duced with 1 g of sodium borohydride in 2 ml of 50% aqueous methanol. Addition of water precipitated 3-oxy-1,2,3,10b-tetrahydrofluoranthene, which after sublimation (100°, 0.5 mm) had mp 112° (lit.[21] mp 130–134° for the alcohol obtained by reduction of the ketone with sodium amalgam).

Anal. Calcd for $C_{16}H_{14}O$: C, 86.5; H, 6.3. Found: C, 86.2; H, 6.2.

The alcohol was heated under reflux with 2 ml of pyridine and 0.5 ml of acetic anhydride for 15 hr, after which water and ether were added. After the ether phase was washed with 1 *N* HCl and 5% $NaHCO_3$, it was dried and evaporated to yield crude acetate, which was dissolved in toluene and passed through a packed tube at 470°. The pyrolysate was washed from the Dry Ice–acetone cooled trap with toluene, the toluene was evaporated, and the residue was crystallized from ethanol and then sublimed at 60° (1 mm) to give 1,10b-dihydrofluoranthene: mp 78–79°; uv max 235 nm (ε 18,900), 267 (21,000), 275 (20,700), 286 (18,500 311 (3000), 323 (3400), 341 (2300), 357 (2300); nmr τ 6.13 (q, 1, Ar_2CH), 3.93 (m, 1, ArC=CH), 3.45 (d, 1, ArCH=C).

Anal. Calcd for $C_{16}H_{12}$: C, 94.1; H, 5.9. Found: C, 93.8; H, 6.1.

(21) J. von Braun and G. Manz, *Justus Liebigs Ann. Chem.*, **488**, 111 (1931).

Registry No.—**1**, 205-94-7; **3**, 35324-19-7; **5c**, 35324-20-0; **5d**, 35324-21-1; **5d** MeI, 35324-22-2; **8**, 14310-97-5; **9**, 35324-24-4; **10a**, 35324-25-5; **10b**, 35324-26-6; **11**, 209-69-8; **12**, 208-69-5; 3-oxy-1,2,3,-10b-tetrahydrofluoranthene, 35324-28-8; 1,10b-dihydrofluoranthene, 35324-29-9.

β-Carbonylamides in Peptide Chemistry. β-Aminoenones and β-Aminoenediones from *N*-Acetoacetyl Derivatives of Secondary Amino Acids

FERNANDO FILIRA, CARLO DI BELLO, AUGUSTO C. VERONESE, AND FERRUCCIO D'ANGELI*

Nucleo di Chimica delle Macromolecole, C. N. R., Istituto di Chimica Organica dell'Universita', Padova, Italy

Received February 15, 1972

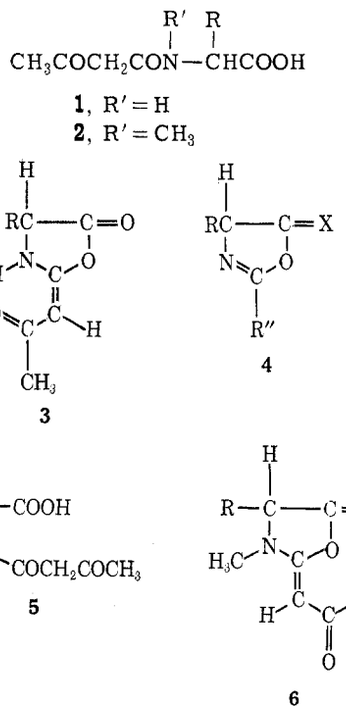
A comparative study on the behavior of some *N*-acetoacetyl (AcA) derivatives of secondary amino acids with dicyclohexylcarbodiimide was made. *N*-Methyl-AcA-amino acids yield 2-acetonylideneoxazolidin-5-ones (**6**), whose stereochemistry and condensation with nucleophiles are reported. *N*-AcA-Proline, in turn, forms a bicyclic azlactone (**7**) and a tetramic derivative (**8**); the latter reacts with nucleophiles yielding diastereomeric β-aminoenediones (**10**, **10'**) stabilized through hydrogen bonding.

