Tetrahedron, 1966, Vol. 22, pp. 2575 to 2580. Pergamon Press Ltd. Printed in Northern Ireland

A REVISED STRUCTURE FOR THE CONDENSATION PRODUCT OF 2-CARBETHOXYCYCLOPENTANONE AND ETHYL CYANOACETATE

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(*Received* 19 *February* 1966)

Abstract—The condensation product of 2-carbethoxycyclopentanone and ethyl cyanoacetate is ethyl 2-carbethoxycyclopentylidene cyanoacetate (IIa) and not the one described by Kon and Nanji. Similarly, 2-carbomethoxycyclopentanone and methyl cyanoacetate yield methyl 2-carbomethoxycyclopentylidene cyanoacetate (IIb). The by-products obtained in the first reaction are cyclopentylidene cyanoacetate (IV) and the enamine of 2-carbethoxycyclopentanone (VIa).

Recently, Anderson *et al.*[1] reported that 2-carbethoxycyclopentanone reacted with ethyl cyanoacetate under Cope's conditions[2] to furnish ethyl 2-carbethoxy-Δ'-cyclopentenyl cyanoacetate (I) in better yield than that reported by Ayerst and Schofield.[3] These authors[1,3] assumed the condensation product to be I based on the report of previous workers,[4-6] who had earlier carried out the reaction with piperidine as the condensing agent. The bis-phenylhydrazone of the diketone (III), formed by ozonolysis of the condensation product, was the only evidence claimed by Kon and Nanji[4] in support of structure I.

As Cope condensation of cyclopentanone compounds generally furnishes cyclopentylidene derivatives,[7-9] the structure of the condensation product was reinvestigated. According to the procedure of Anderson *et al.*[1] and employing pure[10] 2-carbethoxycyclopentanone, the reported yield could not be realized, and only 40% was obtained. Invariably, a low boiling fraction, obtained as a by-product in this reaction, showed UV max at 238 $m\mu$ (ε 11,800) and 356 $m\mu$ (ε 270) and IR bands at 2227 (conjugated $C{\equiv}N$),[11] 1724 (conjugated ester) and 1613 cm^{-1} ($C{=}C$). These spectral characteristics together with elemental analyses are in agreement with structure IV which in the light of Johnson's work,[12] might have resulted from the condensation of ethyl cyanoacetate with cyclopentanone formed by the decarboxylation of 2-carbethoxycyclopentanone under the reaction conditions.

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[1] A. G. Anderson, Jr., W. F. Harrison and R. G. Anderson, *J. Amer. Chem. Soc.* **85**, 3448 (1963).

[2] A. C. Cope, C. M. Hofmann, C. Wyckoff and E. Hardenbergh, *J. Amer. Chem. Soc.* **63**, 3452 (1941).

[3] G. G. Ayerst and K. Schofield, *J. Chem. Soc.* 4097 (1958).

[4] G. A. R. Kon and H. R. Nanji, *J. Chem. Soc.* 2426 (1932).

[5] V. Prelog and O. Metzler, *Helv. Chim. Acta* **29**, 1170 (1946).

[6] M. Protiva, V. Mychajlyszyn and J. O. Jilek, *Chem. Listy.* **49**, 1045 (1955).

[7] Sukh Dev, *J. Indian. Chem. Soc.* **30**, 443, 665, 815 (1953).

[8] T. R. Kasturi, *J. Indian Inst. Science* (Golden Jubilee Res. Vol.) p. 45 (1959).

[9] D. K. Banerjee, private communication.

[10] P. S. Pinkney, *Organic Syntheses* Coll. Vol. II; p. 116. Wiley, N. Y. (1943).

[11] C. N. R. Rao, *Chemical Applications of Infrared Spectroscopy* p. 268. Academic Press, N. Y. (1963).

[12] W. S. Johnson, B. Bannister, R. Pappo and J. E. Pike, *J. Amer. Chem. Soc.* **78**, 6354 (1956).

