tene, 38202-46-9; 1,2-dimethylcycloheptene oxide, 38202-47-0; 1-methylcyclooctene oxide, 16240-40-7; (2-hydroxy-2-methylcyclooctyl)methyldiphenylphosphonium iodide, 38202-49-2; *trans*-2-methylcyclooctene, 38229-26-4; adduct of diphenylisobenzofuran and *trans*-2-methylcyclooctene, 38215-60-0.

Preparation and Reactions of Nitrate Esters of *N*-Acylserine and -threonine Derivatives

RICHARD DEALTON CAMPBELL[1a] AND FRED ERIC BEHR[1b]

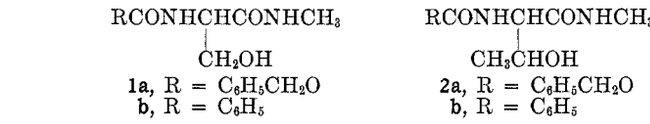
Department of Chemistry, University of Iowa, Iowa City, Iowa 52242

Received May 8, 1972

Nitrate esters of *N*-carbobenzoxyserinemethylamide, *N*-benzoylserinenmethylamide, *N*-carbobenzoxythreoninemethylamide, *N*-carbobenzoxyalanylserine methyl ester, *N*-benzoylallothreoninemethylamide, and *N*-carbobenzoxyglycylserylglycine ethyl ester were prepared from the corresponding amino acid derivatives and acetyl nitrate. Treatment of the first four compounds with ammonia causes an elimination of nitrate ion and formation of substituted acrylic acid and crotonic acid derivatives, respectively.

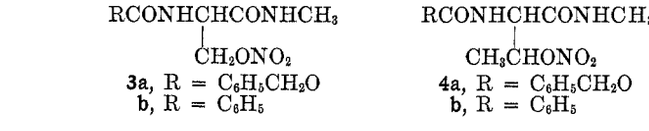
The reaction of acetyl nitrate with *N*-acylserine and -threonine derivatives has been studied to determine if the hydroxyl group present would cause the selective introduction of a nitro group on the amide nitrogen. Such a reaction would be important in the selective cleavage of peptides containing these amino acids. The resulting *N*-nitroamide bond would undergo cleavage with aqueous ammonia[2] more readily than the unmodified peptide bonds. The actual results obtained in the nitration were different from those expected and were considered important enough to report.

Treatment of *N*-acylserinemethylamide (**1**) and *N*-acylthreoninemethylamide (**2**) with fuming nitric acid



1a, R = $C_6H_5CH_2O$; **b**, R = C_6H_5 — **2a**, R = $C_6H_5CH_2O$; **b**, R = C_6H_5

and acetic anhydride in acetic acid gave exclusively the *O*-nitrate derivative (**3**, **4**) rather than the *N*-nitro derivatives. The use of fuming nitric acid and acetic anhydride alone gave lower yields of the nitrate ester. The behavior of a mixture of cupric nitrate and acetic anhydride[3] was not general and gave the *O*-nitro derivative with **1b** and the *O*-acetyl derivative with **1a**.

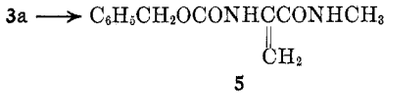


3a, R = $C_6H_5CH_2O$; **b**, R = C_6H_5 — **4a**, R = $C_6H_5CH_2O$; **b**, R = C_6H_5

Evidence for the location of the nitro group on the oxygen rather than on the nitrogens was based on nmr and infrared spectra. The nmr spectrum of **3a** showed broad absorptions for the two NH groups at δ 5.53 and 6.21. The former was a doublet and would correspond to the NHCH group. The infrared spectra for the nitrates showed frequencies for amide groups which were not markedly different from the *N*-acylamino acid derivatives. In contrast, the frequency for the carbonyl of the *N*-nitrobenzamide derivatives[3] was reported to be in the 5.85-μ region.

Nitration on nitrogen is apparently slow under the conditions employed, since *N*-carbobenzoxyalaninemethylamide was not affected.