During previous research[1] on the reactions of *N*-acetoacetylamino acids (AcA-aa, **1**) with dicyclohexylcarbodiimide (DCCI) we obtained 2-acetonylideneoxazolidin-5-ones **3**, which behave as possible intermediates in the condensation with nucleophiles; in some cases, we observed a condensation–racemization ratio more favorable than known for 2-oxazolin-5-ones (**4**, X = O), which racemize through enolates or mesoionic species.[2]

A 2-acetonyloxazoline structure (**4**, R'' = CH_2C-OCH_3, X = R_2 or RH), tautomerically related to **3**, was recently proposed, in turn, for the transformation products of pertinent acetoacetamides.[3]

In this paper we report on the behavior of AcA derivatives of *N*-methylamino acids and proline in the presence of the same activator of the carboxyl groups, namely DCCI. Furthermore, we studied how the eventual formation of oxazole derivatives would affect the retention of configuration in the condensation reaction.

N-Methyl-AcA-aa (**2**) condenses with amino acid esters in the presence of DCCI to give racemized *N*-methyl-AcA dipeptides. On the other hand, when **2** is treated with DCCI in the absence of nucleophiles, the very reactive 2-acetonylidene-3-methyloxazolidin-5-ones (**6**) are obtained in almost quantitative yields. Structure **6** is supported by strong carbonyl absorption at 1840 cm^{-1}, β-aminoenone maximum near 275 nm (ε >20,000),[4] and the presence of singlets for the vinyl proton and the CH_3CO group at δ 4.8 and 2.3, respectively. The hypsochromic–hyperchromic shift of the uv maximum and the strong shift of the vinyl proton with respect to the chelated structures **3** [uv max 285 nm (ε *ca.* 12,000); =CH at δ 5.2],[1] confirm that the present compounds have the thermodynamically favored trans configuration **6**. In no reaction could the alternative diastereomer be detected. This contrasts with the related β-aminoalkenoates and β-aminoenones, which are obtained under proper conditions as cis–



(1) C. Di Bello, F. Filira, and F. D'Angeli, *J. Org. Chem.*, **36**, 1818 (1971), and references cited therein.

(2) *Cf.* M. Goodman and C. Glaser in "Peptides, Chemistry and Biochemistry," B. Weinstein and S. Lande, Ed., Marcel Dekker, New York, N. Y., 1970.

(3) T. Kato and M. Sato, *Chem. Pharm. Bull.*, **17**, 2405 (1969); T. Kato, Y. Yamamoto, and M. Sato, *Yakugaku Zasshi*, **91**, 384 (1971).

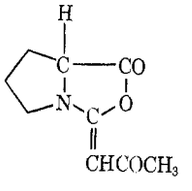
(4) D. L. Ostercamp, *J. Org. Chem.*, **35**, 1632 (1970).

trans mixtures.[5] Further studies on the stereochemistry of the compounds described in this paper will be reported;[6a] circular dichroism data on **3** and **6** have been published.[6b]

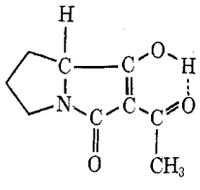
When an azlactone (**6**) was treated with an amino acid ester or amine, the corresponding peptide or amide was obtained, as in the straightforward condensation of an *N*-methyl-AcA-aa with the nucleophile in the presence of DCCI. We investigated the retention of optical activity both in the stepwise and in the direct condensation. In spite of the fact that some *N*-acyl-*N*-alkylamino acids have a smaller tendency to racemize than *N*-acylamino acids,[2] we obtained under both sets of conditions partially racemized *N*-methyl-AcA-L-valine benzylamide, in contrast with the related AcA-L-leucine benzylamide and analogous valine derivatives.[1] The loss of optical purity may be due in part to the positive charge at the tertiary nitrogen of the trans aminoenone chromophore.[4,5]

When *N*-AcA-L-proline (**5**) was treated with an amino acid ester in the presence of DCCI, each *N*-AcA-L-prolyl dipeptide was obtained in rather low yield, and was contaminated by a second condensation product which displayed β-aminoenedione properties. This was somehow unexpected, although complications accompany the synthesis of prolyl peptides due, in part, to the rigidity at the C_α–N bond.[7]

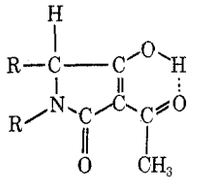
The outcome of parallel reactions of **5** with DCCI in the absence of a nucleophile led to the elucidation of the nature of the unexpected β-aminoenediones. The reaction mixtures obtained in various solvents absorbed at 1845 cm^{-1} and contained an acylating species, which we believe to be the azlactone **7** and not



