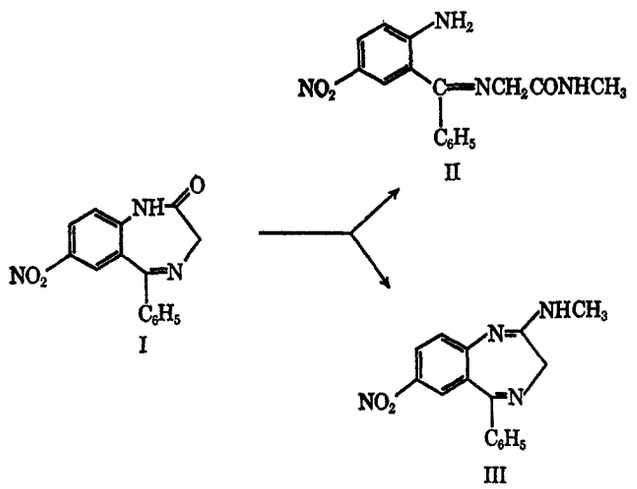
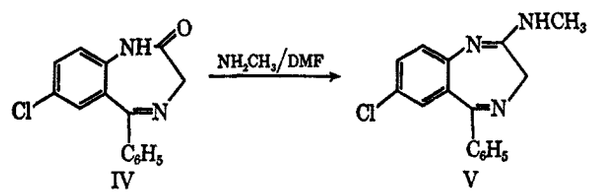
compound II formed by a transamidation reaction (Scheme I).[5]



Amidines could also be prepared directly from some benzodiazepin-2-ones in the absence of the Lewis acid catalyst but in lower yield. Thus a solution of 7-chloro-1,3-dihydro-5-phenyl-2H-1,4-benzodiazepin-2-one (IV) in dimethylformamide could be converted into 7-chloro-2-methylamino-5-phenyl-1,4-benzodiazepine (V) by treatment with methylamine under pressure. These reactions without the use of titanium



tetrachloride were restricted to compounds which were not substituted in the 7 position with a nitro group. In the case of the 7-nitro compounds the only products isolated (up to 90%) were the open amides of type II.[5]

Experimental Section

Melting points were determined microscopically on a hot stage and are corrected. Where the expected products were known compounds, mixture melting points were determined with authentic samples and infrared spectra were compared in order to confirm the expected structural changes.

Substituted Benzoyl-3,4-dihydroquinoxalin-2-(1H)-ones (Compounds 1–3, Table III).—A suspension of 7.4 g (5 mmol) of crude 3,4-dihydroquinoxalin-2(1H)-one[6] in 100 ml of ether was treated with 5 mmol of the appropriate benzoyl chloride. The mixture was stirred at room temperature for 40 min while 50 ml of 1 *N* sodium hydroxide solution was added in portions large enough to maintain the aqueous phase slightly alkaline. The solids were collected, washed with ether and water, and then dried to give the desired product.

Amidines from Amides (Compounds 4a–9a, 10b, 11–17, Tables I and II).—A solution of 0.0184 mol of the amide in 125 ml of dry tetrahydrofuran was added to a solution of 15 g of the amine in 100 ml of dry tetrahyrofuran. The mixture was contained in a three-necked round-bottomed flask fitted with a stirrer, dropping funnel and Dry Ice condenser. The flask was externally cooled in an ice bath. A tetrahydrofuran–titanium tetrachloride complex prepared by adding 1.8 g (0.01 mol) of titanium tetrachloride to 60 ml of tetrahydrofuran was added slowly (20 min) to the reaction mixture. The resulting mixture was continually stirred and allowed to reach room temperature. After 4 hr or when thin layer chromatography indicated that the reaction was complete, the reaction mixture was treated with 10 ml of water and then filtered. The filtrates were evaporated to dryness, and the residue was dissolved in 500 ml of dichloromethane. The organic solution was washed with 20 ml of dilute ammonium hydroxide, two 100-ml portions of saturated brine solution, dried over anhydrous sodium sulfate, filtered and evaporated. The residue was recrystallized from a mixture of the appropriate solvent to give the amidine.

