Anal. Calcd. for $C_{22}H_{26}O_4S_2$: C, 63.13; H, 6.26. Found: C, 63.10; H, 6.25.

1-Methyl-4,5-di-*p*-toluenesulfonylcyclohexene.—To a solution of 2.0 g. of 1,2-di-*p*-toluenesulfonylethylene in 50 ml. of benzene was added 15 ml. of freshly distilled isoprene. The resulting solution was refluxed for two days. The excess diene and the solvent were removed under reduced pressure. The residue was a viscous oil, weight 2.3 g. (96%). After standing in a refrigerator for two weeks, the adduct crystallized. After recrystallization from ethanol the product melted at 130–132°.

Anal. Calcd. for $C_{21}H_{24}O_4S_2$: C, 62.35; H, 5.98. Found: C, 62.48; H, 6.24.

4,5-Di-*p*-toluenesulfonylcyclohexene.—A mixture of 1.0 g. of 1,2-di-*p*-toluenesulfonylethylene, 20 ml. of butadiene and 50 ml. of benzene was sealed in a steel bomb and heated on a steam-bath for 24 hours. The excess diene was allowed to escape and the solvent was removed under reduced pressure. The resulting oil was dissolved in hot ethanol. The product which crystallized from the cooled solution weighed 1.0 g. (95%). After recrystallization from ethanol the adduct was a white solid, m.p. 164–165° dec.

Anal. Calcd. for $C_{20}H_{22}O_4S_2$: C, 61.51; H, 5.68. Found: C, 61.80; H, 5.92.

The Adducts Derived from Anthracene and 1,2-Di-*p*-toluenesulfonylethylene.—A mixture of 0.5 g. of 1,2-di-*p*-toluenesulfonylethylene and 0.265 g. of anthracene was fused and heated at 155–160° for 20 hours. The reaction mixture was boiled with 50 ml. of ethanol. The cooled mixture was filtered and concentrated to half its original volume. The white solid which crystallized when the solution cooled was removed by filtration; it weighed 0.18 g. (24%). After recrystallization from acetone–water this material melted at 254–255°.

Anal. Calcd. for $C_{30}H_{26}O_4S_2$: C, 70.01; H, 5.09. Found: C, 70.30; H, 5.28.

The ethanol-insoluble material (0.22 g., 28%) was triturated with hot ethanol. Recrystallization from acetone–water produced a white solid, m.p. 239.5–241°.

Anal. Calcd. for $C_{30}H_{26}O_4S_2$: C, 70.01; H, 5.09. Found: C, 69.74; H, 5.17.

The mixed melting point of the two substances was 212–240°. The infrared spectra of the two compounds were very similar, with slight displacements of the bands due to the sulfonyl groups. These compounds are believed to be the *meso* and racemic forms of the adduct.

URBANA, ILLINOIS

[Contribution No. 870 from the Department of Chemistry, University of Pittsburgh]

The Preparation of δ-Ketoacids and δ-Ketonitriles from Monocyanoethylated β-Ketoesters[1]

By Clayton W. Yoho and Robert Levine

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A method has been developed for the indirect monocyanoethylation of methyl ketones at the methyl group. The procedure involves treating the appropriate β-ketoesters with acrylonitrile and hydrolyzing the compounds so formed to give either δ-ketonitriles or δ-ketoacids.

Numerous investigators[2] have found that the base-catalyzed Michael condensation of acrylonitrile with active hydrogen compounds leads to the formation of polycyanoethylated derivatives as the main reaction products. To our knowledge,[2] very few ketones have been monocyanoethylated with acrylonitrile and in each case low yields of product were obtained.

