value of 10 for 0.005 molar concentrations of the complex ions and with low salt concentration lead to a rough value of 2800 minutes for the half-time of the exchange. The final entries in the table show that, just as for the oxalate case, the rate of exchange is increased by neutral salt; the half-time in the presence of 2.4 molar sodium perchlorate is approximately 300 minutes.

TABLE IV

EXCHANGE AT 23° BETWEEN $Ni(CN)_4^=$ AND $Ni^*(Tr)^-$

Concn. of $Ni(Tr)^-$ and $Ni(CN)_4^=$ M	Concn. other	pH	t, min.	Exch., %
0.005	0.005 M KOH	9.7	6	1
	.01 M K_2Tr			
.005	.005 M KOH	10.2		
	.01 M K_2Tr	(a)	25	0
		(b)	981	22
		(c)	40100	62
.005	.005 M NaOH	10.3		
	.01 M Na_2Tr	(a)	30	11
	2.4 M $NaClO_4$	(b)	154	27

The over-all picture of the exchange of nickel between tetracyanonickelate ion and other complex ions containing nickel is surprisingly consistent. There is no indication that the extent of dissociation of the second complex ion is of much importance. Otherwise one might expect larger differences than observed between complexes of the same charge and one might have expected the exchange listed in Table IV involving the ethylenediamine complex and excess ethylenediamine to be relatively slower. In contrast the charge of the second complex ion appears to be quite significant. Exchanges between complex ions of the same sign are slow; those between ions of opposite charge are fast. The slow rate of exchange between the tetracyanonickelate ion and free nickel ion constitutes an apparent exception to this last statement. However this experiment actually involves a competitive process; the only definite conclusion is that the rate of exchange is slow compared to the rate of precipitation of nickel cyanide and the latter may well be very fast.

The fact that added salt slows down the exchanges between complex ions of opposite charge and speeds up those with similar charge makes a direct bimolecular exchange process a plausible one. The comparative independence of rate of exchange on stability of the complex ions also suggests this mechanism. However a more detailed kinetic investigation is needed to settle this point.

RECEIVED APRIL 26, 1950

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Cyanoalkylation. III. Structural Effects in the Reaction of Mercaptans with α-Alkylacrylonitriles

BY ROBERT M. ROSS, HAROLD L. BUSHEY AND ROBERT J. ROLIH

The conjugate addition of mercaptans to α-alkylacrylonitriles has been investigated. In the presence of a piperidine–mercaptan salt catalyst, primary, tertiary and aromatic mercaptans have been added to α-methylacrylonitrile, α-ethylacrylonitrile, α-isopropylacrylonitrile and α-n-amylacrylonitrile. Of the mercaptans examined as addenda, thiophenol afforded the best results and rather poor reaction was realized with t-butyl mercaptan. The nature of the alkyl group, situated on the alpha carbon atom of the nitrile, appeared to have little, if any, effect upon the ease with which conjugate addition took place.

Previous communications[1,2] from this Laboratory have revealed that catalysts of the piperidine-salt type are effective in promoting the conjugate addition of certain mercaptans to β-alkylacrylonitriles and 1-cyano-1-cyclohexene. The present investigation was undertaken primarily to determine whether or not these catalysts would be equally efficient in causing satisfactory addition of mercaptans to α-alkylacrylonitriles. As a direct result of the program, a secondary objective was resolved into a study of the effects of mercaptan and nitrile structure upon the course of reaction.

Primary, tertiary and aromatic mercaptans were found to be cyanoalkylated with α-methylacrylonitrile, α-ethylacrylonitrile, α-isopropylacrylonitrile and α-n-amylacrylonitrile provided that a piperidine–mercaptan salt was employed as a catalyst in the reaction. Data for the additions are incorporated in Table I.

Use of the salt as a catalyst was particularly rewarding in the cases of the aromatic and primary mercaptans, wherein the corresponding adducts were isolated in yields which ranged from 60–99%. Thiophenol appeared to be the most active agent within the group of mercaptans studied. On the other hand, it is recognized that the differences in reactivity of thiophenol and benzyl mercaptan, as was adjudged by the quantities of adducts produced, were not marked.

The poorest results were realized when t-butyl mercaptan was employed as the addendum. Because steric factors were not considered to play prominently in conjugate additions of this nature, the slight nucleophilic activity of t-butyl mercaptan was held responsible[3] for the unsatisfactory reaction.

When the mercaptan, bis-(2-mercaptoethyl) sulfide, was dicyanoalkylated with α-methylacrylonitrile, an interesting tris-thio ether was isolated in surprisingly good yields. The adduct proved to be thermally stable at its boiling point of 225° (0.1 mm.).

(1) R. M. Ross, THIS JOURNAL, **71**, 3458 (1949).

