alcohol solution of the oxamate reagent. The crystalline form and filterability of the derivative are improved by continuous shaking or longer standing. The solubilities of the oxamides appear to be related to the oxamates from which they are prepared. The more soluble reagents, I and II, are convenient when large amounts of amines are available while the other reagents are indicated when testing for smaller quantities.

The melting points of the derivatives of IV, V and

TABLE I  
MELTING POINTS OF  $\text{ArNHCOCONHR}$ , °C. (COR.)

Amine <sup>a</sup>	Reagent					
	I	II	III	IV	V	VI
Methyl	185	230	256	293	295	271
Ethyl	170	167	245	223	227	224
Propyl	162	171	230	197	198	198
<i>i</i> -Propyl	172	195	233	...	234	255
<i>n</i> -Butyl	152	154	222	189	191	196
<i>i</i> -Butyl	176	182	222	200	208	214
<i>s</i> -Butyl	157	169	211	...	...	...
<i>n</i> -Amyl	132	151	213	182	184	185
<i>i</i> -Amyl	146	170	215	190	191	187
<i>s</i> -Amyl	158	156	206	...	...	...
<i>n</i> -Hexyl	130	148	208	174	178	181
1,3-Dimethylbutyl	155	149	202	...	...	...
<i>n</i> -Heptyl	128	142	205	158	162	168
<i>s</i> -Heptyl	156	153	192	...	...	...
<i>n</i> -Octyl	126	133	202	154	155	163
<i>n</i> -Decyl	122	121	194	147	149	157
<i>n</i> -Dodecyl	117	116	187	141	143	153
<i>n</i> -Hexadecyl	118	117	180	135	140	146
<i>n</i> -Octadecyl	124	123	177	131	137	142
Benzyl	172	167	228	185	201	212
Spread	68	114	79	162	158	129

<sup>a</sup> Grateful acknowledgment is made to Sharples Chemicals, Inc., for most of the amines through octyl and to Armour Chemical Division, Armour and Co. for the higher amines studied.

(1) This work was begun in 1943 (E. E. R.) when most of the reagents and a few of the derivatives were prepared in Personal Laboratory, Johns Hopkins University.

(2) (a) Wm. P. Poythress and Co., Inc., Richmond, Va.; (b) to whom enquiries concerning this work should be addressed.

(3) H. Klinger, *Ann.*, **184**, 263 (1877).

(4) *Ibid.*, **184**, 285 (1877).

(5) F. D. Chattaway and W. H. Lewis, *J. Chem. Soc.*, **89**, 158 (1906).

(6) H. Klinger, *Ann.*, **184**, 267 (1877).

(7) F. D. Chattaway and A. J. Constable, *J. Chem. Soc.*, **105**, 129 (1914).

(8) O. Wallach, *Ann.*, **184**, 66 (1877).

(9) K. A. de Vries, *Rec. trav. chim.*, **61**, 223 (1942).

(10) H. Suida, *Monatsh.*, **31**, 583 (1910); **32**, 197 (1911).