7

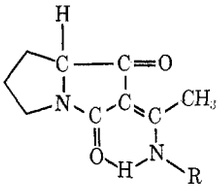


8

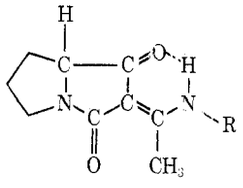


9

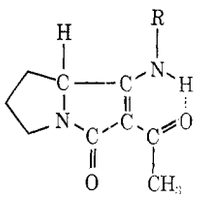
an anhydride;[8] **7** could not be isolated in sufficiently pure state to allow stereochemical conclusions. Instead, we isolated an isomer of **7**, namely the pyrrolizine derivative **8**. Uv, ir, and nmr spectra of **8**, as well as of the β-aminoenediones, fit the properties of related "tetramic acids" **9**;[9e,10] furthermore, **8** reacts promptly with nucleophiles, yielding the β-aminoenediones. In agreement with the preferred orientation in the reactions of nucleophiles onto tetramic acids[9a,f] and other tricarbonylic substrates,[10a] we believe that the aminoenediones bear the amino ester residue linked to the chain. We assume that such orientation will yield two diastereomers almost equally stabilized through hydrogen bonding (**10**, **10′**); actually, the nmr spectrum at 90 Mc of each reaction product displays two lines for the ethylidene methyl group near δ 2.5 and two distinct signals for the amino group near δ 11, in agreement with the proposed structure.



10



10′



11

The available data indicate that an irreversible intramolecular C → C attack competes with the straightforward condensation and/or an intramolecular O → C attack leading to the acylating intermediate (**7**). Alternative hypotheses, such as the existence of slowly interconverting prolinamide rotamers[11] or fast equilibrating diastereomers (**10**, **10′**) admixed with an isomer (**11**) formed by attack on the ring, are ruled out.

AcA-prolyl dipeptide esters undergo deacetoacetylation with hydroxylamine[1] to the pertinent prolyl dipeptide esters; the β-aminoenedione (**10**, **10′**) undergoes, under the same conditions, displacement of the amino acid ester, in analogy with amine replacements reported for related aminoenones and aminoenediones.[10b] In a series of reactions of many AcA-aa with DCCI, particularly in DMF solution,[12] no tetramic derivatives could be detected, although the reaction mixtures were examined carefully by chromatography. This stresses the special effect of proline on the reaction outcome.

In conclusion, as regards the behavior of AcA-aa (**1**),[1] *N*-methyl-AcA-aa (**2**), and AcA-proline (**5**) toward carboxyl group activation *via* DCCI, **1** and **2** yield 2-acetonylideneoxazolidin-5-ones (**3**, **6**), which have the opposite stereochemistry at the olefin side chain. **5**, on the other hand, undergoes a major side reaction and yields the unexpected pyrrolizine derivatives **8** and **10**.

(5) H. Kessler, *Angew. Chem., Int. Ed. Engl.*, **9**, 219 (1970), and references cited therein; Y. Shvo and H. Shanan-Atidi, *J. Amer. Chem. Soc.*, **91**, 6683 (1969); Y. Shvo and I. Belsky, *Tetrahedron*, **25**, 4649 (1969); J. Sandstrom and I. Wennerbeck, *Chem. Commun.*, 1088 (1971).

(6) (a) F. Filira, M. Acampora, and F. D'Angeli, unpublished results; (b) C. Di Bello, F. Filira, and C. Toniolo, *Biopolymers*, **10**, 2283 (1971).

(7) R. H. Mazur and J. M. Schlatter, *J. Org. Chem.*, **28**, 1025 (1963).

(8) E. Schnabel, "Peptides," L. Zervas, Ed., Pergamon Press, Oxford, 1966, p 71; D. F. De Tar, R. Silverstein, and F. F. Rogers, Jr., *J. Amer. Chem. Soc.*, **88**, 1024 (1966).

(9) (a) R. N. Lacey, *J. Chem. Soc.*, 850 (1954); (b) S. A. Harris, L. V. Fisher, and K. Folkers, *J. Med. Chem.*, **8**, 478 (1965); (c) H. Yuki, Y. Tohira, B. Aoki, T. Kano, S. Takama, and T. Yamazaki, *Chem. Pharm. Bull.*, **15**, 1107 (1967); (d) A. Aebi, H. U. Daeniker, and J. Druey, *Pharm. Acta Helv.*, **38**, 616 (1963); (e) C. W. Holzapfel, *Tetrahedron*, **24**, 2101 (1968); (f) G. Büchi and G. Lukas, *J. Amer. Chem. Soc.*, **86**, 5654 (1964).