(2) R. M. Ross and F. W. Raths, *ibid.*, **73**, 129 (1951).

(3) For other examples of conjugate additions of a similar type which are not affected greatly by bulky groups, see references 1 and 2, and R. C. Fuson and H. L. Jackson, *ibid.*, **72**, 1637 (1950).

TABLE I

β-ARYL-(ALKYL)-MERCAPTO-α-ALKYLPROPIONITRILES $RSCH_2\overset{R'}{\underset{|}{C}}HCN$ AND $S(CH_2CH_2SCH_2\overset{CH_3}{\underset{|}{C}}HCN)_2$

RSH R-	g.	$CH_2=\overset{R'}{\underset{|}{C}}CN$ R'-	g.	Catalyst, g.	Yield of distilled adduct, %	B. p. °C.	Mm.	$n^{20}D$	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	MRD Calcd.	MRD Found
C_6H_5-	19.8	CH_3-	12	2.4	92–99	79	0.04	1.5598	67.76	68.00	6.25	6.11	52.50	52.66
C_6H_5-	22.2	C_2H_5-	16.2	3.4	79–80	90	.04	1.5541	68.70	69.02	7.33	7.51	57.12	57.22
C_6H_5-	12.8	$(CH_3)_2CH$-	10	2.0	66–69.5	90	.04	1.5494	70.20	69.98	7.36	7.49	61.73	61.83
C_6H_5-	16.2	n-C_5H_{11}-	16	3.2	88.1–98.4[c]	115	.2	1.5348	72.05	71.89	8.21	8.51	70.97	71.26
$C_6H_5CH_2$-	22.3	CH_3-	12	2.4	70–73.5	89.5	.02	1.5515	69.07	69.24	6.85	6.98	57.12	57.05
$C_6H_5CH_2$-	18.65	C_2H_5-	12.2	2.44	60–71.3	90	.02	1.5456	70.2	70.13	7.36	7.56	61.74	61.63
$C_6H_5CH_2$-	14.2	$(CH_3)_2CH$-	10	2.0	71.5–72.4	97	.05	1.5420	71.18	71.20	7.81	7.86	66.35	66.29
$C_6H_5CH_2$-	16.5	n-C_5H_{11}-	14.8	3.0	78.1–89.5	118	.03	1.5318	72.82	72.53	8.56	8.74	75.58	75.57
$HOCH_2CH_2$-	14.1	CH_3-	11.5	1.2	62–74[e]	102	.08	1.5013	48.49	48.69	7.63	7.90	39.15	38.76
$S(CH_2CH_2-)_2$[i]	9	CH_3-	7.85	1.5	73[d]	225	.1[f]	1.5485	[g]	[g]	[g]	[g]	[g]	[g]
t-C_4H_9-	19.4	CH_3-	13.4	2.7	13.7–14.3	43	.04	1.4662	[h]	[h]	[h]	[h]	[h]	[h]
t-C_4H_9	13.5	C_2H_5-	12.2	2.44	9–11.2	46	.11	1.4672	[h]	[h]	[h]	[h]	[h]	[h]
t-C_4H_9	11.4	$(CH_3)_2CH$-	12	2.4	14–20	47	.2	1.4713	[h]	[h]	[h]	[h]	[h]	[h]

[a] The catalyst was generated *in situ* by adding calculated quantities of piperidine to the mercaptan used in each experiment. [b] Yield is based on at least two experiments unless otherwise noted. [c] In experiments which were carried out for a reflux period of only three hours, yields of 61.5% and 58.4% of β-phenylmercapto-α-methylpropionitrile and β-phenylmercapto-α-n-amylpropionitrile, respectively, were obtained. [d] Because of an accident, 20–25% of the adduct was lost prior to distillation. A second experiment was not attempted. [e] This adduct was too soluble in water to be purified in the usual manner, therefore the residue was purified by distillation only. [f] The adduct was purified by distillation through a short path apparatus and even at the high temperatures required, there was little evidence of decomposition. [g] No attempt was made to purify the viscous adduct because of its high boiling point. Conversion to the trisulfone was effected, however, and a satisfactory analysis of the latter was obtained (see Table II). [h] Insufficient product was isolated for purification by fractional distillation. Thus, the adduct was converted to the corresponding solid sulfone which was analyzed (see Table II). [i] Dr. A. H. Markhart was kind enough to furnish us with this material.