In the presence of alkali (1N NaOH) the product (IV) showed UV max at 248 (ε 9,400) and 356 mμ (ε 12,950), the intensity of the latter peak being very high (Fig. 1). The normal peak at 238 mμ is characteristic of β,β-dimethyl-α-cyanoacrylic ester moiety,[13] and the one at 356 mμ is indicative of extended conjugation as in species V, probably present in small amounts in alcoholic solution. The high intensity of this peak in alkaline medium may be due to the increased concentration of this species (V). The maximal absorption at 238 mμ (high ε value) is difficult to explain on the basis of structure I, proposed by Kon and Nanji.[4]

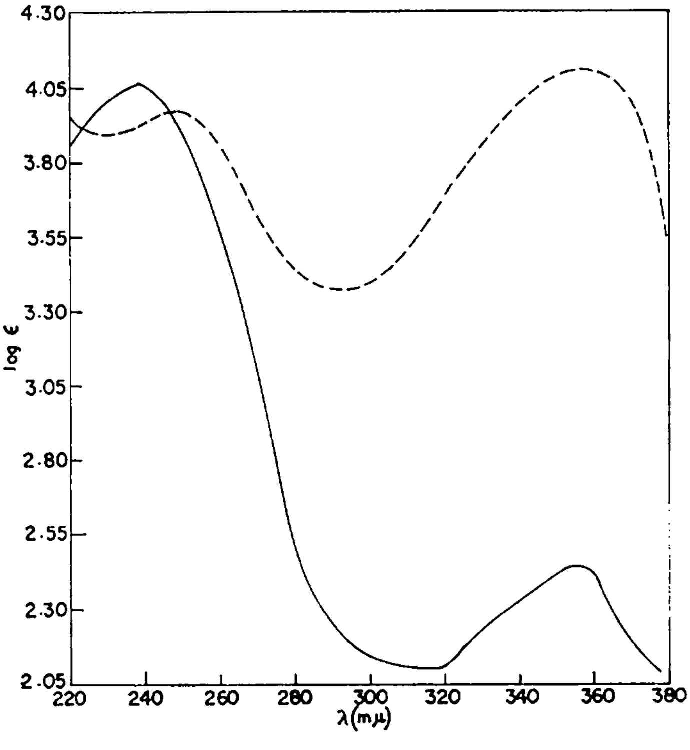

FIG. 1. UV spectrum of IIa
(——) in ethanol
(- - -) in alkaline ethanol

In the NMR spectrum, the peaks centred around 75 (6H, $2COOCH_2CH_3$), 120 (4H, $2CH_2$), 172 (2H, allylic CH_2) and 245 c/s (5H, $2COOCH_2CH_3$ and allylic —CH—) are in agreement only with structure IIa. The significant absence of a sharp singlet in the downfield region, characteristic of proton *a*, clearly rules out the possibility of structure I.

The NMR spectrum of the corresponding methylester (IIb) prepared from methyl cyanoacetate and 2-carbomethoxycyclopentanone under similar conditions, supports structure IIa. Figure 2 shows peaks at 115 (4H, CH_2—CH_2—), 175 (2H, allylic CH_2)

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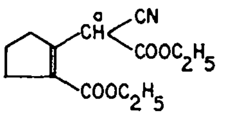
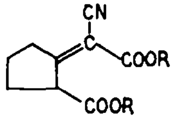
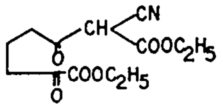
[13] P. Bagchi, F. Bergmann and D. K. Banerjee, *J. Amer. Chem. Soc.* **71**, 989 (1949).



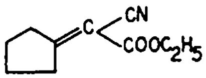
I



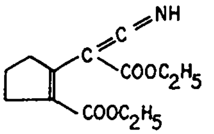
IIa, $R=C_2H_5$
IIb, $R=CH_3$



III



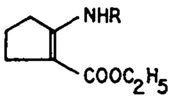
IV



V

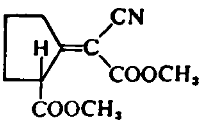
$C_6H_5CH_2NH\,CO\,CH_2CN$

VII

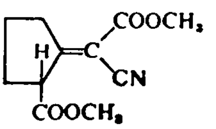


VIa, R = H
VIb, $R=CH_3$
VIc, $R=CH_2C_6H_5$

and 247 c/s (1H, allylic —*CH*—). In addition, it shows two pairs of doublets at 223 (4H) and 227 c/s (2H), which must be ascribed to the two methyls of the carbomethoxy groups. The appearance of a pair of doublets for the methyls of COOMe is probably due to the different deshielding of the two ester groups in the two possible geometrical isomers (IIb_1 and IIb_2). All attempts to isolate IIb_1 and IIb_2 for detailed NMR study were not successful.



IIb_1



IIb_2

Ozonolysis of IIa under the conditions employed by Kon and Nanji,[4] yielded only 2-carbethoxycyclopentanone, identified by comparison of its IR spectrum with that of an authentic sample and supported by identical IR spectra of the 2,4-dinitrophenylhydrazones. The β-keto ester (III), reported by Kon and Nanji[4] could not be isolated.

