

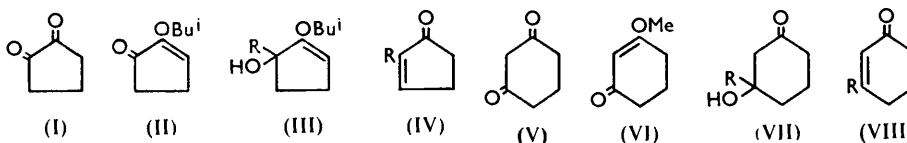
59. Reduced Cyclic Compounds. Part VII.* A New Route to 2-Substituted cyclopent-2-enones.

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A convenient and unambiguous route to 2-substituted *cyclopent-2-enones* by way of 2-isobutoxycyclopent-2-enone is described, with ten examples.

IN connexion with other investigations^{1*} we required a convenient and unambiguous method for the preparation of 2-substituted *cyclopent-2-enones* (IV). The reported general routes are: (a) from the 1-substituted *cyclopentene* *via* the nitroso-chloride (for IV, R = Me,² Pr,³ *n*-pentyl,² and Ph⁴); (b) cyclisation of alkenoic acids (or the lactones of the related hydroxy-acids) or alkenoyl chlorides (for IV, R = Me,¹ Et,¹ Prⁿ,¹ Prⁱ,¹ Buⁿ,^{5,6} *n*-pentyl,⁷ and *n*-hexyl⁷⁻⁹); (c) dehydrohalogenation of 2-substituted 2-halogenocyclopentanones (for IV, R = Me,¹⁰ Et,¹ and Ph,^{4,11}); and (d) from *cyclopentane-1:2-dione* by treatment with a Grignard reagent followed by dehydration (for IV, R = Me¹²). The cyclisation and concomitant hydration of suitably constituted dienes¹³ or the cyclisation of dicarbonyl compounds¹⁴ has been used as a route to *cyclopent-2-enones* substituted in the 2- and other positions. 2-Phenyl*cyclopent-2-enone* has been prepared¹⁵ from 3-oxo-2-phenyl*cyclopentane-1-carboxylic acid* by treatment with polyphosphoric acid, and the same reagent converts 2-isopropylidene*cyclopentanone* into 2-isopropyl*cyclopent-2-enone*.¹

Of the available methods for the preparation of 2-substituted *cyclopent-2-enones*, (a) is somewhat indirect and has been described¹⁶ as being of little practical importance; (b) is ambiguous, as it can also give rise to 2-substituted *cyclohex-2-enones*^{1,9} and 2-substituted *cyclopent-4-enones*;^{7,9} and (c) involves preferential halogenation in the preparation of the starting material. Method (d) uses a readily available, although somewhat unstable, starting material and a molar excess of the Grignard reagent, but does constitute a convenient and unambiguous synthesis. We considered that the method could be further improved, by analogy with the route (V—VIII) devised by Born, Pappo,



and Szmuszko¹⁷ for the preparation of 3-substituted *cyclohex-2-enones*. We have therefore prepared 2-isobutoxycyclopent-2-enone (II), a stable liquid, from *cyclopentane-1:2-*

* Part VI, *J.*, 1958, 3956.

¹ Ansell and Brown, *J.*, 1958, 2955.

² Rinkes, *Rec. Trav. chim.*, 1938, **57**, 176.

³ Meerwein, *Annalen*, 1914, **405**, 129.

⁴ Amiel, Löffler, and Ginsburg, *J. Amer. Chem. Soc.*, 1954, **76**, 3625.

⁵ Dominquez, Diaz, and Slim, *Ciencia*, 1956, **16**, 151.

⁶ Isikawa, Sakurai, and Someno, *Sci. Reports Tokyo Bunrika Daigaku*, 1940, **3**, A, No. 74, 293; *Chem. Abs.*, 1941, **35**, 8206.

⁷ Plattner and St. Pfau, *Helv. Chim. Acta*, 1937, **20**, 1474.

⁸ Maschmeijer, F.P. 765,515.

⁹ Frank, Armstrong, Kwiatek, and Price, *J. Amer. Chem. Soc.*, 1948, **70**, 1379.