2-[(2-Amino-5-nitrophenyl)phenylmethylenimino]-N-methylacetamide (II) and 2-Methylamino-7-nitro-5-phenyl-3H-1,4-benzodiazepine (III).—A solution of 5 g (0.0178 mol) of 1,3-dihydro-7-nitro-5-phenyl-2H-1,4-benzodiazepin-2-one in 150 ml of dry tetrahydrofuran was added to a solution of 10 g of methylamine in 100 ml of dry tetrahydrofuran. The resulting solution was cooled and treated with a solution of 2.4 g (0.017 mol) of titanium tetrachloride in 50 ml of dry benzene. The mixture was allowed to warm to room temperature and stirred overnight. Approximately 10 ml of water was added to decompose excess titanium tetrachloride and the solution was filtered. Solvent was removed and the residue was treated with 50 ml of ethanol. The open amide, compound II,[5] was removed by filtration [4.1 g (74%), mp 190–192°] and the mother liquors were concentrated to yield the other product. Recrystallization from methanol gave 1.0 g (19%) of pure III as prisms.

Registry No.—**1**, 18756-07-5; **2**, 18756-08-6; **3**, 18756-09-7; **4a**, 18756-10-0; **5a**, 18756-11-1; **6a**, 18756-12-2; **7a**, 18756-13-3; **8a**, 18756-14-4; **9a**, 17953-25-2; **10b**, 18756-16-6; **11**, 13677-83-3; **15**, 18756-18-8; **16**, 3712-28-5.

Acknowledgment.—We are indebted to Dr. F. Scheidl and his staff for the microanalyses and to Mr. S. Traiman for the determination of infrared spectra.

(5) We have previously shown [R. I. Fryer, J. V. Earley, and L. H. Sternbach, *J. Org. Chem.*, **32**, 3798 (1967)] that compounds of type I react with amines to give only the transamidation products.

(6) W. H. Perkin and G. C. Riley, *J. Chem. Soc.*, **123**, 2403 (1923).

Acid-Catalyzed Reaction of Isocyanide with a Schiff Base. New and Facile Syntheses of Imidazolidines

TAKEO SAEGUSA, NAOTAKE TAKA-ISHI, IWAO TAMURA, AND HIROYASU FUJII

Department of Synthetic Chemistry, Kyoto University, Kyoto, Japan

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Recently we reported the reaction of alkyl isocyanides with carbonyl compounds in the presence of a Lewis acid catalyst at −78°, in which 1:2 and 2:3 cyclic cooligomers were formed by the opening of the carbon–oxygen double bond and the α,α addition of the isocyanide carbon.[1,2]

The present communication describes the cationic reaction of alkyl isocyanide with the carbon–nitrogen double bond. In the presence of a Lewis acid catalyst, alkyl isocyanide reacts with benzaldehyde N-alkylimine (a Schiff base of aliphatic amine) to produce a derivative of imidazolidine, namely the 1:2 cyclic cooligomer.

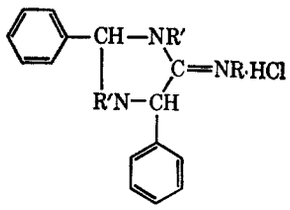
Table I illustrates the preparations of some 2,5-diphenylimidazolidines. The structures of the products were clearly established by elemental analysis, molecular weight determination and ir and nmr spectra. As catalyst, an equimolar amount of $AlCl_3$ was required. The 1:1 complexization of $AlCl_3$ with the imidazolidine product probably deactivated a stoichio-

(1) T. Saegusa, N. Taka-ishi, and H. Fujii, *Polymer Lett.*, **5**, 779 (1967).

(2) T. Saegusa, N. Taka-ishi, and H. Fujii, *Tetrahedron*, **24**, 3795 (1968).

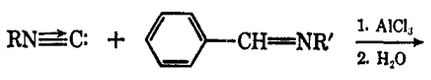
TABLE I

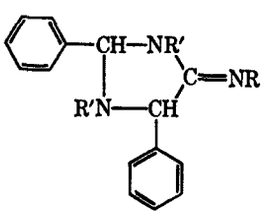
2,5-DIPHENYLIMIDAZOLIDINE–HYDROCHLORIDE SALTS



Compd no.	R	R′	Yield,[a] %	Mp,[b] °C	Formula	Calcd, % C	H	N	Cl	Found, % C	H	N	Cl
Ia		CH_3	98	196–197	$C_{23}H_{29}N_3 \cdot HCl$[c]	71.95	7.88	10.94	9.23	71.52	8.02	10.71	9.51
Ib		C_2H_5	81	211–212	$C_{25}H_{33}N_3 \cdot HCl$[d]	72.88	8.32	10.20	8.60	72.81	8.38	9.94	8.35
Ic	t-C_4H_9	CH_3	80	173–174	$C_{21}H_{27}N_3 \cdot HCl$[e]	70.47	7.89	11.74	9.91	70.70	8.15	11.54	10.20