Furthermore, while from structural considerations, symmetrical dialkyl ketones such as acetone, diisopropyl ketone and diisobutyl ketone; and alkyl aryl and alkyl heterocyclic ketones such as acetophenone, methyl 2-thienyl ketone and methyl 2-furyl ketone could give rise to only one monocyanoethylated derivative; unsymmetrical dialkyl ketones such as methyl ethyl ketone, methyl isopropyl ketone and methyl isobutyl ketone might give rise to isomeric monocyanoethylated products. Actually,[2] as shown in the following equation, the condensation of acrylonitrile with methyl alkyl ketones occurs at that α-carbon atom which is more highly substituted to give dicyanoethylated products if the α-carbon carries two hydrogen atoms.

$$CH_3COCH_2CH(CH_3)_2 + 2CH_2CHCN \xrightarrow{OH^-} CH_3COC(CH_2CH_2CN)_2CH(CH_3)_2$$

For some time now we have been interested in developing methods for monocyanoethylating or monocarboxyethylating methyl alkyl ketones and in determining whether the reactions could be effected at the α-methyl group carbon atom of these compounds. Recently,[3] we studied the reaction of several methyl alkyl ketone anions (prepared from the ketones and sodium amide) with β-chloropropionitrile and found that the chloronitrile underwent β-elimination to form acrylonitrile, which then condensed at the α-methylene or α-methinyl carbon atom of the ketone to give either a monocyanoethylated compound or a mixture of mono- and dicyanoethylated products.

It occurred to us that, as shown in the following scheme, it might be possible to monocyanoethylate or monocarboxyethylate ketones indirectly by treating β-ketoesters with acrylonitrile under appropriate reaction conditions and hydrolyzing the resulting condensation products to the corresponding δ-ketonitriles or δ-ketoacids. Thus, if R is the isopropyl group, ethyl isobutyrylacetate,

$$RCOCH_2CO_2C_2H_5 \xrightarrow{CH_2CHCN} RCOCH(CH_2CH_2CN)CO_2C_2H_5 \xrightarrow{\text{hydrolysis}} RCO(CH_2)_3CN \text{ or } RCO(CH_2)_3CO_2H$$

prepared by the general method of Levine and Hauser,[4] may be cyanoethylated to give ethyl α-(β-cyanoethyl)-isobutyrylacetate which may then

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[1] This report is based on a thesis presented by Clayton W. Yoho to the graduate faculty of the University of Pittsburgh in partial fulfillment of the requirements for the M.S. degree.

[2] See H. A. Bruson, in "Organic Reactions," Vol. 5, John Wiley and Sons, Inc., New York, N. Y., 1949, Chapter 2.

[3] L. B. Barkley and R. Levine, This Journal, **72**, 3699 (1950).

[4] R. Levine and C. R. Hauser, *ibid.*, **66**, 1768 (1944).

