crystalline. Found: C, 72.14, 72.41; H, 8.96, 9.03; N, 11.30, 11.27. Calcd. for $C_{15}H_{22}ON_2$: C, 73.18; H, 8.94; N, 11.39. Insufficient material was available for further purification or characterization.

The mother liquors from fraction II, the undistilled residue and the base obtained from extract B yielded further quantities of rhombinine isolated as perchlorate.

Hydrogenation of Rhombinine.—Rhombinine (0.5 g.), obtained from the perchlorate, was dissolved in water (75 cc.) and hydrogenated in the presence of Raney nickel (*ca.* 0.2 g.) for three hours at 65° and 460 lb. and three hours at 105° and 520 lb. pressure. The content of the bomb was filtered to remove the catalyst, and potassium hydroxide (10 g.) was dissolved in the filtrate which was then repeatedly extracted with chloroform. The base recovered from the combined extract was fractionated *in vacuo*. The bulk (0.3 g.) distilled at 120–130° (0.08 mm.) as a colorless oil which was dissolved in a little methanol and the solution made just acid to congo with 65% perchloric acid. The crystalline perchlorate which separated was recrystallized once from hot methanol from which it separated on cooling as clusters of small, colorless, stout prisms melting at 213° either alone or after admixture with the perchlorate of naturally occurring hydrorhombinine $[\alpha]_D$ −40.3° (c = 1.06 in water). Calcd. for $C_{16}H_{30}O_2N_2 \cdot HClO_4$: N, 7.32. Found: N, 7.35.

Summary

1. *Lupinus Macounii*, Rydb., has been shown to contain three alkaloids, the main one of which is identical with rhombinine, previously isolated from *Thermopsis rhombifolia*.

2. The second alkaloid, hydrorhombinine, is identical with the product of the catalytic hydrogenation of rhombinine.

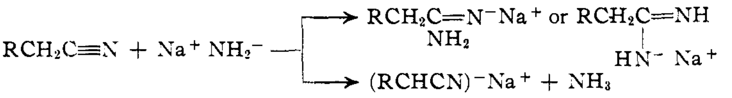
OTTAWA, CANADA RECEIVED JANUARY 28, 1946

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

The Acylation and Carbethoxylation of Nitriles in the Presence of Sodium Amide[1]

BY ROBERT LEVINE[2] AND CHARLES R. HAUSER

In the presence of the amide ion, nitriles having α-hydrogen may undergo two different types of reaction. One involves the addition of the amide ion to the nitrile group to form the amidine (as an anion), while the other consists in the removal of the α-hydrogen of the nitrile to form the nitrile anion, which is the reactive intermediate in carbon-carbon condensations such as the acylation, alkylation or self-condensation of nitriles. These two courses of reaction may be represented, thus



$$RCH_2C{\equiv}N + Na^+\,NH_2^- \longrightarrow \begin{cases} RCH_2C(NH_2){=}N^-Na^+ \text{ or } RCH_2C(=NH)\text{—}HN^-\,Na^+ \\ (RCHCN)^-Na^+ + NH_3 \end{cases}$$

Phenylacetonitrile forms the nitrile anion apparently exclusively but acetonitrile and especially higher aliphatic nitriles may form the amidine in addition to the nitrile anion.[3] However, even diethylacetonitrile, in which the α-hydrogen is relatively unreactive, appears to be converted to the nitrile anion since, under certain conditions, it may be alkylated with allyl chloride to form diethylallylacetonitrile[4]; in the absence of the alkyl halide, the corresponding amidine is obtained in good yield.[4]

In the present investigation the anions of phenylacetonitrile and acetonitrile, prepared by means of sodium amide in ether suspension, have been acylated with ordinary esters to form β-keto nitriles and carbethoxylated with diethyl carbonate to form α-cyano esters. The products and yields are listed in Table I. These reactions may be illustrated with phenylacetonitrile, thus

$$RCO_2C_2H_5 + (C_6H_5CHCN)^-Na^+ \longrightarrow RCOCH(C_6H_5)CN$$

$$C_2H_5OCO_2C_2H_5 + (C_6H_5CHCN)^-Na^+ \longrightarrow C_6H_5CH(CN)CO_2C_2H_5$$

It can be seen from Table I that the yields are good with phenylacetonitrile and fairly good with acetonitrile.[5] As in the acylation[6] or carbethoxylation[7] of ketones the presence of excess sodium amide improves the yield (based on the nitrile). An attempt to carbethoxylate caprylonitrile has failed. Apparently, the corresponding amidine was formed, since caprylamide, a hydrolysis product,[3] was obtained from the aqueous acid solution.