[a] Based on Schiff base. [b] Samples for analysis were prepared by recrystallization from acetone. [c] Ir $\nu_{C=N}$ at 1680 cm^{-1}; nmr ($CDCl_3$) τ 2.52 (s, phenyl), 4.94 (m) and 5.27 (m, methine), 6.77 (s) and 7.80 (s, methyl). [d] Ir $\nu_{C=N}$ at 1670 cm^{-1}; nmr ($CDCl_3$) τ 2.55 (s, phenyl), 4.53 (m, methine), 5.42 (q) and 6.80 (q, methylene), 8.75 (t) and 9.14 (t, methyl). [e] Ir $\nu_{C=N}$ at 1640 cm^{-1}; nmr ($CDCl_3$) τ 2.53 (s, phenyl), 4.80 (m) and 5.02 (m, methine), 6.66 (s) and 7.75 (s, methyl), 8.72 (s, t-butyl).

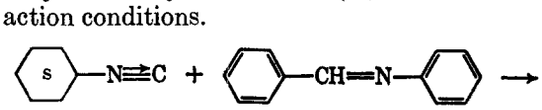


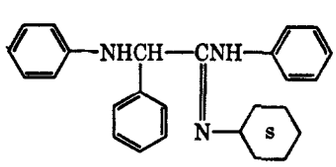


Ia, R = cyclohexyl; R′ = CH_3
b, R = cyclohexyl; R′ = C_2H_5
c, R = t-C_4H_9; R′ = CH_3

metric amount of $AlCl_3$. Not only $AlCl_3$, but also $SnCl_4$ and $BF_3 \cdot Et_2O$ induced the formation of the same cyclic cooligomer in decreased yields.

The reaction of cyclohexyl isocyanide with the Schiff base of aromatic amine, however, gave only an acyclic product of N,N′-diphenyl-1-phenyl-2-cyclohexyliminoethylenediamine (II) under the same reaction conditions.





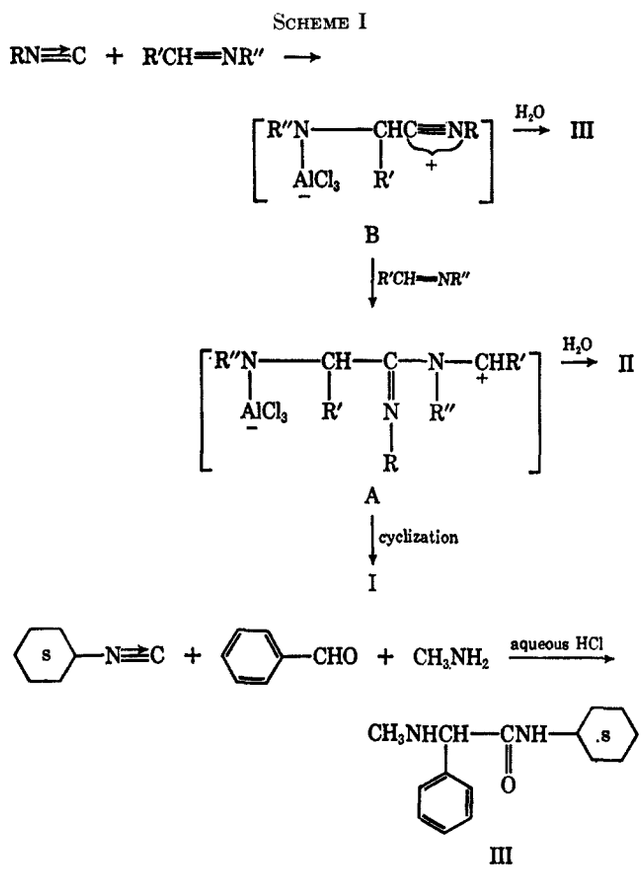
II

It is of interest to compare the reactions of the present study with the HCl-catalyzed reaction of isocyanide with a Schiff base producing a derivative of α-amino acid amide.[3]

In the present study, cyclohexyl isocyanide was treated with benzaldehyde–methylamine in the presence of HCl according to Ugi's procedure. The product was N-cyclohexyl-2-(methylamino)-2-phenylacetamide (III) and Ia was not detected.