(10) (a) J. F. Stephen and E. Marcus, *J. Org. Chem.*, **34**, 2527 (1969), and references cited therein; (b) J. D. Edwards, J. E. Page, and M. Pianka, *J. Chem. Soc.*, 5200 (1964); H. Junek and A. R. O. Schmidt, *Monatsh. Chem.*, **100**, 570 (1969).

(11) *Cf.* H. L. Maia, K. G. Orrell, and H. N. Rydon, *Chem. Commun.*, 1209 (1971), and references cited therein.

(12) Details of these reactions are omitted for sake of brevity.

Experimental Section[13]

N-Acetoacetyl-N-methylamino acids (2) and N-acetoacetyl-L-proline (5) were obtained by stirring a solution of N-methylamino acid[14] or L-proline in the equivalent amount of 2 N sodium hydroxide, with 1 mol of diketene at 0° until the latter was completely dissolved (1–2 hr). The solution was washed with ether, acidified to pH 1, and extracted with ethyl acetate. The extracts were dried (Na_2SO_4) and concentrated to give AcA-L-proline,[1,9b] $[\alpha]$ −58° (*c* 2.0), and the following new N-methyl AcA-aa.

N-Acetoacetyl-N-methyl-L-alanine (2a) was an oil (80%), uv max 256 nm (ε 3800), $[\alpha]$ −33.4° (*c* 2.0). It was analyzed as the dicyclohexylammonium salt, mp 146–147°. *Anal.* Calcd for $C_8H_{13}NO_4 \cdot C_{12}H_{23}N$: C, 65.18; H, 9.85; N, 7.60. Found: C, 65.55; H, 9.74; N, 7.59.

N-Acetoacetyl-N-methyl-L-valine (2b) was an oil (82%), uv max 257 nm (ε 5370), $[\alpha]$ −94.0° (*c* 2.0). *Anal.* Calcd for $C_{10}H_{17}NO_4$: C, 55.80; H, 7.96; N, 6.51. Found: C, 55.20; H, 7.69; N, 6.47.

N-Acetoacetyl-N-methyl-L-leucine (2c) was colorless prisms: mp 85–86° (68%), $[\alpha]$ −31.9° (*c* 2.0); uv max 254 nm (ε 5630). *Anal.* Calcd for $C_{11}H_{19}NO_4$: C, 57.62; H, 8.35; N, 6.11. Found: C, 57.44; H, 7.90; N, 6.12.

2-Acetonylidene-3,4-dimethyloxazolidin-5-one (6a).—The solution of AcA-N-methyl-L-alanine (**2a**) (167 mg, 0.89 mmol) in 3 ml of dioxane was added to DCCI (190 mg, 0.89 mmol); after 2 hr standing, the DCU (182 mg, 92%) was filtered off and the solution was lyophilized. An oil was obtained: $[\alpha]$ −3° (*c* 1.5); uv max 278 nm (ε 24,000); nmr δ 1.5 (d, C_4CH_3), 2.25 (s, $COCH_3$), 2.9 (NCH_3), 4.15 (q, C_4H), 4.7 (s, =CH). *Anal.* Calcd for $C_8H_{11}NO_3$: C, 56.79; H, 6.55; N, 8.28. Found: C, 56.70; H, 6.45; N, 8.23.

Compounds **6b,c** were obtained in an identical way from AcA-N-methyl-L-valine and AcA-N-methyl-L-leucine, respectively, and had the following properties.

2-Acetonylidene-3-methyl-4-isopropyloxazolidin-5-one (6b) was colorless prisms: mp 89–90°; $[\alpha]$ −4.3° (*c* 1.85); uv max 276 nm (ε 20,900). *Anal.* Calcd for $C_{10}H_{15}NO_3$: C, 60.89; H, 7.67; N, 7.10. Found: C, 60.31; H, 7.72; N, 7.28.

2-Acetonylidene-3-methyl-4-isobutyloxazolidin-5-one (6c) had mp 59–60°; $[\alpha]$ −0.7°; uv max 275 nm (ε 26,900). *Anal.* Calcd for $C_{11}H_{17}NO_3$: C, 62.54; H, 8.11; N, 6.63. Found: C, 62.62; H, 8.76; N, 6.74.