TABLE II: YIELDS AND ANALYSES FOR  $N$ -ARYL- $N'$ -ALKYLOXAMIDES,  $ArNHCOCOONHR$ 

Amine (R)	$Ar = C_6H_5$			$Ar = p\text{-}CH_3C_6H_4$			$Ar = p\text{-}ClC_6H_4$			$Ar = p\text{-}BrC_6H_4$			$Ar = p\text{-}IC_6H_4$		
	Yield, %	Calcd. Nitrogen, %	Found, %	Yield, %	Calcd. Nitrogen, %	Found, %	Yield, %	Calcd. Nitrogen, %	Found, %	Yield, %	Calcd. Nitrogen, %	Found, %	Yield, %	Calcd. Nitrogen, %	Found, %
Methyl	56	15.72	15.47	57	14.58	14.55	74	11.02	11.05	47	13.15	13.22	50	10.86	10.91
Ethyl	47	14.58	14.48	67	13.58	13.48	67	10.44	10.45	44	12.34	12.40	44	10.30	10.25
<i>n</i> -Propyl	48	13.58	13.69	68	12.72	12.62	63	9.94	9.97	62	11.63	11.55	52	9.80	9.84
<i>i</i> -Propyl	58	13.58	13.49	62	12.72	12.70	35	9.94	9.91	..	..	..	14	9.80	9.78
<i>n</i> -Butyl	64	12.72	12.75	68	11.96	11.86	67	9.47	9.38	67	10.99	10.98	63	9.34	9.30
<i>i</i> -Butyl	54	12.72	12.79	51	11.96	11.92	44	9.47	9.42	55	10.99	11.02	50	9.34	9.36
<i>s</i> -Butyl	45	12.72	12.65	51	11.96	12.01	17	9.47	9.49	..	..	..	..	..	..
<i>n</i> -Amyl	49	11.96	12.10	72	11.28	11.08	61	9.04	8.96	56	10.42	10.33	44	8.92	8.88
<i>i</i> -Amyl	60	11.96	12.05	44	11.28	11.25	42	9.04	9.00	59	10.42	10.39	51	8.92	8.90
<i>s</i> -Amyl	43	11.96	12.02	48	11.28	11.25	16	9.04	9.02	..	..	..	..	..	..
<i>n</i> -Hexyl	76	11.28	11.24	72	10.68	10.58	68	8.64	8.67	60	9.90	9.88	61	8.54	8.60
1,3-Dimethylbutyl	48	11.28	11.24	49	10.68	10.64	15	8.64	8.61	..	..	..	..	..	..
<i>n</i> -Heptyl	80	10.68	10.64	72	10.14	10.18	65	8.29	8.30	64	9.43	9.40	64	8.19	8.23
<i>s</i> -Heptyl	57	10.68	10.63	54	10.14	10.17	18	8.29	8.30	..	..	..	..	..	..
<i>n</i> -Octyl	83	10.14	10.20	69	9.66	9.59	68	7.96	7.89	77	9.01	9.05	67	7.89	7.90
<i>n</i> -Decyl	72	9.20	9.17	63	8.80	8.84	66	7.37	7.38	65	8.27	8.22	60	7.30	7.26
<i>n</i> -Dodecyl	69	8.43	8.49	66	8.09	8.12	63	6.87	6.90	65	7.63	7.70	60	6.80	6.78
<i>n</i> -Hexadecyl	68	7.21	7.18	64	6.96	6.91	58	6.04	6.06	59	6.62	6.58	53	5.98	6.00
<i>n</i> -Octadecyl	58	6.72	6.69	67	6.51	6.65	53	5.70	5.63	58	6.21	6.23	56	5.65	5.63
Benzyl	76	11.02	11.21	71	10.44	10.50	63	8.49	8.55	69	9.73	9.76	59	8.44	8.50

VI are remarkably close together as are the melting points of the reagents themselves. For this reason V and VI may be eliminated. The inactivity of reagent IV with primary amines having substituents on the  $\alpha$ -carbon makes it particularly useful when used in conjunction with reagents I, II or III. By use of boiling points of the amines and reagents II and IV, it is possible to definitely identify each of the amines studied, boiling below 200°.

### Experimental

**Preparation of Reagents.**—The aromatic amine is dissolved in an excess of ethyl oxalate and the mixture refluxed 3 or 4 hours.<sup>11</sup> The replacement of ethoxyl goes in two stages, forming  $ArNHCOCOOC_2H_5$  and  $ArNHCOCOONHAr$ . The first is favored by an excess of ethyl oxalate but both are always obtained. The mixture is cooled and filtered and the filter cake washed with water and/or dilute alcohol. The diaryloxamide is relatively insoluble and remains behind when the dried filter cake is extracted with boiling aqueous alcohol. For reagent I 25% alcohol is used, for II 40%, for III 70% and 95% for IV, V and VI.

**Ethyl *N*-*p*-xenyloxamate,**  $p\text{-}C_6H_5C_6H_4NHCOCOOC_2H_5$ , the only new member of this series, melts at 132°. *Anal.* Calcd. for  $C_{18}H_{15}O_3N$ : N, 5.20. Found: 5.19.

**Preparation of Derivatives.**—The desired amount of reagent, conveniently 0.01 mole for the more soluble, is dissolved in the required amount of alcohol and the amine added in moderate excess. The mixture is shaken for several minutes and let stand for an hour, or several hours for the less reactive amines. The derivative which separates out is recrystallized from alcohol or aqueous alcohol to constant melting point. Benzene is a convenient solvent for derivatives from reagents IV and V.

**Identification of Small Quantities of Amines.**—Fifty milligrams of each of the primary alkyl amines, except methyl, used in this study were tested with equimolar quantities of ethyl *N*-*p*-xenyloxamate in 10 to 15 ml. of ethanol, according to the above procedure. The methyl amine, 50 mg., was added in the form of a standardized alcohol solution. The yields of pure oxamates were 75 to 200 mg., sufficient for identification.

**Identification of Primary Amines in Presence of Secondary.**—To three flasks, each containing 1.93 g. (0.01 mole) of reagent I in 20 ml. of alcohol were added, respectively, 0.01 mole each of ethyl and diethyl, propyl and dipropyl and butyl and dibutyl amines. The flasks were stoppered and shaken for 3 minutes and let stand overnight. The precipitates which formed were filtered off, washed with petroleum ether, dried and their melting points determined. These crude products melted within 3° of the figures in Table I. One crystallization brought them to the recorded values. The secondary amines were found in the filtrates.

RICHMOND, VIRGINIA

(11) In the case of *p*-iodoaniline, the reaction mixture was boiled for only 10 minutes.