Earlier workers have reported the carbethoxylation,[8] acetylation[9] and propionylation[9] of phenylacetonitrile in the presence of a slight excess of sodium amide. We confirmed their yield for the carbethoxylation but were able to approach their high yield of 70% for acetylation only when we used an extra equivalent of sodium amide. We were able even with this extra equivalent to obtain only a 60% yield instead of their 75% yield for the propionylation.

Sodium amide appears to be as good as or superior to sodium ethoxide for the acylation or carbethoxylation of phenylacetonitrile or acetonitrile, although only the latter base (or sodium) has been satisfactory with higher aliphatic ni-

---

[1] Paper XXXIV on "Condensations"; paper XXXIII, THIS JOURNAL, **68**, 672 (1946).

[2] Present address: Mathieson Alkali Works, Niagara Falls, New York.

[3] See especially Bergstrom and Fernelius, *Chem. Rev.*, **12**, 136–138 (1933); Shriner and Neumann, *ibid.*, **35**, 359 (1944).

[4] Ziegler and Ohlinger, *Ann.*, **495**, 84 (1932).

[5] Propionyl acetonitrile, from ethyl propionate and acetonitrile, has been alcoholyzed to ethyl propionylacetate in 60% yield by the method described previously for other β-keto nitriles (ref. 12, 13, 14). It was hoped that these reactions would furnish a satisfactory method for the preparation of this β-keto ester but the over-all yield from acetonitrile has been only 24%.

[6] Adams and Hauser, THIS JOURNAL, **66**, 1220 (1944).

[7] Levine and Hauser, *ibid.*, **66**, 1768 (1944).

[8] Nelson and Cretcher, *ibid.*, **50**, 2758 (1928).

[9] Bodroux, *Bull. soc. chim.*, [4] **7**, 848 (1910).

TABLE I

Product	B. p. or m. p., °C.	Yield, %
α-Acetylphenylacetonitrile	89–90[a]	68 (45)[h]
Propionylacetonitrile	109–110 (20)[b]	40
α-Propionylphenylacetonitrile	71–72.5[c]	60
n-Butyrylacetonitrile	103–105 (11)[d]	33
α-Benzoylphenylacetonitrile	89–90[e]	61[i] (50)[i,j]
Ethyl cyanoacetate	106–107 (22)[f]	40 (20)[i,j]
Ethyl α-cyanophenylacetate	152–154 (11)[g]	69[i,j]

[a] This melting point and that (112–113°) of the oxime agree with those reported in ref. 10, 11. [b] The boiling point reported by Henry [*Bull. classe sci. Acad. roy. Belg.*, [4] **2**, 62 (1900)] and by Van Reymenant [*ibid.*, [4] **2**, 743 (1900)] is 164–165°. Our product was characterized by alcoholysis to ethyl propionylacctate which was identified by its copper salt, m. p. 143–144° (Dupont, *Compt. rend.*, **148**, 1524 (1909). [c] The melting point reported by Bodroux (ref. 9) is 73° and that by Walther and Schickler (ref. 10) is 58°. [d] Agrees with boiling point reported in ref. 14. [e] This boiling point and the melting point (160–161.5°) of the oxime agree essentially with those reported in ref. 10. [f] Agrees with boiling point reported in literature (see ref. 15). [g] Nelson and Cretcher (ref. 8) report 145° at 7 mm. and 165° at 19 mm. [h] Yield with 0.3 mole each of reactants. [i] Only 0.38 mole of ester used. [j] Only 0.33 mole of sodium amide used.

triles. Thus, sodium amide has produced considerably better yields than sodium ethoxide[10] in the propionylation or benzoylation of phenylacetonitrile; however, sodium ethoxide[11] as well as sodium amide produces good yields in the acetylation of this nitrile. Sodium ethoxide has been employed in the isobutyrylation[12] or benzoylation[13] of acetonitrile but apparently not in the propionylation or *n*-butyrylation of this nitrile for which sodium amide has been fairly satisfactory.[14] Sodium ethoxide[15] as well as sodium amide produces good yields in the carbethoxylation of phenylacetonitrile but only the latter base has produced even a fairly satisfactory yield in the carbethoxylation of acetonitrile. In general, sodium amide effects these reactions in less time than sodium ethoxide.