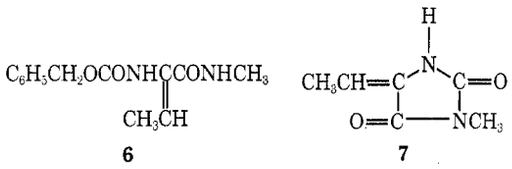
Treatment of **3a** with methanolic ammonia gave ammonium nitrate and α-*N*-carbobenzoxyaminoacrylmethylamide (**5**).



5

Proof for the structure of **5** was the spectra and chemical behavior. Treatment with dilute hydrochloric acid gave benzyl carbamate. The other hydrolysis product, *N*-methylpyruvamide, was difficult to isolate because of its high solubility in water. Catalytic hydrogenation gave alaninemethylamide. Oxidation with potassium dichromate gave *N*-carbobenzoxy-*N'*-methyloxamide, which on catalytic hydrogenation gave *N*-methyloxamide.

The reaction of alcoholic ammonia with **4a** gave ammonium nitrate, α-*N*-carbobenzoxyaminocrotonmethylamide (**6**), and 1-methyl-4-ethylidenehydantoin (**7**).



6 **7**

The structure of the hydantoin **7** was demonstrated by catalytic hydrogenation to 1-methyl-4-ethylhydantoin.

The hydantoin **7** is formed in this reaction by a base-catalyzed cyclization of the crotyl derivative **6**. The feasibility of such a reaction was demonstrated by cyclizing **6** with sodium hydroxide to **7**.

Changing the protecting group from carbobenzoxy to benzoyl did not change the course of the reaction with alcoholic ammonia but gave a more reactive species from **3b**; polymeric *N*-benzoylaminoacrylmethylamide was isolated. Substitution of sodium hydroxide in methanol for alcoholic ammonia in the reaction with **3b** gave *N*-benzoyl-*O*-methylserinemethylamide and benzamide.

The reaction of *N*-carbobenzoxyalanylserine methyl ester proceeded similarly and produced the *O*-nitrate,

(1) (a) Deceased. Inquiries should be addressed to S. Wawzonek. (b) Abstracted in part from the Ph.D. Thesis of F. E. B., Aug 1971.

(2) C. J. Peterson, Ph.D. Thesis, The University of Iowa, 1964.

(3) R. D. Campbell and C. J. Peterson, *J. Org. Chem.*, **28**, 2294 (1963).

TABLE I

N-ACYLAMINO ACID METHYLAMIDES

Compd	Mp, °C	Formula		C, %	H, %	N, %	Ir (Nujol), μ: OH	NH	CO
1a	129–129.5[b]	$C_{12}H_{16}N_2O_4$	Calcd	57.13	6.39	11.10	2.96	3.02	5.95, 6.05
			Found	57.23	6.44	11.38			
1b	149–149.5[c]	$C_{11}H_{14}N_2O_3$	Calcd	59.45	6.35	12.61	2.88	2.98	5.96, 6.05
			Found	59.56	6.35	12.84			
2a	129–130[d]	$C_{13}H_{18}N_2O_4$	Calcd	58.63	6.81	10.52	2.78–2.85	2.92	5.86, 6.06
			Found	58.57	6.97	10.66			
2b	183.5–184[e]	$C_{12}H_{16}N_2O_3$	Calcd	60.91	6.82	11.84	2.90		6.00, 6.08
			Found	60.87	7.02	12.27			
CAMA[a]	113–115[f]	$C_{12}H_{16}N_2O_3$	Calcd	61.00	6.83	11.86		2.95	5.88, 6.00
			Found	60.89	6.75	11.59			

[a] *N*-Carbobenzoxyalaninemethylamide. [b] Recrystallized from acetone. [c] Recrystallized from ethanol–ether and twice from water. [d] Two recrystallizations from acetone–hexane. [e] Recrystallized from aqueous ethanol. [f] Two crystallizations from acetone–hexane.