The courses of the reactions of the present study as well as of Ugi's reaction will be well summarized by Scheme I. A cyclization of a dipolar adduct (A) consisting of one molecule of isocyanide and two molecules of Schiff base would lead to the formation of I. Acyclic products II and III would be derived from the hydrolysis of the two intermediates of A and B, respectively.

SCHEME I



It is of interest to note that the unit ratio of isocyanide–Schiff base in imidazolidine is $^1/_2$, whereas that of isocyanide–carbonyl compound in their cyclic cooligomers is $^2/_1$ or $^3/_2$. Further studies including the mechanistic one will be reported in the near future.

Experimental Section

General Method for the Preparation of 2,5-Diphenylimidazolidines (Ia–c).—A solution of 10 mmol of $AlCl_3$ in 20 ml of ethyl

(3) I. Ugi and C. Steinbrückner, *Chem. Ber.*, **94**, 734 (1961).

ether was added dropwise at room temperature to an equimolar mixture of an alkyl isocyanide and a Schiff base of benzaldehyde in 10 ml of ethyl ether. A white precipitate appeared immediately. The reaction system was kept at room temperature for 1 day. Then a water–methanol mixture was added to terminate the reaction. The precipitate was washed with petroleum ether, extracted with chloroform and finally recrystallized from acetone.

N,N'-Diphenyl-1-phenyl-2-cyclohexyliminoethylenediamine (II).—A solution of 20 mmol of $BF_3 \cdot OEt_2$ in 5 ml of ethyl ether was added dropwise at 0° to a solution of 30 mmol of cyclohexyl isocyanide and benzylidene aniline in 30 ml of ethyl ether. After standing 1 day at the same temperature, the reaction was stopped by the addition of a water–methanol mixture. From the ether-soluble part, 1.5 g of II was obtained by recrystallization: yield 13% (based on isocyanide); mp 136–137°; nmr (in CCl_4) τ 2.5–3.8 (phenyl, multiplet, 15 H), 4.30 (NH, multiplet, 1 H), 5.08 (CH, singlet, 1 H), 6.15 (CH of cyclohexyl ring, multiplet, 1 H), 6.30 (NH, multiplet 1 H), 7.8–9.0 (CH_2 of cyclohexyl ring, multiplet, 10 H). *Anal.* Calcd for $C_{26}H_{29}N_3$: C, 81.42; H, 7.62; N, 10.96. Found: C, 81.07; H, 7.81; N, 10.79.

N-Cyclohexyl-2-(methylamino)-2-phenylacetamide (III).—At 0°, 2.73 g of cyclohexyl isocyanide (25 mmol) was added dropwise to a mixture of 3.18 g of benzaldehyde (30 mmol), 3 ml of methylamine (30% in water, 30 mmol), 3 ml of 10 *N* HCl and 5 ml of methanol. After standing for 1 hr, the reaction system was acidified with 20 ml of 2 *N* HCl, and extracted with benzene. The water layer was neutralized with 10 ml of 40% aqueous NaOH and extracted with methylene chloride. From the methylene chloride soluble part, 1.91 g of III was obtained by recrystallization from 1:5 benzene–petroleum ether (bp 30–60°): yield 31%; mp 82–83°; nmr (in $CDCl_3$) τ 2.68 (phenyl, singlet, 5 H), 5.97 (CH, singlet, 1 H), 7.55 (CH_3, singlet, 3 H), 8.0–9.0 (CH_2 of cyclohexyl ring, multiplet, 10 H). *Anal.* Calcd for $C_{15}H_{22}N_2O$: C, 73.13; H, 9.00; N, 11.37. Found: C, 73.18; H, 9.09; N, 11.15.

Registry No.—Ia, 18742-13-7; Ib, 18742-14-8; Ic, 18742-15-9; II, 18742-16-0; III, 18742-17-1.