Experimental

Sodium amide (0.6 mole) was prepared in liquid ammonia as previously described.[7] The reaction flask was placed on a steam-bath and absolute ether was added at such a rate as to maintain 300 cc. of liquid in the flask. After evaporation of the ammonia the ether began to boil, and 0.3 mole of phenylacetonitrile or acetonitrile in 50 cc. of absolute ether was added with stirring. The mixture was boiled for one-half hour. Longer heating appeared to be undesirable, since preliminary experiments with acetonitrile and diethyl carbonate indicated that the maximum concentration of nitrile anion is attained within fifteen to thirty minutes.

The ethyl ester (0.6 mole) to be condensed, dissolved in 50 cc. of absolute ether, was added, and the mixture was boiled under reflux and stirred for two hours; then it was poured on 100 g. of ice and acidified with concentrated hydrochloric acid. The ethereal phase was separated and the water layer was extracted with two 100-cc. portions of ether. The combined extracts were dried over Drierite, the solvent was distilled, and the residue was recrystallized, or distilled *in vacuo;* the data are given in Table I.

When 0.3 mole of caprylonitrile was treated with two equivalents each of sodium amide and diethyl carbonate as described above, none of the condensation product was obtained,[16] but the aqueous acid phase deposited on standing caprylamide, m. p. 105–105.5°,[17] in 30% yield.

Summary

1. The acylation and carbethoxylation of certain nitriles with certain esters have been effected in the presence of sodium amide.

2. The two courses of reaction of nitriles with sodium amide are discussed.

(10) Walther and Schickler, *J. prakt. Chem.*, **55**, 305 (1897).

(11) "Organic Syntheses," Coll. Vol. II, 487 (1943).

(12) Kroeker and McElvain, THIS JOURNAL, **56**, 1172 (1934).

(13) Dorsch and McElvain, *ibid.*, **54**, 2962 (1932).

(14) Sodium triphenylmethide also, has been employed in the *n*-butyrylation of acetonitrile; Abramovitch and Hauser, *ibid.*, **64**, 2720 (1942).

(15) Wallingford, Jones and Homeyer, *ibid.*, **64**, 576 (1942).

(16) Since Ziegler and Ohlinger (ref. 4) have reported that higher aliphatic nitriles may be alkylated by adding sodium amide to a mixture of the nitrile and alkyl halide at the boiling point of ether, an attempt was made to carbethoxylate caprylonitrile in this manner; however, the nitrile was recovered. Since little diethyl carbonate was recovered, it appeared that the sodium amide reacted with this ester rather than with the nitrile.

(17) Hofmann, *Ber.*, **17**, 1408 (1884).

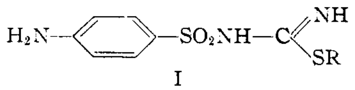
DURHAM, NORTH CAROLINA RECEIVED OCTOBER 13, 1945

[CONTRIBUTION FROM THE DANIEL SIEFF RESEARCH INSTITUTE]

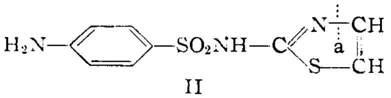
Sulfathiourea[1]

BY FELIX BERGMANN

The synthesis of sulfanilyl-isothioureas of the general formula I was initiated by the idea that these compounds are derived from sulfathiazole, II, by opening the thiazole ring along line a.[2,3,4] If it is assumed that sulfa drugs act by adsorption at an essential enzymatic system of the living cell, then the isothiourea derivatives I could replace II because of their structural resemblance.



I



II

[1] This name is proposed as abbreviation of the more accurate designation of the compound as "sulfanilyl-thiourea."

[2] Cox, *J. Org. Chem.*, **7**, 307 (1942).

[3] Hungarian Patent 127,731; *C. A.*, **36**, 2270 (1942).

[4] Winnek, *et al.*, THIS JOURNAL, **64**, 1682 (1942); *C. A.*, **36**, 5791 (1942). This paper, like many others cited in this publication, was available to the author only from the *C. A.*