N-Acetoacetyl-N-methylvaline Benzylamide.—A sample of N-methyl-AcA-L-valine (**2b**) (215 mg, 1 mmol), dissolved in 5 ml of dioxane, was treated with DCCI (206 mg, 1 mmol) and allowed to stand for 2 hr. The DCU was filtered and the solution was treated with benzylamine (107 mg, 1 mmol) and left overnight. Concentration yielded an oil (A) that was redissolved in ethyl acetate and washed with aqueous sodium bicarbonate and then with water. The solution, taken to dryness, gave an oil (220 mg, 70%), $[\alpha]$ −7.2° (*c* 4.2). *Anal.* Calcd for $C_{17}H_{24}N_2O_3$: C, 67.08; H, 7.95; N, 9.20. Found: C, 67.14; H, 7.92; N, 9.14.

N-Benzyloxycarbonyl-N-methylvaline Benzylamide.—A sample of the above crude oil (A) obtained in an identical run was dissolved in 2 ml of ethanol–acetic acid–water (4:1:1) and added with 70 mg (1 mmol) of hydroxylamine hydrochloride. The mixture was heated at 40° for 30 min and the resulting solution was taken to dryness. After working up,[1] the aqueous extract, containing N-methylvaline benzylamide hydrochloride, was treated with benzyloxycarbonyl chloride in the presence of sodium hydroxide at 0°. An oil separated and was extracted with chloroform. After washing with water, 1.0 N HCl, and water, the solution was taken to dryness. A thick oil (90%) was obtained, $[\alpha]$ −22.9° (*c* 1.8, ethanol). *Anal.* Calcd for $C_{21}H_{26}N_2O_3$: C, 71.16; H, 7.39; N, 7.30. Found: C, 71.0; H, 7.20; N, 7.22.

The same product was obtained by treating (Z)-L-valine with benzylamine in the presence of DCCI, *via* symmetric anhydride,[15] yield 93%, $[\alpha]$ −80.1° (*c* 2.02, ethanol), indicative that in the preparation *via* the N-methyl-AcA-aa (**2b**) (see above) there had been 37.5% racemization. Finally, a third sample of N-methyl-(Z)-valine benzylamide was obtained by N-deacetoacetylation followed by N-benzyloxycarbonylation of a sample of the oil (A) prepared in turn by treating **2b** with benzylamine and then with DCCI; this sample had $[\alpha]$ −17.6°, indicative that extensive racemization had occurred also in this case.

N-Acetoacetyl-N-methylvalylglycine Ethyl Ester.—A sample of compound **2b** (645 mg, 3 mmol) in 5 ml of acetonitrile was added with DCCI (618 mg, 3 mmol), allowed to stand for 2 hr, and treated with a solution of glycine ethyl ester hydrochloride (460 mg, 3.3 mmol) and triethylamine (313 mg, 3.1 mmol) in 5 ml of acetonitrile. The mixture was let stand overnight, the DCU was filtered off, and the solution was taken to dryness. The oil was redissolved in ethyl acetate and washed with water, 0.1 N HCl, water, aqueous sodium bicarbonate, and again water; the solution was dried and concentrated *in vacuo*. An oil was obtained (800 mg, 87%), $[\alpha]$ −2° (*c* 3.6), uv max 253 nm (methanol). *Anal.* Calcd for $C_{14}H_{24}N_2O_5$: C, 55.98; H, 8.05; N, 9.32. Found: C, 55.61; H, 8.30; N, 9.29.

N-Acetoacetyl-N-methylvalyl-L-valine Methyl Ester.—This compound was prepared from **2b** and L-valine methyl ester, as an oil (85%); it consisted probably of a diastereomeric mixture, but no resolution was apparent on tlc. *Anal.* Calcd for $C_{16}H_{28}N_2O_5$: C, 58.51; H, 8.59; N, 8.53. Found: C, 58.08; H, 8.42; N, 8.25.

1-Hydroxy-2-acetyl-3-oxo-3,5,6,7,7a-pentahydropyrrolizine (8).

A.—AcA-L-proline[1,9b] was converted into its methyl ester and then into the corresponding tetramic derivative (**8**,[9b] sodium salt) (10.0 g, 98%).[9b] A sample was dissolved in 0.1 N hydrochloric acid. Extraction with ethyl acetate gave a solution that was washed with a little water and taken to dryness as an oil, $[\alpha]$ −95.2° (*c* 2.1), uv max 277 nm (ε 12,600). *Anal.* Calcd for $C_9H_{11}NO_3$: C, 59.66; H, 6.12; N, 7.73. Found: C, 59.74; H, 6.35; N, 7.58.