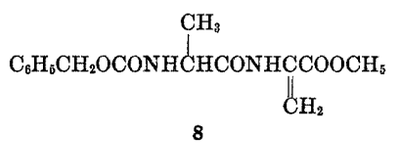
TABLE II

N-ACYL-*O*-NITROAMINO ACID METHYLAMIDES

Compd	Mp, °C	Formula		C, %	H, %	N, %	Ir (Nujol), μ: NH	CO
3b	142–143[a]	$C_{11}H_{13}N_3O_3$	Calcd	49.35	4.89	15.70	3.97, 3.63	5.96, 6.10
			Found	49.84	5.05	15.60		
4a	148–149[a]	$C_{13}H_{17}N_3O_6$	Calcd	50.16	5.56	13.50	2.99	5.75, 6.05
			Found	50.10	5.56	13.45		
4b	158–159 dec[b]	$C_{12}H_{15}N_3O_5$	Calcd	51.24	5.38	14.94	2.93, 3.03	6.00, 6.10
			Found	50.79	5.41	14.81		

[a] Recrystallized from ethyl acetate–petroleum ether (bp 60–68°). [b] No further purification.

since treatment with alcoholic ammonia gave the acrylic acid derivative **8**. This structure was based on elemental analysis and the ir and nmr spectra.



8

Work with a tripeptide, *N*-carbobenzoxyglycylserylglycine ethyl ester, was carried out only through the nitration step.

The elimination reaction observed with the nitrate derivatives **3** and **4** proceeds more easily than when this group is absent. *N*-Carbobenzoxyserinemethylamide is stable toward methanolic ammonia. Substitution methanolic sodium hydroxide for the ammonia in this example caused elimination to a slight degree.

β elimination of the type described has been observed with cystine peptides,[4] and tosyl and phosphorylated serine derivatives.[5,6]

Experimental Section

General.—Melting points are corrected. Infrared spectra were obtained with a Perkin-Elmer Model 21 spectrophotometer and Infracord and nmr spectra were obtained using Varian A-60 and HA-100 spectrometers. DL-Amino acids were used in all reactions.

Amidation of Methyl Esters of *N*-Acylamino Acids.—The methyl ester (0.035 mol) was treated with anhydrous methylamine (20 ml) in a precooled glass-lined Parr bomb and the mixture was allowed to stand at room temperature for 12 hr. Removal of the methylamine gave a viscous oil, which upon trituration with ether gave a white solid. Yields of 99% were obtained for all the compounds listed in Table I except **2a** (79%).

Nitration of *N*-Acylamino Acid Methylamides.—A suspension of the methylamide (0.00734 mol) in glacial acetic acid (25 ml) and acetic anhydride (20 ml) at 0° was treated with fuming nitric acid (sp gr 1.52) (0.4 ml). The resulting solution was stirred at 0° for 6 hr and at room temperature for 1 hr and then was poured onto ice. The solid obtained was filtered, washed with water, and dried. The yields obtained for the compounds listed in Table II were as follows: **3b**, 79%; **4a**, 81%; and **4b**, 49%.

***N*-Carbobenzoxy-*O*-nitroserinemethylamide (3a)** was obtained in a 50% yield and in contrast to the other examples was extracted from the water mixture with methylene chloride. Removal of the solvent gave an oil which was crystallized from ether: mp 127–127.5° [two further crystallizations from petroleum ether (bp 86–100°) did not change the melting point]; ir (Nujol) 2.90 (NH), 5.98, 6.10 μ (CON); nmr ($DCCl_3$) δ 2.78 (d, CH_3N, J = 5 cps), 4.64 (m, $CHCH_2$), 5.10 (s, $C_6H_5CH_2$), 5.53 (broad d, NHCOO), 6.20 (broad s, $NHCH_3$), 7.30 (s, C_6H_5).

Anal. Calcd for $C_{12}H_{15}N_3O_6$: C, 48.48; H, 5.10; N, 14.14. Found: C, 48.60; H, 5.17; N, 13.94.