In trying to improve the yield of IIa by adopting the well-known lot addition technique,[14] an additional by-product was obtained showing an intense UV max at

[14] E. J. Cragoe, Jr., C. M. Robb and J. M. Sprague, *J. Org. Chem.* **15**, 381 (1950).

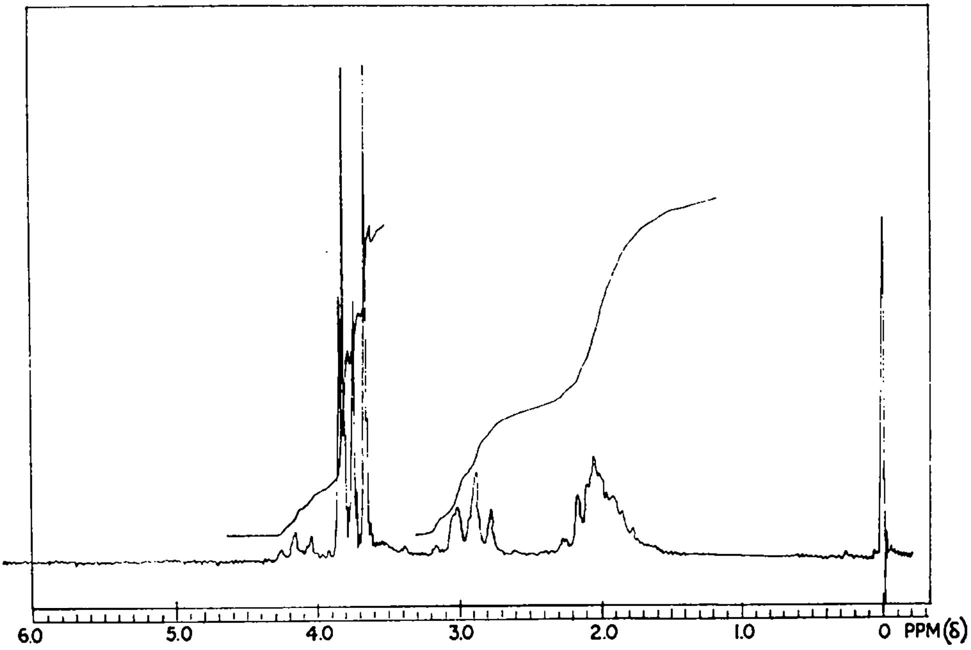


Fig. 2. NMR Spectrum of IIb

282 mμ. In the IR spectrum, it showed strong peaks at 1653 and 1626 cm^{-1} (assignment in sequel), but no peak characteristic of a nitrile group.[11] In the NMR spectrum it showed peaks at 74 (triplet, 3H), 110 (multiplet, 2H), 146 (multiplet, 4H), 243 (quartet, 2H) and 295–350 c/s (broad), clearly indicating the presence of —CH_2—CH_3 and NH groups. The elemental analyses, corresponding to $C_8H_{13}NO_2$, was in good agreement with the mol. wt. of the compound (mass spectrum* 155). The same compound could also be obtained by treatment of IIa with ammonium hydroxide. Consequently, this compound was assigned the enamine structure (VIa), confirmed by comparison of its IR spectrum with that of an authentic sample.[15] Presumably, ammonia from excess ammonium acetate used reacts with 2-carbethoxycyclopentanone. In the reaction of IIa with ammonium hydroxide to give VIa, a retro-Cope reaction takes place. Similarly, the corresponding enamine derivatives (VIb and VIc) were obtained when IIa was treated with methylamine and benzylamine respectively. With benzylamine, in addition to VIc,[16] a solid exhibiting only benzenoid absorption in the UV and showing nitrile (2273 cm^{-1}) and amide (1639 cm^{-1}) bands in the IR spectra was obtained. This was identical with N-benzylcyanacetamide (VII) by comparison of its IR spectrum with that of an authentic sample,[17] and corresponded with the other fragment of the retro-Cope reaction.

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* We are grateful to Dr. J. S. Shannon, Division of Coal Research, Council of Scientific and Industrial Research Organisation, Chatswood, Australia, for this determination.

[15] T. A. Connors and W. C. J. Ross, *J. Chem. Soc.* 2119 (1960).

[16] W. Treibs, R. Mayer and M. Madejski, *Chem. Ber.* **87**, 356 (1954).