B.—AcA-L-proline was treated with DCCI in dioxane or acetonitrile, following the procedure used to obtain **6a**. DCU was filtered after 10–15 hr from the solution, which absorbed at 1845 cm^{-1}; the solution was concentrated to dryness and taken up with ethyl acetate–aqueous sodium bicarbonate. Concentration of the organic layer and purification on a column of SiO_2 gave N-acetoacetylprolylurea as an oil, $[\alpha]$ 78.3° (*c* 2.67). *Anal.* Calcd for $C_{22}H_{35}N_3O_4$: C, 65.16; H, 8.70; N, 10.36. Found: C, 65.20; H, 8.65; N, 10.41. The aqueous layer was extracted with ethyl acetate at various pH's; the presence of **8** and unchanged N-acetoacetylproline was demonstrated on tlc, by comparison with authentic samples.

2-(α-Ethoxycarbonylmethylamino)ethylidene-1,3-dioxopyrrolizidine (10, 10', R = $CH_2COOC_2H_5$) and N-Acetoacetyl-L-prolylglycine Ethyl Ester.—Samples of N-acetoacetylproline (4.18 g, 0.021 mol) and glycine ethyl ester hydrochloride (2.9 g, 0.018 mol) were dissolved in a mixture of DMF (20 ml) and acetonitrile (100 ml); triethylamine (2.8 ml, 0.02 mol) was added under stirring and cooling at −10°. The mixture was treated with DCCI (4.66 g, 0.023 mol) and kept for 1 hr at −10° and then for 16 hr at 20° under stirring. From the resulting suspension, the DCU was filtered off (100%) and the solution was evaporated to dryness. The residue was extracted with ethyl acetate that left undissolved the triethylammonium hydrochloride formed (100%); the extract was washed with water and 1 N HCl until neutral, dried, and concentrated to a solid. This work-up caused the disappearance of absorption at 1845 cm^{-1}, possibly due to reconversion of the azlactone **7** into AcA-proline **5** (*ca.* 10%). The solid was extracted with ether and recrystallized from ethyl acetate–petroleum ether (bp 40–60°) as colorless prisms (0.8 g, 20%): mp 135–136°; $[\alpha]$ −28° (*c* 2.0, methanol); uv max 305 nm (ε 20,000); ir 3450, 1750, 1710, 1675, 1630, 1600 cm^{-1}; nmr δ 1.3 (t, CH_2CH_3), 1.8–2.3 (m, CH_2CH_2), 2.5, 2.53 (CH_3C=), 2.9–3.3 (m, $C_{7a}H$), 3.55–4.0 (m, CH_2N), 4–4.4 (m, CH_2O, NCH_2CO), 10.95 (t, NH), 11.3 (t, NH). The twin signals at δ 2.5 and 2.53 did not collapse to a single peak upon irradiation of the spectrum; on deuteration, the amino proton peak disappears in about 16 min and uncoupling of the CH_2N was observed. *Anal.* Calcd for $C_{13}H_{18}N_2O_4$: C, 58.63; H, 6.81; N,

(13) Elemental analyses were performed in the Microanalytical Laboratory of the Institute of Organic Chemistry, at the care of Professor Eloisa Celon Mazzucato. Uv and ir spectra and optical activities (line D, at 25°, concentration in parentheses) were measured in dioxane, unless otherwise stated. Nmr spectra were measured in $CDCl_3$, using a Bruker Spectrospin, 90 Mc, and are given in (δ) parts per million, using $(CH_3)_4Si$ as internal standard. The molecular weight of the β-aminoenedione (**10, 10'**) was measured with a vapor pressure osmometer Hewlett-Packard 301A in benzene and with a mass spectrometer Hitachi Perkin-Elmer RMV6, with recorder H.P.E. 196. For tlc, precoated layers of silica gel Merck and ethyl acetate–benzene (2:1) as eluent were used; acetoacetyl derivatives gave blue-violet spots using an iron chloride spray.

(14) H. N. Rydon and P. W. G. Smith, *J. Chem. Soc.*, 3646 (1956).

(15) L. Kisfaludy and M. Löw, "Peptides 1962," G. T. Young, Ed., Pergamon Press, Oxford, 1963, p 93.

10.52; mol wt, 266.3. Found: C, 59.23; H, 6.79; N, 10.64; mol wt, 261 (C_6H_6), *m/e* 266. The same product was obtained by treating the pyrrolizinone **8** with glycine ethyl ester, in the condition described below for **10, 10'a**.