***N*-Carbobenzoxy-*O*-acetylserinemethylamide.**—A mixture of cupric nitrate trihydrate (0.46 g) and acetic anhydride (70 ml) at 0° was treated dropwise with half of a suspension of *N*-carbobenzoxyserinemethylamide (0.453 g) in methylene chloride (20 ml) and acetic anhydride (20 ml). After completion of the addition more cupric nitrate trihydrate (0.255 g) was added and the second half of the amide suspension was added. The amide slowly dissolved and a homogeneous blue solution resulted and was allowed to stand at 0° for 2 hr and at room temperature for 2 hr. The resulting solution was poured onto ice and extracted with methylene chloride. Removal of the solvent gave a white, amorphous powder which after two crystallizations from ethyl acetate melted at 117.5–118°: yield 0.39 g (further purification by column chromatography using silica gel and a 1:1 ethyl acetate–benzene mixture as the eluent raised the melting point to 121–122°); ir (Nujol) 2.90 (NH), 5.70 ($OCOCH_3$), 5.90, 6.04 μ (CONH); nmr ($DCCl_3$) δ 1.99 (s, CH_3CO), 2.76 (d, CH_3N, J = 5 cps), 4.35 (m, OCH_2CH), 5.10 (s, $C_6H_5CH_2$), 6.03 (broad doublet, OCONH), 6.80 (broad singlet, $NHCH_3$), 7.31 (s, C_6H_5).

Anal. Calcd for $C_{14}N_{18}N_2O_5$: C, 57.13; H, 6.16; N, 9.52. Found: C, 57.14; H, 6.10; N, 9.69.

The *O*-acetyl derivative was also prepared by treating *N*-carbobenzoxyserinemethylamide (1.0 g) in ethyl acetate (10 ml) with 5 ml of a mixture containing perchloric acid, 2,4-dinitrobenzenesulfonic acid, and acetic anhydride in ethyl acetate.[7] The resulting solution, after standing for 15 min, was poured

(4) R. G. Hiskey, R. A. Upham, G. M. Beverly, and W. C. Jones, Jr., *J. Org. Chem.*, **35**, 513 (1970).

(5) I. Photaki, *J. Amer. Chem. Soc.*, **85**, 1123 (1963).

(6) G. Riley, J. Turnbull, and W. Wilson, *J. Chem. Soc.*, 1373 (1957).

(7) D. J. Pietrzyk and J. Belisle, *Anal. Chem.*, **38**, 1508 (1966).

into water and extracted with ethyl acetate. Removal of the solvent gave the *O*-acetyl derivative (0.85 g), which after crystallization from a mixture of ethyl acetate–petroleum ether (bp 86–100°) melted at 122–123°.

α-*N*-Carbobenzoxyaminoacrylmethylamide (5).—A solution of the methylamide **3a** (1.9 g) in methanol (50 ml) containing 15 *N* ammonium hydroxide (60 ml) was allowed to stand at room temperature for 24 hr. Removal of the solvent gave a solid (1.8 g) which was extracted with ethyl acetate. The insoluble portion was water soluble and proved to be ammonium nitrate (0.6 g).

Removal of the ethyl acetate gave a solid which was purified by chromatography on silica gel using benzene–ethyl acetate (8:2) as an eluent. The white solid obtained was recrystallized from benzene–petroleum ether (bp 86–100°): yield 1.2 g; mp 102.5–104.5°; ir (Nujol) 2.90 (NH), 5.72, 6.02 (CON), 11.35 μ (=CH_2); nmr ($CDCl_3$) δ 2.78 (d, CH_3N, J = 5 cps), 5.13 [singlet ($C_6H_5CH_2$) superimposed on a doublet (=CH)], 6.0 (d, =CH, J = 1.6 cps), 6.82 (broad singlet, $NHCH_3$), 7.32 (s, C_6H_5), 7.63 (broad singlet, OCONH).

Anal. Calcd for $C_{12}H_{14}N_2O_3$: C, 61.53; H, 6.02; N, 11.96. Found: C, 61.55; H, 6.01; N, 11.99.