Synthesis of the N-Isobutylamide of All-*trans*-2,6,8,10-Dodecatetraenoic Acid

PHILIP E. SONNET

Entomology Research Division, U. S. Department of Agriculture, Beltsville, Maryland 20705

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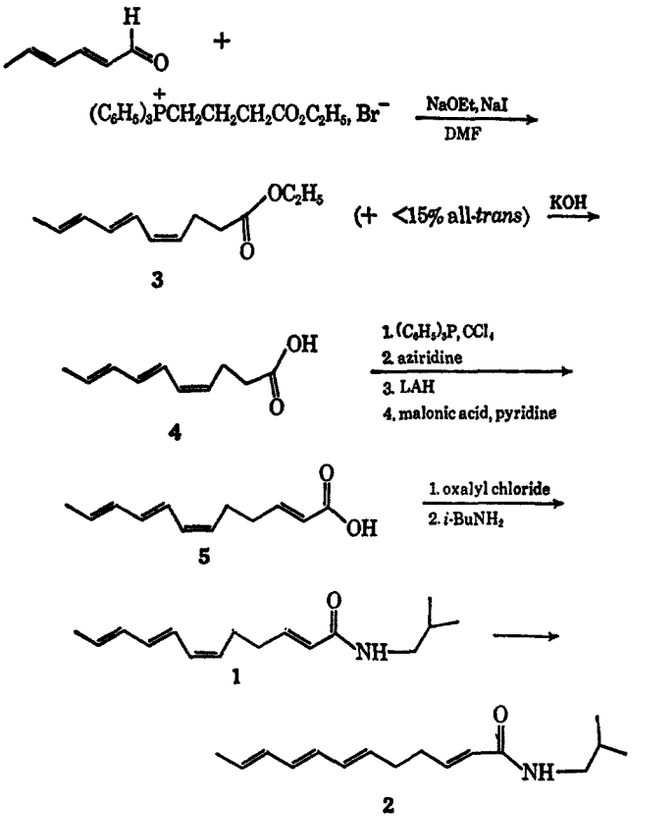
An insecticidal component of American coneflower roots, *Echinacea angustifolia* D.C. and *E. pallida* (Nutt.) Britton (Compositae), has been assigned structure **1**.[1] This same material occurs also in the barks of southern prickly ash, *Zanthoxylum clava-herculis* L.,[2] and the Japanese tree, *Zanthoxylum piperitum* D.C. (Rutaceae).[3] These isolates have been named echinacein, neoherculin, and α-sanshool, respectively. The instability of the material makes purification a formidable problem. The only criterion of purity has been ultraviolet absorption, and there is contamination with the all-*trans* isomer, **2**, which merely changes the extinction coefficients and not the position of the maxima. Treatment of the purified natural insecticide with iodine and uv light produces a crystalline substance of higher melting point, slightly greater maximum uv extinctions, and slightly lower insecticidal activity. This material, β-sanshool, has been assigned the all-*trans* configuration.[3]

We have synthesized **1**, containing an estimated 30% of the 6-*trans* isomer (Chart I). Studies by Bergelson



and coworkers have revealed that Wittig condensations conducted in DMF using alkoxides to generate the ylides produced olefins which were 91–93% *cis*.[4] In addition, they synthesized ethyl α-eleostearate, a conjugated *cis,trans,trans*-triene in this same manner by using the required *trans,trans*-dienal as the starting aldehyde.[5] We employed commercial sorbic aldehyde (>97% *trans* by glpc) and the triphenylphosphonium salt derived from ethyl-4-bromobutyrate. Triene ester **3** was uniform by glpc and was estimated to contain no more than 15% of the all-*trans* isomer using the uv data available for α- and β-eleostearic acids (see Table I). Saponification to the free acid **4** was followed by conversion into the aziridide *via* the acid halide. The usual methods for preparing acid halides were unsuccessful, and the method described by Lee[6] using triphenylphosphine and carbon tetrachloride was used instead. The aziridide was reduced with $LiAlH_4$ to the aldehyde which was then transformed into the required acid, **5**,

(1) M. Jacobson, *J. Org. Chem.*, **32**, 1646 (1967).
(2) L. Crombie, *J. Chem. Soc.*, 995 (1955).
(3) L. Crombie and J. D. Shah, *ibid.*, 4244 (1955); L. Crombie and J. L. Tayler, *ibid.*, 2760 (1957).
(4) L. D. Bergelson, V. A. Vaver, V. Yu Kovtun, L. B. Senyavina, and M. M. Shemyakin, *Zh. Obshch. Khim.*, **32**, 1802 (1962).
(5) L. D. Bergelson, V. D. Solodovnik, and M. M. Shemyakin, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 1315 (1962); *Chem. Abstr.*, **58**, 7824 (1963).
(6) J. B. Lee, *J. Amer. Chem. Soc.*, **88**, 3440 (1966).