The above ether extract was evaporated to dryness, yielding an oil whose physical properties and elemental analysis indicated that it was crude AcA-pro-gly-OEt (4.0 g, 60%). Upon treatment with hydroxylamine hydrochloride[1] it yielded L-prolylglycine ethyl ester hydrochloride, identical with an authentic specimen.[16]

A sample of **10, 10'** was treated with hydroxylamine, under the same conditions;[1] chromatography showed the release of glycine ethyl ester hydrochloride and of a derivative, giving a strong blue spot with iron chloride, identical with the one obtained by mixing equimolecular quantities of **8** and hydroxylamine hydrochloride.[9f,10b]

Several other reactions of AcA-proline with glycine ethyl ester and DCCI were run using different solvents (acetonitrile alone, dioxane, $CDCl_3$); work-up always gave mixtures of **10, 10'** and AcA-prolylglycine ethyl ester.

2-(α-1-Ethoxycarbonyl-1-ethylamino)ethylidene-1,3-dioxopyrrolizidine (10, 10'a, R = $CHCH_3COOC_2H_5$).—A sample of **8** as the sodium salt (812 mg, 0.004 mol), suspended in ethanol (20 ml), was treated with L-alanine ethyl ester hydrochloride (615 mg, 0.004 mol), refluxed for 1 hr, and filtered. The solution was taken to dryness and the residue was redissolved in ethyl acetate. The solution was washed with water, 1 *N* hydrochloric acid, and water, dried on sodium sulfate, and concentrated to dryness as an oil (0.54 g, 49%): uv max 306 nm (ε 20,000); [α] +30.5 (*c* 2.2); nmr δ 1.3 (t, CH_2CH_3), 1.6 (d, CH_3), 1.7–2.3 (m, CH_2CH_2), 2.50, 2.52 (=CCH_3), 2.9–3.4 (m, C_{7a} H), 3.4–3.9 (m, CH_2N), 4.0–4.6 (m, OCH_2, C_α H), 10.8 (d), 11.1 (d, NH). *Anal.* Calcd for $C_{14}H_{20}N_2O_4$: C, 59.98; H, 7.19; N, 9.99. Found: C, 59.81; H, 6.95; N, 9.61.

(16) S. Guttman, J. Pless, and R. A. Boissonas, *Helv. Chim. Acta*, **45**, 170 (1962).

Registry No.—**2a**, 35211-90-6; **2b**, 35191-59-4; **2c**, 35141-03-8; **6a**, 35141-04-9; **6b**, 35141-05-0; **6c**, 35141-06-1; **8**, 2113-85-1; **10** (R = $CH_2CO_2C_2H_5$), 35191-60-7; **10'** (R = $CH_2CO_2C_2H_5$), 35141-08-3; **10** (R = $CHCH_3CO_2C_2H_5$), 35141-09-4; **10'** (R = $CHCH_3CO_2C_2H_5$), 35191-61-8; *N*-acetoacetyl-*N*-methylvaline benzylamide, 35191-62-9; *N*-benzyloxycarbonyl-*N*-methylvaline benzylamide, 35191-63-0; *N*-acetoacetyl-*N*-methylvalylglycine ethyl ester, 35191-64-1; *N*-acetoacetyl-*N*-methylvalyl-L-valine methyl ester, 35141-10-7; *N*-acetoacetylprolylurea, 35191-67-4.

Acknowledgments.—We are indebted to Dr. Mario Acampora for discussions concerning the nmr spectra and to Mr. Adriano Mencini for technical assistance.

Photolysis of Dibenzylamine. Formation of Benzylamino and Dibenzylamino Radicals

M. A. RATCLIFF, JR., AND J. K. KOCHI*

Department of Chemistry, Indiana University, Bloomington, Indiana 47401

Received February 15, 1972

Direct irradiation of *N,N*-dibenzylamine in solution at 254 nm leads to efficient homolysis of the benzyl–nitrogen bond. Product studies show that the subsequent dark reactions observed are primarily those of the *N*-benzylamino radical with dibenzylamine to afford benzylamine and the dibenzylamino radical by abstraction from the N–H bond. There is no evidence for the intermediacy of the isomeric carbon-centered radical. Combination and disproportionation reactions of the benzylamino and the dibenzylamino radicals are discussed.