Reactions of α-*N*-Carbobenzoxyaminoacrylmethylamide (5). A. Catalytic Hydrogenation.—A solution of the acrylmethylamide **5** (0.5 g) in methanol (20 ml) and concentrated hydrochloric acid (1 ml) was reduced using palladium (10% on charcoal) (0.1 g) as a catalyst and hydrogen at 15 psi for 1.5 hr. Filtration of the solution followed by removal of the solvent gave a solid, which after two crystallizations from a mixture of isopropyl alcohol and ethyl acetate melted at 175.5–176°, ir (KBr) 2.80, 3.10 (NH), 5.90 μ ($CONHCH_3$).

Anal. Calcd for $C_4H_{11}N_2OCl$: C, 34.66; H, 8.00; N, 20.21. Found: C, 35.09; H, 7.78; N, 20.26.

The sample was identical with the hydrochloride of alaninemethylamide prepared by the catalytic hydrogenation of *N*-carbobenzoxyalaninemethylamide.

B. Hydrolysis.—A suspension of the acrylmethylamide **5** (1.5 g) in 6 *N* hydrochloric acid was allowed to stand at room temperature for 1.5 hr. The resulting solution was neutralized with sodium bicarbonate and extracted with ethyl acetate. Removal of the ethyl acetate gave a solid, which was dissolved in hot, aqueous methanol. Cooling gave benzyl carbamate (0.375 g), mp 87–88°. The filtrate gave no precipitate with 2,4-dinitrophenylhydrazine.

C. Oxidation.—A solution of the acrylmethylamide **5** (1.5 g) and chromium trioxide (1.7 g) in glacial acetic acid (25 ml) and water (1 ml) was treated at 0–5° with 6 drops of 36 *N* sulfuric acid and heated at 95° for 1 hr. The resulting solution was poured into water and gave *N*-carbobenzoxy-*N'*-methyloxamide, which was recrystallized from aqueous ethanol: yield 1.0 g; mp 166–167°; ir (Nujol) 2.84, 3.00, 3.09 (NH), 5.62, 5.92, 5.98 μ (CON).

Anal. Calcd for $C_{11}H_{12}N_2O_4$: C, 55.93; H, 5.12; N, 11.96. Found: 56.22; H, 5.21; N, 11.52.

Hydrogenation of the oxamide (0.4 g) in methanol (20 ml), water (5 ml), and acetic acid (2 ml) using palladium (10% on charcoal) catalyst at 18 psi of hydrogen for 3 hr gave *N*-methyloxamide (0.14 g), mp 230–231°. A mixture with an authentic sample[8] melted at the same point.

Ammonolysis of *N*-Carbobenzoxy-*O*-nitrothreoninemethylamide (4a).—A solution of the nitrate **4a** (0.76 g) in methanol saturated with ammonia was allowed to stand for 24 hr at room temperature. Removal of the solvent gave a solid which after crystallization from benzene–petroleum ether (bp 86–100°) melted at 128–131°. Chromatography on silica gel using benzene–ethyl acetate (9:1) as the eluent gave α-carbobenzoxyaminocrotonmethylamide (0.156 g), and benzene–ethyl acetate (8:2) as the eluent gave 1-methyl-3-ethylidenehydantoin (0.105 g). The crotonic acid derivative on crystallization from benzene–petroleum ether (bp 60–68°) melted at 137–139°, ir (KBr) 3.06 (NH), 5.81, 5.93 μ (CON).

Anal. Calcd for $C_{13}H_{16}N_2O_3$: C, 62.89; H, 6.50; N, 11.28. Found: C, 62.67; H, 6.53; N, 11.29.

The hydantoin upon crystallization from benzene–petroleum ether (bp 60–68°) melted at 206–207.5°: ir (KBr) 3.07 (NH), 5.56, 5.63, 5.69, 5.79, 5.93 (CO), 13.23 μ (=$CHCH_3$).