TABLE II

β-ARYL-(ALKYL)-SULFONYL α-ALKYLPROPIONAMIDES AND RELATED DERIVATIVES

Sulfones[a] $RSO_2CH_2\overset{R'}{\underset{|}{C}}HCN$ R-	R'-	Yield, %	M. p., °C.	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found
C_6H_5-	CH_3-	49	79–79.6[b]	57.39	57.44	5.30	5.50	..	..
C_6H_5-	C_2H_5-	84.5	65–65.8[b]	59.16	59.03	5.87	5.94	..	..
C_6H_5-	$(CH_3)_2CH$-	89	68.5–69.0[b]	60.73	60.84	6.37	6.21	5.90	5.99
C_6H_5-	n-C_5H_{11}-	[e]	[e]	...	...	..	..	..	..
$C_6H_5CH_2$-	CH_3-	96	71.5–72[b]	59.18	58.93	5.87	6.05	..	..
$C_6H_5CH_2$-	C_2H_5-	87	91–91.8[b]	60.68	60.80	6.37	6.26	..	..
$C_6H_5CH_2$-	$(CH_3)_2CH$-	92.6	84–85[b]	62.12	62.24	6.82	7.01	..	..
$C_6H_5CH_2$-	n-C_5H_{11}	72.5	66–67[b]	64.48	64.67	7.58	7.80	..	..
$HOCH_2CH_2$-[g]	CH_3-[g]	[g]	[g]	...	...	..	..	..	..
t-C_4H_9-	CH_3-	25	78.9–79.5[d]	50.76	50.49	7.99	8.19	..	..
t-C_4H_9-	C_2H_5-	38	69.5–70.2[d]	53.17	53.42	8.43	8.61	..	..
t-C_4H_9-	$(CH_3)_2CH$-	15.6	96–96.4[d]	55.20	53.52[f]	8.81	8.54	..	..
$SO_2(CH_2CH_2SO_2CH_2\overset{CH_3}{\underset{|}{C}}HCN)_2$		96	240–242[c]	37.48	37.28	5.24	5.52	..	..

[a] All sulfones were prepared by hydrogen peroxide oxidation of the corresponding thio ether (see ref. 1). [b] Recrystallized from 95% and absolute ethanol. [c] Recrystallized from the mixed solvent pair dimethylformamide and diisobutyl ketone. [d] Recrystallized from hot water. [e] The β-phenylsulfonyl α-n-amylpropionitrile could not be induced to crystallize by usual techniques. Presumably, the linearity and unsymmetrical nature of the molecule was responsible for the difficulty encountered. Therefore, the crude, oily nitrile was converted to the corresponding amide with concentrated sulfuric acid [see Hurd and Gershbein, THIS JOURNAL, 69, 2328 (1947)]. In this way the β-phenylsulfonyl α-n-amylpropionamide was isolated in 95% yield, m.p. 111–111.5°. *Anal.* Calcd. for $C_{14}H_{21}NO_2S$: C, 59.33; H, 7.47; N, 4.94. Found: C, 59.61; H, 7.58; N, 5.02. [f] The sample was believed to have contained water. [g] Oxidation to a sulfone was not attempted in this case. Unsuccessful attempts were made to prepare p-nitrophenyl and α-naphthylurethans. Hydrolysis to the amide was unsuccessful also.

$$S(CH_2CH_2SH)_2 + 2CH_2=\overset{CH_3}{\underset{|}{C}}CN \longrightarrow S(CH_2CH_2SCH_2\overset{CH_3}{\underset{|}{C}}HCN)_2$$

No significant differences in activity among the various nitriles was disclosed when the additions were carried out under the standard conditions described. Apparently, whether the alpha carbon of the nitrile held a methyl or n-amyl group had little bearing upon the ease with which reaction took place. From the comparative yields obtained with a given mercaptan, such as thiophenol, it would appear at first that α-isopropylacrylonitrile was somewhat less reactive than the other nitriles examined. Impurities were known to have been present, how-