Early photochemical studies of nitrogen-containing systems primarily involved decomposition of ammonia[1] and simple alkylamines[2] in the gas phase. Primary and secondary alkylamines were shown to decompose by a homogeneous cleavage of the N–H bond when subjected to light from a mercury arc lamp.[3,4] Only with tertiary amines, in which no N–H bond was available, did alkyl–nitrogen homolysis become important. The photolysis of a series of primary and secondary methylamines at 77°K afforded esr spectra, which were attributed to nitrogen-centered radicals.[5]

Studies with both *n*-amylamine and *n*-butylamine showed that no decomposition corresponding to a Norrish type II reaction was associated with the photolysis of simple alkylamines.[6a] Extensive polymer formation and product arising from other than simple radical processes have obscured the elucidation of the mechanistic details of the gas-phase reactions. The solution photochemistry of amines subsequently showed that the products initially formed, when both primary and secondary amines were photolyzed in hydrocarbon media, were similar to those formed in the gas phase.[6b,7] Ammonia, always present as a secondary reaction product in photolyses carried out in the vapor phase, however, was shown to be absent in solution.[8,9]

Kinetic studies[10] involving the attack of alkyl radicals

(1) (a) E. Warburg, *Sitzungsber. Preuss. Akad. Wiss.*, 746 (1911); *Chem. Abstr.*, **6**, 20 (1912). (b) E. Warburg, *Sitzungsber. Preuss. Akad. Wiss.*, 216 (1912); *Chem. Abstr.*, **6**, 3356 (1912). (c) W. Kuhn, *C. R. Acad. Sci.*, **177**, 956 (1923); *Chem. Abstr.*, **18**, 789 (1924). (d) W. Kuhn, *C. R. Acad. Sci.*, **178**, 708 (1924); *Chem. Abstr.*, **8**, 1787 (1924). (e) W. Kuhn, *J. Chim. Phys.*, **23**, 521 (1926); *Chem. Abstr.*, **20**, 3646 (1926). (f) J. R. Bates and H. S. Taylor, *J. Amer. Chem. Soc.*, **49**, 2438 (1927). (g) W. E. Groth, U. Schurath, and R. N. Schindler, *J. Phys. Chem.*, **72**, 3914 (1968).

(2) (a) H. J. Emeleus and H. S. Taylor, *J. Amer. Chem. Soc.*, **53**, 3370 (1931); (b) H. J. Emeleus and L. J. Jolley, *J. Chem. Soc.*, 1612 (1935).

(3) C. H. Bamford, *J. Chem. Soc.*, 17 (1939).

(4) J. V. Michael and W. A. Noyes, Jr., *J. Amer. Chem. Soc.*, **85**, 1228 (1963).

(5) S. G. Hadley and D. H. Volman, *ibid.*, **89**, 1053 (1967). See also T. Richerzhagen and D. H. Volman, *ibid.*, **93**, 2062 (1971).

(6) (a) C. H. Bamford and R. G. W. Norrish, *J. Chem. Soc.*, 1504 (1935); (b) G. H. Booth and R. G. W. Norrish, *ibid.*, 188 (1952).

(7) For other photochemical reactions of amines see (a) J. A. Barltrop and R. J. Owers, *Chem. Commun.*, 1462 (1970); (b) D. R. G. Brimage and R. S. Davidson, *ibid.*, 1385 (1971); (c) C. H. Niu and V. I. Stenberg, *ibid.*, 1430 (1971); (d) D. Bryce-Smith, M. T. Clarke, A. Gilbert, G. Klunkin, and G. Manning, *ibid.*, 916 (1971); (e) N. Paillous and A. Lattes, *Tetrahedron Lett.*, 4945 (1971).

(8) The photolysis of both di- and triethylamine has been carried out on the neat liquids with a medium-pressure mercury lamp.[8] Due to the long periods of irradiation (90 hr) and the consequent complexity of the resulting products, mechanistic arguments should be considered tenuous.[9a]

(9) (a) L. T. Allan and G. A. Swan, *J. Chem. Soc.*, 4822 (1965); (b) C. H. Niu and V. I. Stenberg, *Chem. Commun.*, 1430 (1971).

(10) (a) P. J. Kozak and H. Gesser, *J. Chem. Soc.*, 448 (1960); (b) R. K. Brinton, *Can. J. Chem.*, **38**, 1339 (1960); (c) P. Gray and J. C. J. Thynne, *Trans. Faraday Soc.*, **59**, 2275 (1963); (d) P. Gray and A. Jones, *ibid.*, **62**, 112 (1966); (e) P. Gray, A. Jones, and J. C. J. Thynne, *ibid.*, **61**, 474 (1965); (f) D. A. Edwards, J. A. Kerr, A. C. Lloyd, and A. F. Trotman-Dickerson, *J. Chem. Soc. A*, 1500 (1966).