Anal. Calcd for $C_6H_8N_2O_2$: C, 51.48; H, 5.75; N, 19.99. Found: C, 51.31; H, 5.72; N, 20.01.

(8) O. Wallach, *Justus Liebigs Ann. Chem.*, **184**, 67 (1877).

Catalytic hydrogenation of the hydantoin (0.1 g) in methanol (20 ml), water (20 ml), concentrated hydrochloric acid (1.5 ml) using palladium (10% on charcoal), and hydrogen at 18 psi gave 1-methyl-3-ethylhydantoin (0.1 g) which was recrystallized from benzene–petroleum ether (bp 86–100°): mp 99–100.5°; ir (KBr) 2.96, 3.15 (NH), 5.67, 5.84, 5.89 (CO).

Anal. Calcd for $C_6H_{10}N_2O_2$: C, 50.69; H, 7.09; N, 19.71. Found: C, 50.49; H, 7.29; N, 20.12.

A sample of 1-methyl-4-ethylhydantoin was prepared by refluxing 4-ethylhydantoin (1.0 g) in a solution of methanol (10 ml) containing sodium methoxide (6.47 g) with methyl iodide (1.0 ml) for 3 hr. The product melted at 99–100° and gave no lowering in melting point when mixed with the sample obtained by hydrogenation.

Cyclization of α-Carbobenzoxyaminocrotonmethylamide.—A solution of the crotonmethylamide (0.104 g) in methanol (20 ml) was treated with a 50% methanol solution (10 ml) containing sodium hydroxide (1.0 g) and the resulting solution was allowed to stand at room temperature for 24 hr. Removal of the solvent followed by extraction with ethyl acetate gave a solid which was purified by recrystallization from benzene–petroleum ether (bp 60–68°) and column chromatography on silica gel using benzene–ethyl acetate (8:2) as an eluent, yield 0.038 g, mp 207–207.5°. The ir spectrum was identical with that of 1-methyl-3-ethylidenehydantoin and the mixture melting point was the same.

Ammonolysis of *N*-Benzoyl-*O*-nitroserinemethylamide (3b).—A solution of the nitrate **3b** (0.90 g) in methanol (100 ml) and 15 *N* ammonium hydroxide (2 ml) was allowed to stand at room temperature for 24 hr. Removal of the solvent gave a solid (0.3 g), which was insoluble in water and ethyl acetate and melted above 340°: ir (Nujol) 2.90 (NH), 5.69, 5.75, 5.90, 6.00 (CON).

Anal. Calcd for $(C_{11}H_{12}N_2O_2)_x$: C, 64.69; H, 5.92; N, 13.72. Found: C, 63.87; H, 6.33; N, 13.71.

Reaction of *N*-Benzoyl-*O*-nitroserinemethylamide (3b) with Alcoholic Sodium Hydroxide.—A solution of the nitrate **3b** (2.7 g) in methanol (260 ml) and water (5 ml) containing sodium hydroxide (0.5 g) was allowed to stand for 24 hr. Removal of the methanol followed by extraction with ethyl acetate gave a viscous yellow oil which slowly crystallized. Chromatography on silica gel using benzene–ethyl acetate (1:1) as the eluent gave benzamide and ethyl acetate as the eluent gave *N*-benzoyl-*O*-methylserinemethylamide melting at 144.5–146° after one recrystallization from a mixture of benzene–petroleum ether (bp 86–100°), ir (Nujol) 2.85, 2.90 (NH), 5.96, 6.04 (CON), 8.90 μ (CH_2OCH_3).

Anal. Calcd for $C_{12}H_{16}N_2O_3$: C, 61.00; H, 6.81; N, 11.86. Found: C, 61.22; H, 6.93; N, 12.09.