TABLE I

KETONES OF THE TYPE $RCOCHR_1CH_2CH_2R_2$

R	R_1	R_2	Yield, %	B.p. or m.p. °C.	Mm.	Formula[a]	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
CH_3	$CO_2C_2H_5$	CN	40.5	126–127	3^{b}					
CH_3^{c}	H	CN	60.0	72–73	2^{b}					
CH_3^{d}	H	CO_2H	35.7	137–138	$5^{e,f}$					
$n\text{-}C_3H_7$	$CO_2C_2H_5$	CN	52.0	136–138	2.5	$C_{11}H_{17}O_3N$	62.54	62.76	8.11	7.89
$n\text{-}C_3H_7^{d}$	H	CO_2H	54.0	146–148	$5^{g,h}$					
$i\text{-}C_3H_7$	$CO_2C_2H_5$	CN	53.0	134–137	3	$C_{11}H_{17}O_3N$	62.54	62.34	8.11	8.13
$i\text{-}C_3H_7$	H	CO_2H	58.0	138–140	5^{i}	$C_8H_{14}O_3$	60.74	60.73	8.92	8.94
$i\text{-}C_4H_9$	$CO_2C_2H_5$	CN	46.4	132–133	2	$C_{12}H_{19}O_3N$	63.97	64.01	8.50	8.34
$i\text{-}C_4H_9^{j}$	H	CO_2H	55.0	132–133	3.5^{k}	$C_9H_{16}O_3$	62.70	62.50	9.36	8.79
$n\text{-}C_5H_{11}$	$CO_2C_2H_5$	CN	38.5	145–146	2	$C_{13}H_{21}O_3N$	65.24	65.17	8.84	8.51
$n\text{-}C_5H_{11}^{d}$	H	CO_2H	45.7	152–153	2^{l}	$C_{10}H_{18}O_3$	64.49	64.50	9.74	9.55
$n\text{-}C_6H_{13}$	$CO_2C_2H_5$	CN	34.6	154–156	1.3	$C_{14}H_{23}O_3N$	66.37	66.49	9.15	9.06
$n\text{-}C_6H_{13}^{d}$	H	CO_2H	72.0	M. $56\text{–}57^{m}$		$C_{11}H_{20}O_3$	65.96	66.06	10.06	9.87
C_6H_5	$CO_2C_2H_5$	CN	43.2	173–174	2^{b}					
$C_6H_5^{c}$	H	CN	47.0	M. $40\text{–}41^{n}$						
$C_6H_5^{d}$	H	CO_2H	99.0	M. $126\text{–}127^{o,p}$		$C_{11}H_{12}O_3$	68.73	68.96	6.30	6.21
$2\text{-}C_4H_3O^{q}$	$CO_2C_2H_5$	CN	37.1	180–180.5	2.5	$C_{12}H_{13}O_4N$	61.26	61.10	5.57	5.25
$2\text{-}C_4H_3O^{j}$	H	CO_2H	50.5	M. $124\text{–}125^{r}$		$C_9H_{10}O_4$	59.33	59.46	5.53	5.39
$2\text{-}C_4H_3S^{s}$	$CO_2C_2H_5$	CN	64.0	175–176	1	$C_{12}H_{13}O_3NS$	57.13	57.27	5.59	5.29
$2\text{-}C_4H_3S^{d}$	H	CO_2H	44.0	M. $92\text{–}93^{t}$		$C_9H_{10}O_3S$	54.52	54.26	5.45	5.35

[a] Analyses by Mr. George Stragand of the Microanalytical Laboratory of the University of Pittsburgh. [b] See ref. 5. [c] Prepared from the previous compound by sodium carbonate hydrolysis. [d] Prepared from the previous compound by sodium hydroxide hydrolysis. [e] See A. Lipp, *Ber.*, 18, 3281 (1885). [f] Semicarbazone, m.p. 167–168° and 173–174° depending on rate of heating (D. Vorländer, *Ann.*, **294**, 269 (1896). [g] See R. Wolffenstein, *Ber.*, **28**, 1464 (1895). [h] Semicarbazone, m.p. 186° (G. Chavanne and F. Becker, *Bull. soc. chim. Belg.*, **36**, 598 (1927)). [i] Semicarbazone, m.p. 177–178°. *Anal.* Calcd. for $C_9H_{17}O_3N_3$: N, 19.34. Found: N, 19.63. [j] Prepared from the previous compound by acidic hydrolysis. [k] Semicarbazone, m.p. 162–163°. *Anal.* Calcd. for $C_{10}H_{19}O_3N_3$: N, 18.33. Found: N, 18.07. [l] Semicarbazone, m.p. 103–104°. *Anal.* Calcd. for $C_{11}H_{21}O_3N_3$: N, 17.68. Found: N, 17.55. [m] Semicarbazone, m.p. 126–127°. *Anal.* Calcd. for $C_{12}H_{23}O_3N_3$: N, 16.33. Found: N, 16.05. [n] See ref. 6. [o] See ref. 7. [p] Semicarbazone, m.p. 196–197°. *Anal.* Calcd. for $C_{12}H_{15}O_3N_3$: N, 16.86. Found: N, 17.10. [q] This is the 2-furyl radical. [r] Semicarbazone, m.p. 191–191.5°. *Anal.* Calcd. for $C_{10}H_{13}O_4N_3$: N, 17.57. Found: N, 17.31. [s] This is the 2-thienyl radical. [t] Semicarbazone, m.p. 192–193°. *Anal.* Calcd. for $C_{10}H_{13}O_3N_3S$: N, 16.46. Found: N, 16.33.