[17] K. G. Naik and Y. N. Bhat, *J. Indian Chem. Soc.* **4**, 547 (1927); T. Mukaiyama, H. Takei and Y. Koma, *Bull. Chem. Soc. Japan* **36**, 95 (1963).

EXPERIMENTAL[18]

Ethyl 2-carbethoxycyclopentylidene cyanoacetate (IIa)

A mixture of ethyl cyanoacetate (13·2 g), 2-carbethoxycyclopentanone (20 g), ammonium acetate (1·3 g), glacial AcOH (1·8 ml) and dry benzene (25 ml) was heated under reflux till no more water separated (72 hr). The cooled reaction mixture was washed several times with water and the benzene removed *in vacuo*. On distillation of the residue, three fractions were isolated:

(a) b.p. 75–80°/1·5 mm; 7 g; mixture of ethyl cyanoacetate and 2-carbethoxycyclopentanone.

(b) b.p. 110–113°/1·5 mm; 3·5 g; crystallized in white needles from aq. EtOH, m.p. 54–55°; (Found: C, 67·23; H, 7·48; N, 7·45. $C_{10}H_{13}NO_2$ requires: C, 67·04; H, 7·26; N, 7·82%). UV λ_{max} 238 mμ (ε 15,164); IR (Nujol): 2227 (conjugated C≡N), 1724 (conjugated ester) and 1613 cm^{-1} (C=C). This fraction was identified as ethyl cyclopentylidenecyanoacetate (IV)[2].

(c) b.p. 145–148°/1·5 mm; 8·5 g; n_D^{25} 1·4828; UV λ_{max} 238 (ϵ 11,800) and 356 mμ (ϵ 270); $\lambda_{max}^{alkaline\ EtOH}$ 248 (ϵ 9400) and 356 mμ (ϵ 12,950); IR (thin film): 2227 (conjugated C≡N), 1724 (conjugated ester) and 1626 cm^{-1} (C=C). This fraction was identified as ethyl 2-carbethoxycyclopentylidenecyanoacetate (IIa).

The above experiment was repeated using ethyl cyanoacetate (13·2 g), 2-carbethoxycyclopentanone (20 g), ammonium acetate (2·6 g), glacial AcOH (1·8 ml) and dry benzene (25 ml), the ammonium acetate being added every 24 hr in 4 equal lots. The mixture was refluxed for 96 hr and yielded 3 fractions:

(a) b.p. 75–80°/1·5 mm; mixture of ethyl cyanoacetate and 2-carbethoxycyclopentanone.

(b) b.p. 112–120°/1·5 mm; 4 g.

(c) b.p. 145–148°/1·5 mm; 8·5 g; same as fraction (c) above.

Fraction (b) was repeatedly fractionated to give 2 pure products in equal amounts;

(i) m.p. 54–55°; recrystallized from aq. EtOH and found to be identical with IV.

(ii) m.p. 55–56°; recrystallized from pet. ether as pale yellow plates; (Found: C, 61·97; H, 8·25; N, 8·87. $C_8H_{13}NO_2$ requires: C, 62·13; H, 8·32; N, 8·97%). UV λ_{max} 282 mμ (ϵ 19,950); IR (Nujol): 3546, 3425 (—NH), 1653 (chelated ester) and 1626 cm^{-1} (C=C); mol. wt (mass spectrum) 155. This was identified as the enamine of 2-carbethoxycyclopentanone.[16]

Ozonolysis of IIa. Into a solution of IIa (2 g) in AcOEt (40 ml) at 0° was passed ozonized O_2 for 2 hr. The solvent was removed *in vacuo* and the residue shaken with water (30 ml) for 10 hr at room temp.[4] It was then extracted with ether and the extract washed several times with ice cold 5% NaOHaq. On removal of ether, a neutral material (1 g), which was not further investigated, was obtained. The alkali extract, after acidification, was extracted with ether. The extract was successively washed with water, $NaHCO_3$aq and water and dried (Na_2SO_4). The ether was distilled off to give an oil (450 mg) which showed purple colouration with alcoholic $FeCl_3$ solution. This was purified to give 2-carbethoxycyclopentanone (b.p. 115°/35 mm; n_D^{25} 1·4502). The 2,4-dinitrophenylhydrazone, prepared by the H_2SO_4 method, melted at 107–108° after one crystallization from EtOH. The m.p. remained undepressed on admixture with an authentic sample of the 2,4-dinitrophenylhydrazone of 2-carbethoxycyclopentanone[19] and the IR spectra of the two were identical.