***N*-Carbobenzoxyalanyl-*O*-nitroserine Methyl Ester.**—*N*-Carbobenzoxyalanylserine methyl ester (3.0 g) was treated in a mixture of acetic acid (30 ml) and acetic anhydride (5 ml) at 0–5° with fuming nitric acid (1.0 ml). The mixture was stirred for 1.5 hr at 0–5° and for 5 hr at room temperature and then poured onto ice. The white solid obtained was recrystallized from ethyl acetate and melted at 123–124.5°: yield 3.3 g (a further recrystallization from benzene raised the melting point to 125–126.5°); ir (Nujol) 2.92 (NH), 5.64 ($COOCH_3$), 5.84, 5.96, 6.08 μ (CON).

Anal. Calcd for $C_{15}H_{19}N_3O_8$: C, 48.78; H, 5.19; N, 11.38. Found: C, 48.59; H, 5.15; N, 11.34.

Ammonolysis of *N*-Carbobenzoxyalanyl-*O*-nitroserine Methyl Ester.—A solution of the nitrate (0.32 g) in 15 *N* ammonium hydroxide (15 ml) was allowed to stand for 24 hr at room temperature. Removal of the ammonia was followed by extraction with ethyl acetate. Chromatography on silica gel using benzene–ethyl acetate (6:4) as the eluent gave a solid (0.12 g) which was crystallized from benzene–petroleum ether (bp 86–100°): mp 91–92°; ir (Nujol) 2.94 (NH), 5.74 ($COOCH_3$), 5.79, 5.94 (CON), 10.96 μ (=CH_2); nmr ($CDCl_3$) δ 1.37 (d, CH_3CH, J = 8 cps), 3.80 (s, $COOCH_3$), 4.33 (m, CH), 5.12 (s, $C_6H_5CH_2$), 5.89 (s, =CH), 6.58 (s, =CH), 7.32 (s, C_6H_5), 8.38 (broad s, C=CNH).

Anal. Calcd for $C_{15}H_{18}N_2O_5$: C, 58.82; H, 5.92; N, 9.15. Found: C, 58.78; H, 5.97; N, 8.94.

***N*-Carbobenzoxyglycyl-*O*-nitroserylglycine Ethyl Ester.**—Fuming nitric acid (0.40 ml) was added to a suspension of *N*-carbobenzoxyglycylserylglycine ethyl ester (0.663 g) in acetic acid (30 ml) and acetic anhydride (1.0 ml) at 0–5° and the mixture was stirred at room temperature for 9 hr and poured onto ice. Extraction with ethyl acetate gave a solid which was chromatographed on silica gel using benzene–ethyl acetate (40:60) as an

eluent, yield 0.70 g. Crystallization from ethyl acetate–petroleum ether (bp 60–68°) gave a melting point of 58–60°; ir (Nujol) 2.85, 2.89 (NH), 5.56 ($COOC_2H_5$), 5.82, 5.86, 6.04 μ (CON).

Anal. Calcd for $C_{17}H_{22}N_4O_9$: C, 47.89; H, 5.20; N, 13.14. Found: C, 47.61; H, 4.92; N, 13.05.

Registry No.—**1a**, 38215-61-1; **1b**, 33628-81-8; **2a**, 38229-27-5; **2b**, 38215-63-3; CAMA, 38215-64-4; **3a**, 38215-65-5; **3b**, 38215-66-6; **4a**, 38215-67-7; **4b**, 38215-68-8; **5**, 38215-69-9; **6**, 38215-70-2; **7**, 38215-71-3; **8**, 38215-72-4; alaninemethylamide (HCl), 38215-73-5; *N*-carbobenzoxy-*N'*-methyloxamide, 38215-74-6; 1-methyl-3-ethylhydantoin, 36650-99-4; polymeric *N*-benzoylaminoacrylmethylamide, 38193-79-2; *N*-benzoyl-*O*-methylserinemethylamide, 38215-76-8; carbobenzoxyalanylserine methyl ester, 38660-05-8; *N*-carbobenzoxyalanyl-*O*-nitroserine methyl ester, 38660-06-9; *N*-carbobenzoxyglycylserylglycine ethyl ester, 33660-07-0; *N*-carbobenzoxyglycyl-*O*-nitroserylglycine ethyl ester, 38660-08-1.