be cleaved to 5-keto-6-methylheptanoic acid. The monocyanoethylated β-ketoesters were hydrolyzed by one of the following methods: (1) refluxing with aqueous sodium carbonate solution to yield the corresponding δ-ketonitrile, which was then hydrolyzed with aqueous sodium hydroxide solution; (2) direct hydrolysis to the δ-ketoacid by aqueous sodium hydroxide; and (3) direct hydrolysis with a mixture of acids to the δ-ketoacid. It should be noted that this indirect method for cyanoethylating ketones *via* β-ketoesters results in the type of compound that would have been obtained if it were possible to directly monocyanoethylate methyl ketones at the methyl group.

After the present study was in progress, Albertson,[5] using procedures quite similar to those employed by us, reported the monocyanoethylation of two of the compounds (ethyl acetoacetate and ethyl benzoylacetate) which we also investigated, and hydrolyzed these intermediates to the corresponding δ-ketonitrile with aqueous sodium carbonate solution. The pertinent data on the monocyanoethylated β-ketoesters, δ-ketonitriles and δ-ketoacids, which we have prepared, are summarized in Table I.

From the work of Barkley and Levine,[3] there were available the semicarbazones of three δ-ketoacids which are isomeric with three of those obtained in the present study. When mixed melting points were taken of the three pairs of isomeric semicarbazones, a depression in the melting point was noted in all cases. These data are summarized in Table II.

TABLE II

MELTING POINTS OF SEMICARBAZONES OF ISOMERIC δ-KETOACIDS

Ketone	Semicarbazone, m.p., °C. CH_3 derivative[a]	Semicarbazone, m.p., °C. CH_2 derivative[b]	Mixed m.p., °C.
Methyl isopropyl	177–178.5	185–186	160–165
Methyl isobutyl	153–154	165.5–166	135–148
Methyl *n*-hexyl	126–127	136–137	119–123

[a] Present study. [b] See ref. 3.

Experimental

General Procedure for the Preparation of Monocyanoethylated β-Ketoesters.—In a three-neck, round-bottom flask equipped with ground-glass joints, a mercury-sealed stirrer, an addition funnel and a condenser (protected from atmospheric moisture by a drying tube filled with Drierite) was placed 100 ml. of 95% ethanol in which 0.3–0.8 g. of sodium metal and one mole of the appropriate β-ketoester (or proportionate amounts of the reactants) had been dissolved. The solution was stirred rapidly and 0.8 mole of acrylonitrile was added at such a rate as to keep the temperature at 40–45°. After the addition of the nitrile was completed, the mixture was allowed to cool to room temperature (30–60 minutes), the solvent was removed under reduced pressure, the residue neutralized by the addition of glacial acetic acid and then the mixture was dissolved in ether and washed with water until the washings were neutral to litmus. The organic layer was dried over Drierite, filtered, the Drierite washed with ether, the solvent removed and the residue distilled in vacuum. Thus, from 0.785 mole (156 g.) of ethyl 2-thenoylacetate, b.p. 110–113° at 1 mm., 0.6 g. of sodium and 0.628 mole (33.3 g.) of acrylonitrile, there was obtained 101.2 g. (64%) of ethyl α-(β-cyanoethyl)-2-thenoylacetate, b.p. 175–176° at 1 mm.

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(5) N. F. Albertson, THIS JOURNAL, **72**, 2594 (1950).