¹⁰ Nazarov, Bergelson, Torgov, and Ananchenko, *Bull. Acad. Sci. U.S.S.R.*, 1953, 787.

¹¹ Winternitz, Mousseron, and Rouzier, *Bull. Soc. chim. France*, 1954, 316.

¹² Inhoffen and Krämer, *Chem. Ber.*, 1954, **87**, 488.

¹³ *Inter al.*, Nazarov and Bakhmutskaya, *Zhur. obschei Khim.*, 1948, **18**, 1077.

¹⁴ Hunsdiecker, *Ber.*, 1942, **75**, 455.

¹⁵ Baker and Jones, *J.*, 1951, 787.

¹⁶ Raphael in "Chemistry of Carbon Compounds," ed. E. H. Rodd, Elsevier, Amsterdam, 1950, Vol. IIa, p. 96.

¹⁷ Born, Pappo, and Szmuszko, *J.*, 1953, 1779.

dione (I) by treatment of the latter with *isobutyl* alcohol in the presence of toluene-*p*-sulphonic acid. The former (II) reacts readily with a Grignard reagent to yield compound (III) which on treatment with dilute acid undergoes hydrolysis and dehydration to yield the 2-substituted *cyclopent-2-enone* (IV). The use of strong acid at this stage causes polymerisation (cf. ref. 9). The validity of this method depends on the exclusive formation of an endocyclic double bond on dehydration of the intermediate hydroxy-ketone. That this should be so is supported by the observation¹ that 2-*isopropylidene*cyclopentanone isomerises to 2-*isopropyl*cyclopent-2-enone in the presence of acid, which is in keeping with the greater stability of an endo- than of an exo-cyclic double bond in a five-membered ring.¹⁸

We have applied this method to the preparation of two new and eight known 2-substituted *cyclopent-2-enones* (see Table). The constants we obtained agree with the

2-Substituted *cyclopent-2-enones* (IV). (Previous constants are in parentheses.)

No.	2-Subst. R	B. p./mm.	n_D^*	M. p. of 2 : 4-dinitrophenylhydrazone	M. p. of semicarbazone
1 ¹	Me	48—50°/14 (51—52°/13)	1.4744 (1.4798)	221—222° (221—222°) ^b	— ^a
2 ¹	Et	69—72°/16 (76—78°/23)	1.4728 (1.4747)	219—220° (219—220)	209—210° ^d (196—198°)
3 ¹	Pr ⁿ	85—86°/20 (90—91°/24)	1.4730 (1.4743)	198—199° (177—178)	217—219° (217—218)
4 ¹	Pr ^l	88—90°/22 (84.5—85°/25)	1.4720 (1.4721)	— (202—203)	205—207° ^f (203—204)
5 ^{5,6}	Bu ⁿ	98—100°/12 (95—102°/30; 102°/5)	1.4749 (1.4657, † 1.4759)	137—138° ^f (128—130.5, 177.4)	199—200° ^e (200—201, —)
6 ⁷	<i>n</i> -Pentyl	114—116°/15 (108°/10)	1.4743 (1.473)	99—100° ^f (—)	200—201° (199—200)
7 ^{5,9}	<i>n</i> -Hexyl	88—89°/1 (126—129°/30; 97—100°/5)	1.4744 (1.4729, † 1.4675)	88—89° ^f (92—93, —)	196—197° (190—191, 194.5—196)
8 ¹⁵	Ph	107—109°/1 (110—113°/2) ^g	— (—)	209—210° (209—210)	235—236° ^b (235—237)
9	Ph·[CH ₂] ₂	97—98°/0.1	1.5490	153—154° ^d	254—256° ^f
10	Ph·[CH ₂] ₃	131—132°/0.1	1.5437	118—119° ^e	190—191

* At 20°, but † at 30°. ^a Oxime, m. p. 127—128° (lit.,¹ 127—128°).

^b Prisms. ^c Needles. Plates. ^g M. p. 72—73° (lit.,¹⁵ m. p. 72°).

Tablets. Laths.