Methyl 2-carbomethoxycyclopentylidene cyanoacetate (IIb)

A mixture of 2-carbomethoxycyclopentanone (11 g), methyl cyanoacetate (7·7 g) and piperidine (2 ml) was set aside for 48 hr at room temp.[3] After diluting with ether, the mixture was washed with 5% HClaq, then with water and dried (Na_2SO_4). The solvent was removed *in vacuo* and the residue distilled to give IIb (9·1 g), b.p. 145–147°/2 mm; n_D^{24} 1·4935; (Found: N, 6·31; $C_{11}H_{13}NO_4$ requires: N, 6·28%). UV λ_{max} 237 (ϵ 11,800) and 355 mμ (ϵ 282); IR (film): 2227 (conjugated C≡N), 1730 (ester) and 1618 cm^{-1} (C=C).

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[18] All m.ps are uncorrected. UV spectra were determined in 95% EtOH using a Beckmann DU Model spectrophotometer. IR spectra were recorded with a Perkin–Elmer Model 137B Infracord spectrophotometer. NMR spectra were taken on a Varian A-60 spectrometer. Chemical shifts are quoted in c/s units downfield from TMS as internal standard. Pet. ether, b.p. 40–60°, only was used. Microanalyses were carried out by Messrs. B. R. Seetharamia and H. S. Tyagaraj of this department.

[19] D. H. Johnson, *J. Chem. Soc.* 1624 (1958).

Reaction of IIa *with bases*

(a) *With ammonia.* The IIa (2 g) was stirred with NH_4OH (10 ml) for 48 hr at room temp. Ammonia was removed *in vacuo* at room temp, water (50 ml) was added and the residue extracted with ether. The extract, after washing once with water was dried (Na_2SO_4). The solvent was removed and the residue (0·95 g) was recrystallized from pet. ether to yield VIa, m.p. 55–56°, which did not depress the m.p. of an authentic sample.

(b) *With methylamine.* The IIa (2 g) was stirred with 30% $MeNH_2$ solution (10 ml) for 48 hr at room temp and yielded the corresponding enamine VIb (1·25 g), which crystallized from aq. EtOH, m.p. 45–46°. (Found: C, 63·82; H, 8·55; N, 8·22; $C_9H_{15}NO_2$ requires: C, 63·9; H, 8·87; N, 8·28%). UV λ_{max} 295 mμ (ϵ 20,004); IR (Nujol): 3448 (—NH), 1653 (chelated ester carbonyl) and 1613 cm^{-1} (C═C); NMR ($CDCl_3$): triplet centred at 74·8 (3H, —CH_2—*CH_3*), multiplet centred at 110 (2H, *CH_2*), 152 (4H, allylic *CH_2*), doublet centred at 172·5 (3H, J = 5 c/s, —NH—*CH_3*) and a quartet centred at 245 c/s (2H, *CH_2*—CH_3).

(c) *With benzylamine.* The IIa (2 g) was stirred with benzylamine (3·2 g) for 48 hr at room temp and yielded a residue (3 g), which was triturated with pet. ether. The solid was filtered off and the pet. ether soluble portion (2·4 g) purified by short-path distillation to yield VIc.[16] (Found: N, 5·43; $C_{15}H_{19}NO_2$ requires: N, 5·71%). UV λ_{max} 295 mμ (ϵ 20,590); IR (film): 3448 (—NH), 1669 (chelated ester carbonyl) and 1600 cm^{-1} (aromatic C═C) as a thick oil.

The pet. ether insoluble solid (0·5 g) was recrystallized from benzene as yellow needles, m.p. 123–124°. (Found: C, 69·25; H, 5·4; N, 16·13; $C_{10}H_{10}N_2O$ requires: C, 68·96; H, 5·74; N, 16·09%). UV λ_{max} 248 (ϵ 181), 252 (ϵ 203), 259 (ϵ 232) and 264 mμ (ϵ 174); IR (Nujol): 3356 (—NH), 2273 (saturated C≡N), 1639 (—CO—NH) and 1550 cm^{-1} (aromatic C═C) and was identified as N-benzyl cyanacetamide.[17]

Acknowledgments—We are thankful to Prof. D. K. Banerjee for his interest in the work. We are grateful to Prof. George R. Pettit, Arizona State University and Dr. T. R. Govindachari, Ciba Research Centre, India, for recording the NMR spectra reported here. One of us (A. S.) thanks the Indian Institute of Science, Bangalore, for the award of a predoctoral Fellowship.