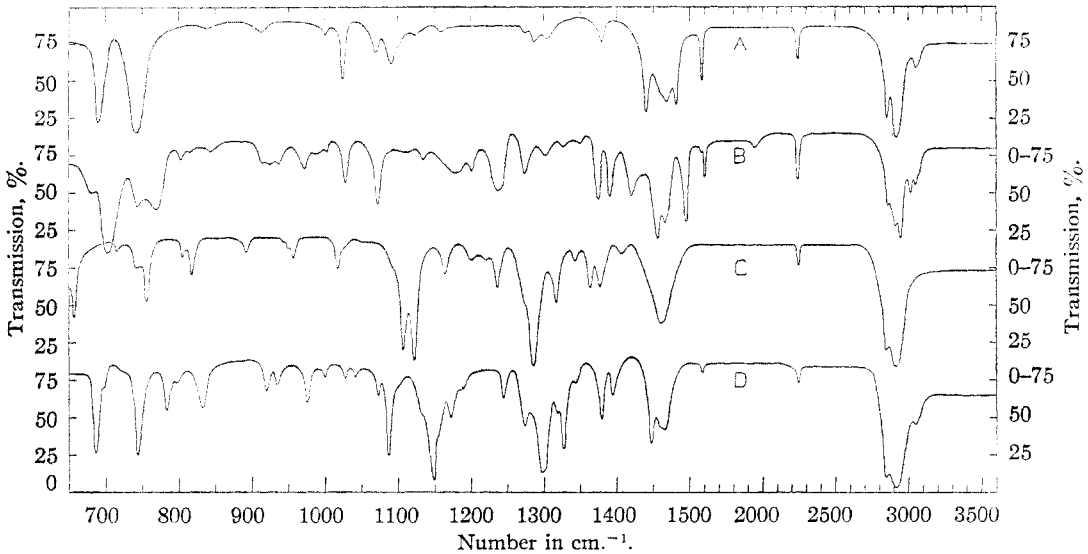


Fig. 1.—Infrared absorption spectra: A, β-phenylmercapto α-*n*-amylpropionitrile; B, β-benzylmercapto α-isopropylpropionitrile; C, β-*t*-butylsulfonyl α-ethylpropionitrile; D, β-phenylsulfonyl α-isopropylpropionitrile (the liquids A and B were examined in a cell of 0.025 mm. thickness; the solids C and D were examined in Nujol).

ever, in the samples of α-isopropylacrylonitrile[4] used; these may have prevented smooth reaction from taking place.

All the adducts were converted to the corresponding sulfonyl derivatives. Characterization of the thio ethers and the sulfones was aided by infrared analysis,[5] and representative examples of several absorption curves are illustrated in Fig. 1.

(4) Our preparation of α-isopropylacrylonitrile followed that which was described by C. S. Marvel and W. R. Miller, THIS JOURNAL, **72**, 5408 (1950). The latter authors have pointed out that the product they obtained was unstable and therefore impure. In attempting to purify the nitrile, even careful fractionation failed, and a satisfactory analytical sample has not been prepared as yet.

(5) We are indebted to Miss Elizabeth M. Petersen for the infrared analyses, their interpretation, and the tracing of the absorption curves.

Experimental[6,7]

Nitriles.—α-Methylacrylonitrile was purchased from Shell Chemical Corporation. All other nitriles were prepared according to the method of Marvel and Miller (see citation 4).

Cyanoalkylations.—A detailed procedure for similar cyanoalkylations has been described in an earlier communication.[1] Quantities of reactants and other pertinent data are listed in Tables I and II.

All additions were carried out over a reflux period of 48 hours; *t*-butyl alcohol was used as the solvent.

(6) All melting points are corrected and were determined on a brass micro melting point apparatus. Reported boiling points are not corrected.

(7) Microanalyses were carried out by Miss Emily Davis, Miss Rachel Kopel and Mr. Maurice Dare to whom we are indebted.

URBANA, ILL. RECEIVED AUGUST 7, 1950

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF PARKE, DAVIS & CO.]

Chloromycetin.[1] Synthesis of DL-*threo*-2-Dichloroacetamido-1-(4-nitro-1-naphthyl)-1,3-propanediol

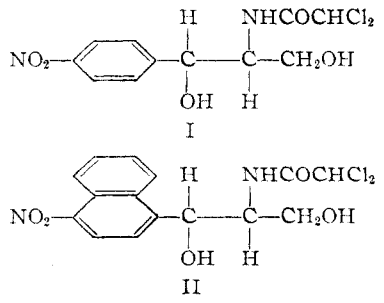
BY LOREN M. LONG AND H. D. TROUTMAN

Two compounds related to the antibiotic, Chloromycetin, have been prepared, These derivatives contain a 4-nitro-1-naphthyl or a 2-naphthyl group in place of the *p*-nitrophenyl group present in the antibiotic.

During the course of our investigation of the chemistry of D-(*levo*)-*threo*-2-dichloroacetamido-1-*p*-nitrophenyl-1,3-propanediol (Chloromycetin) it became desirable to prepare certain compounds related to the antibiotic. One of these, DL-*threo*-2-dichloroacetamido-1-(4-nitro-1-naphthyl)-1,3-propanediol, is the subject of this paper. Structure I, established by Rebstock, *et al.*,[2] represents Chloromycetin while structure II is that of the 4-nitro-1-naphthyl derivative. In addition the 2-naphthyl derivative was prepared.

(1) Parke, Davis & Co. registered trademark for chloramphenicol.

(2) M. C. Rebstock, H. M. Crooks, Jr., J. Controulis and Q. R. Bartz, THIS JOURNAL, **71**, 2458 (1949).



The principal steps involved in the synthesis are illustrated in the series of reactions. This