No. †		Found (%)			Formula	Required (%)		
		C	H	N		C	H	N
2	Ketone	76.3	9.2	—	C ₇ H ₁₀ O	76.3	9.2	—
2	SC	56.9	7.9	25.3	C ₈ H ₁₃ ON ₃	57.5	7.8	25.1
3	Ketone	77.6	9.5	—	C ₉ H ₁₂ O	77.4	9.7	—
3	DNP	55.1	5.3	18.0	C ₁₄ H ₁₆ O ₄ N ₄	55.3	5.3	18.4
5	Ketone	78.0	9.8	—	C ₉ H ₁₄ O	78.2	10.2	—
5	DNP	—	—	17.5	C ₁₅ H ₁₆ O ₄ N ₄	—	—	17.6
5	SC	61.6	8.8	21.3	C ₁₀ H ₁₇ ON ₃	61.5	8.8	21.5
6	DNP	—	—	16.9	C ₁₆ H ₂₀ O ₄ N ₄	—	—	16.9
7	DNP	—	—	16.4	C ₁₇ H ₂₂ O ₄ N ₄	—	—	16.2
7	SC	64.9	9.7	18.8	C ₁₂ H ₂₁ ON ₃	64.5	9.5	18.8
9	Ketone	83.5	7.8	—	C ₁₃ H ₁₄ O	83.8	7.6	—
9	DNP	61.8	5.0	15.1	C ₁₉ H ₁₄ O ₄ N ₄	62.3	5.0	15.3
9	SC	68.9	6.6	17.6	C ₁₄ H ₁₇ ON ₃	69.1	7.0	17.3
9	Oxime §	—	—	6.5	C ₁₃ H ₁₅ ON	—	—	7.0
10	Ketone	83.9	8.2	—	C ₁₄ H ₁₆ O	84.0	8.0	—
10	DNP	—	—	14.9	C ₂₀ H ₂₀ O ₄ N ₄	—	—	14.7
10	SC	70.3	7.6	16.0	C ₁₅ H ₁₉ ON ₃	70.0	7.4	16.3

† SC = Semicarbazone; DNP = 2 : 4-dinitrophenylhydrazone. § M. p. 81—82°.

recorded values when the *cyclopent-2-enones* have been prepared by unambiguous methods, but discrepancies appear when the latter have previously been obtained by method (b).

¹⁸ Turner and Garner, *J. Amer. Chem. Soc.*, 1958, **80**, 1424.

EXPERIMENTAL

2-isoButoxycyclopent-2-enone.—A solution of *cyclopentane-1:2-dione*¹⁹ (22 g., 0.26 mole) and toluene-*p*-sulphonic acid (2 g.) in benzene (390 ml.) and *isobutyl* alcohol (96 ml.) was heated under reflux for 2 hr., the water formed in the reaction being removed by a Dean and Stark separator. The cold reaction mixture was washed with 5% sodium hydrogen carbonate solution, 5% sodium hydroxide solution and water, dried (MgSO₄), and distilled, to yield, after removal of the solvent, *2-isoButoxycyclopent-2-enone* (26 g., 67%), b. p. 130—132°/15 mm., n_D^{20} 1.4770 (Found: C, 69.6; H, 8.8. C₉H₁₄O₂ requires C, 70.1; H, 9.1%).

2-Substituted cyclopent-2-enones.—*2-isoButoxycyclopent-2-enone* (4 g., 0.025 mole) in ether (20 ml.) was added to a stirred solution of the required Grignard reagent (0.03 mol.) in ether (40 ml.) at such a rate that gently refluxing was maintained. After being stirred for 30 min. at room temperature the mixture was poured on ice and ammonium chloride, and 2*N*-hydrochloric acid added until two phases were obtained. The aqueous layer was separated and extracted with ether, and the combined ethereal solutions were washed with 5% aqueous sodium hydrogen carbonate and water, dried (MgSO₄), and distilled, to yield the *2-substituted cyclopent-2-enone* (45—75%). The 2:4-dinitrophenylhydrazones (orange to crimson) were crystallised from ethanol-chloroform, and the oximes and semicarbazones from ethanol.

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¹⁹ Dutch P. 58,279; *Chem. Abs.*, 1947, **41**, 4807.