A Kinetic Study of the Thermal Decomposition of 1,1-Diphenylpropyl Hydrogen Phthalate Ester in Solution

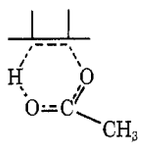
RAPHAEL M. OTTENBRITE,*[1] JAMES W. BROCKINGTON,[2] AND KENNETH G. RUTHERFORD

Department of Chemistry and Pharmaceutical Chemistry, Virginia Commonwealth University, Richmond, Virginia 23220

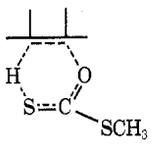
Received September 14, 1972

The rate of thermal decomposition of 1,1-diphenylpropyl hydrogen phthalate ester, using nmr techniques, was determined in DMSO solution over temperatures ranging from 65 to 92°. The pyrolysis reaction followed first-order kinetics. Values for the activation energy and the entropy of activation were calculated to be 30.2 kcal/mol and 7.3 eu, respectively. This positive entropy is indicative of a heterolytic or homolytic type cleavage and precludes a cyclic transition state for this decomposition. A decrease in rate was observed when the acid ester was converted to the corresponding methyl diester. Further, the reaction was completely curtailed when the acid ester was converted to the sodium salt. It seems evident that the proton of the orthocarboxylate acid function is playing a significant role in the mechanism of the decomposition of tertiary hydrogen phthalate esters, probably by intramolecular hydrogen bonding.

Ester pyrolyses have received a considerable amount of attention, both for their utility in the formation of olefinic compounds as well as for their mode of decomposition.[3] In general, the presently accepted mechanism for the decomposition of acetate esters, xanthate esters, and related esters involves a concerted six-membered cyclic transition state.



acetate ester



xanthate ester

The above mechanism can only account for cis-elimination products, even though there have been instances of varying amounts of trans-elimination products reported.[4] Briggs and Djerassi[5] have recently found in their pyrolysis studies of epimeric *cis*- and *trans*-9-methylcyclohexyl-*S*-methyl xanthates and acetates that the cis isomers yield considerable trans-elimination product. Kinetic deuterium isotope studies led these authors to propose an ionic mechanism for the net trans-elimination process. This is in agreement with Sixma and coworkers,[6] who reported predominantly positive entropies of activation for a number of tertiary acetate pyrolyses. In contrast, recent vapor-phase ^{18}O studies by Smith, *et al.*,[7] with ethyl acetate and Kwart and Slutsky[8] with *tert*-butyl *N*,*N*-dimethyl carbamate esters showed an absence of randomization of the ^{18}O label in the unreacted ester after pyrolysis, thus supporting a concerted transition state in these cases.

Recently, Rutherford[9] reported the pyrolyses of a new ester system, tertiary hydrogen phthalate esters, which decompose at low temperatures (less than 150°) to yield exclusively olefinic products and phthalic acid. On decomposition of *trans*-1,2-dimethylcyclohexyl hydrogen phthalate, 19% of trans-elimination product was obtained. It was, therefore, suggested that carbonium ion character was evident (at least in part) in the transition state during the pyrolysis. It was further found that *trans*-2-methyl-1-phenylcyclohexyl hydrogen phthalate ester yielded 6% trans product on pyrolysis[10] as well.

We later showed that partial decomposition of ^{18}O-enriched carbonyl oxygen of the *trans*-1,2-dimethylcyclohexyl hydrogen phthalate ester resulted in the enrichment of ^{18}O in the alkyl portion of the undecomposed ester.[11] This increase in ^{18}O abundance represents a 17% exchange, which was explained by invoking an ionic intermediate state in the decomposition.

More recently,[10] a detailed kinetic study was made of the decomposition of *cis*- and *trans*-1,2-dimethylcyclohexyl hydrogen phthalate esters and *cis*- and *trans*-2-methyl-1-phenylcyclohexyl hydrogen phthalate esters. Pyrolysis of these compounds, both neat and in DMF, showed that the rate-determining step involved ion pair formation.

(1) To whom correspondence should be addressed.
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