Hydrolysis of Cyanoethylated β-Ketoesters. (1) The Aqueous Sodium Carbonate Method. (a) Preparation of δ-Ketonitriles.—To a solution of two moles of sodium carbonate in 1800 ml. of water was added one mole of the cyanoethylated β-ketoester (or a proportionate amount of the reactants) and the mixture refluxed 10–14 hours. The mixture was cooled to room temperature and, if necessary, the product was salted out with potassium carbonate. After several extractions with ether, the extracts were dried over Drierite, filtered, the solvent distilled and the residue fractionated in vacuum or crystallized. Thus, after a 14-hour reflux period, a mixture of 0.5 mole of sodium carbonate, 450 ml. of water, 0.25 mole (61.3 g.) of ethyl α-(β-cyanoethyl)-benzoylacetate gave 20 g. (47%) of γ-benzoylbutyronitrile, m.p. 40–41°.[6]

(b) Preparation of δ-Ketoacids.—To a solution of two moles of sodium hydroxide in 400 ml. of water was added one mole of the δ-ketonitrile (or a proportionate amount of the reactants) and the mixture was refluxed until the evolution of ammonia ceased. The mixture was cooled to room temperature, extracted with ether to remove any unreacted nitrile and acidified with concentrated hydrochloric acid. The free acid was isolated by filtration if it was a solid or by extraction with ether followed by distillation in vacuum if it is a liquid. Thus from a mixture of 0.2 mole of sodium hydroxide in 80 ml. of water and 0.1 mole (17.3 g.) of γ-benzoylbutyronitrile there was obtained 19 g. (99%) of 4-benzoylbutanoic acid, m.p. 126–127°[7] (from water).

(2) Dilute Sodium Hydroxide Method.—A mixture of three moles of sodium hydroxide in 1480 ml. of water and one mole of the monocyanoethylated β-ketoester (or a proportionate amount of reactants) was treated as described above in part 1b. Thus, from a mixture of 0.75 mole (30 g.) of sodium hydroxide, 380 ml. of water, 0.25 mole (65.4 g.) of ethyl α-(β-cyanoethyl)-heptoylacetate, there was obtained 36.1 g. (72%) of 4-heptoylbutanoic acid, m.p. 56–57° (from anhydrous ether).

(3) Acid Method.—Following the method of Hudson and Hauser[8] for the cleavage of simple β-ketoesters, a mixture one mole of cyanoethylated β-ketoester, 100 ml. of concentrated sulfuric acid, 300 ml. of glacial acetic acid and 100 ml. of water (or a proportionate amount of the reactants) was refluxed until the evolution of carbon dioxide ceased. The free δ-ketoacid was then isolated as described above in part Ib. Thus, from a mixture of 5 ml. of concentrated sulfuric acid, 15 ml. of glacial acetic acid, 5 ml. of water and 0.1 mole (23.2 g.) of ethyl α-(β-cyanoethyl)-isovalerylacetate, there was obtained 9.5 g. (55%) of γ-isovalerylbutyric acid, b.p. 132–133° at 3.5 mm.

PITTSBURGH 13, PENNA.

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[6] C. F. H. Allen and W. L. Ball, THIS JOURNAL, **59**, 686 (1937).

[7] A. Ahmed, R. D. Desai, R. F. Hunter and S. M. Makhdhum Mohammad, *J. Chem. Soc.*, 1013 (1937).

[8] B. E. Hudson, Jr., and C. R. Hauser, THIS JOURNAL, **63**, 3163 (1941).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

Evidence for α- and β-Elimination from Deutero Alkyl Halides with Potassium Amide[1,2]

BY DOUGLAS G. HILL, WILLIAM A. JUDGE, PHILIP S. SKELL, SIMON W. KANTOR AND CHARLES R. HAUSER

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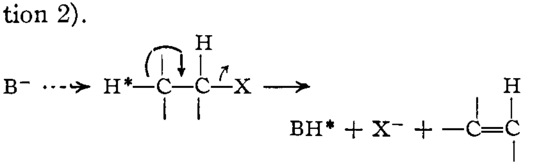
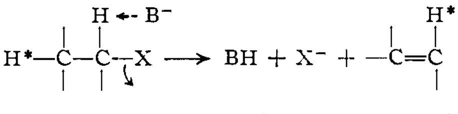
A study of the elimination reaction of appropriate deutero alkyl halides with potassium amide in liquid ammonia has shown that 2-ethylbutyl bromide exhibits β-elimination, while n-octyl halides exhibit α-elimination as well as β-elimination. Hydrogen halide was found to be eliminated more readily than deuterium halide. It was shown that rearrangement did not occur during the conversion of n-octyl alcohol to bromide with hydrogen bromide. Evidence was obtained indicating that in both α- and β-elimination reactions, the proton (or deuteron) and the halide ion are removed simultaneously.

The removal of hydrogen halide from alkyl halides by bases (E2 mechanism) might conceivably involve either β-elimination of H* and X (equation 1) or α-elimination of H and X accompanied by the shift of H* from the β- to the α-carbon atom (equation 2).



$$\mathrm{B^- \dashrightarrow H^*{-}\underset{|}{\overset{|}{C}}{-}\underset{|}{\overset{H}{\overset{|}{C}}}{-}X \longrightarrow BH^* + X^- + {-}\overset{|}{C}{=}\underset{|}{\overset{H}{\overset{|}{C}}}} \quad (1)$$



$$\mathrm{H^*{-}\underset{|}{\overset{|}{C}}{-}\underset{|}{\overset{H \leftarrow B^-}{\overset{|}{C}}}{-}X \longrightarrow BH + X^- + {-}\overset{|}{C}{=}\underset{|}{\overset{H^*}{\overset{|}{C}}}} \quad (2)$$

In recent years β-elimination has commonly been assumed and, indeed, it has been supported by considerable indirect evidence, principally of a theoretical nature.[3] In the present investigation, the mode of elimination brought about by potassium amide in liquid ammonia was determined by the use of deuterium labeled alkyl halides. The results show that although β-elimination occurs exclusively with certain alkyl halides, some α-elimination also takes place with certain others.

Deutero Alkyl Halides.—Deutero analogs of the straight chain alkyl halide, n-octyl halide and of the alkyl halide having branching on the β-carbon atom, 2-ethyl butyl halide, were chosen for study since they could be prepared readily and would produce, on elimination, olefins of convenient volatility. These deutero analogs were prepared by the reactions illustrated in equations 3–6 and analyzed for deuterium by burning the sample and measuring the D_2O content of the water by the interferometer method.[4] The deuterium content, expressed as atoms of D per molecule and considered accurate to ±0.02 D, is given under the halides and some of the intermediates.

$$\begin{array}{lll} \mathrm{RCH_2CO_2Et} \xrightarrow[\mathrm{AcOD}]{\mathrm{Na}} & \mathrm{RCH_2CD_2OH} \xrightarrow[\mathrm{SOCl_2}]{\mathrm{HBr\ or}} & \\ \mathrm{R} = n\text{-}\mathrm{C_6H_{13}} & 1.98\ \mathrm{D} & \\ & & \mathrm{RCH_2CD_2X} \quad (3) \\ & & (\mathrm{X = Br\ or\ Cl}) \\ & & \mathrm{I,\ 1.98\ D} \end{array}$$

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[1] A preliminary report was given at the Buffalo Meeting of the American Chemical Society, September, 1942.

[2] This work was supported in part by the Office of Naval Research.

[3] W. Hanhart and C. K. Ingold, *J. Chem. Soc.*, 997 (1927); C. K. Ingold and M. A. T. Rogers, *ibid.*, 722 (1935).

[4] R. H. Crist, G. M. Murphy and H. C. Urey, *J. Chem. Phys.*, **2**, 112 (1934).