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A SYNTHESIS AND SOME REACTIONS OF 2-THIOCYANATO-2-ETHYLENIC CARBONYL COMPOUNDS

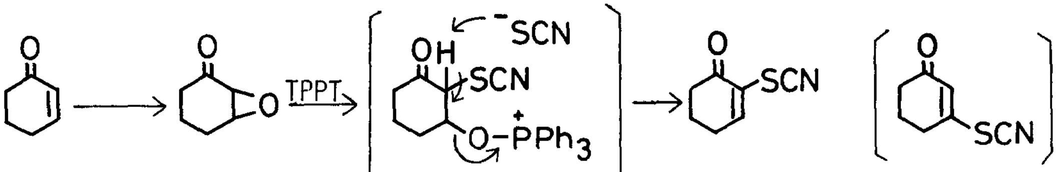
Y. Tamura*, T. Kawasaki, N. Gohda and Y. Kita
Faculty of Pharmaceutical Sciences, Osaka University
133-1, Yamada-kami, Suita, Osaka, Japan

Summary: A synthesis of 2-thiocyanato-2-ethylenic carbonyl compounds was achieved by the reaction of epoxy ketones with $Ph_3P(SCN)_2$ (TPPT). Some useful transformations of 2-thiocyanato-2-cyclohexenone to 2,3-disubstituted cyclohexanones and iminothiazolines are described.

Previously unreported 2-thiocyanato-2-ethylenic carbonyl compounds (I) are expected to be quite attractive intermediates in organic synthesis, since compounds (I) presumably can serve as electron deficient olefins such as Michael receptors and also undergo a rich variety of reactions due to the ability of thiocyanate functional group either as a pseudohalide group or as a sulfenyl cyanide group[1]. Generally, 2-substituted 2-ethylenic carbonyl compounds are prepared by the reaction of epoxy ketones (II) with nucleophilic substrates such as ^-OR[2,3], ^-SR[2,4], $^-NRR'$[2,5], ^-X[6] and ^-CN[7]. Our attempts to use this method for the preparation of (I) by using KSCN or NH_4SCN gave poor preparative results[8]. We now wish to report a novel, simple and facile synthesis of (I) involving the reaction of $Ph_3P(SCN)_2$ (TPPT)[9] with (II), and some attracting reactions of (I).

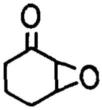
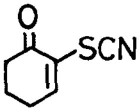
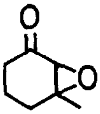
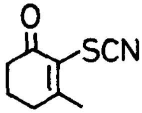
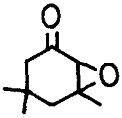
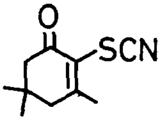
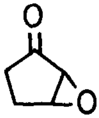
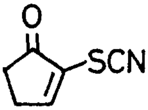
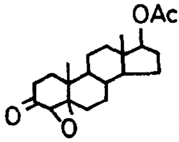
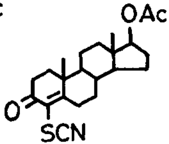
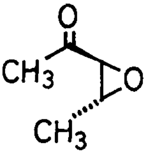
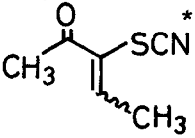
Synthesis of 2-Thiocyanato-2-ethylenic Carbonyl Compounds

The starting epoxy ketones (IIa-f) were readily prepared by epoxidation of 2-ethylenic carbonyl compounds (IIIa-f) under ordinary conditions such as alkaline hydrogen peroxide in methanol at 0-15°. A typical experimental procedure for thiocyanation is illustrated in the reaction of 2,3-epoxycyclohexanone (IIa) with TPPT. A solution of (IIa; 1 mmole) in methylene chloride (6 ml) was reacted with freshly prepared TPPT[9] (ca. 1.2 mmole in 10 ml CH_2Cl_2) under nitrogen at -40° for several hrs and at room temperature overnight. An excellent yield of pure 2-thiocyanato-2-cyclohexenone (Ia) [mp 54-54.5° (pet. ether)] was obtained simply by concentration of the reaction mixture, followed by chromatography of the crude product on silica-gel column (elution with $CHCl_3$). The structure was determined by its elemental, mass [m/e 153(M^+)], i.r. [$\nu_{max}^{CHCl_3}cm^{-1}$ 2170, 1675 and 1610] and n.m.r. data [δ ($CDCl_3$) 7.35 (t, 1H, -HC=), 2.9-2.4 (m, 4H, $-COCH_2$ and $-\underline{CH_2}CH=$) and 2.4-1.8 (m, 2H, $-CH_2-$)]. The reaction selectively proceeded to give (Ia) free of the isomeric (Ia'). In a similar manner, a number of epoxy ketones (IIb-f) were converted to the corresponding 2-thiocyanato-2-ethylenic carbonyl compounds (Ib-f) regioselectively in considerable yields. The results are shown in Table.



IIIa IIa Ia Ia'

Table 2-Thiocyanato-2-ethylenic Carbonyl Compounds (Ia-f)

	Epoxy ketone (II)	Product (I)	Yield* (%)	I.R. $\nu_{max}^{CHCl_3}$ cm^{-1}	N.M.R. δ (CCl_4)	m/e** (M^+)
a			92	2170,1675,1610	7.35(t,1H,=CH-) 2.9-2.4(m,4H,=CHC$\underline{H}_2$-, -COC$\underline{H}_2$-) 2.4-1.8(m,2H,-CH_2-)	153
b			71	2170,1670,1595	2.75-2.3(m,4H,-CH_2-×2) 2.34(s,3H,-CH_3) 2.25-1.95(m,2H,-CH_2-)	167
c			73	2170,1675,1595	2.50(s,2H,-CH_2CO-) 2.44(s,2H,-CH_2-C=) 2.34(s,3H,-CH_3) 1.07(s,6H,-CH_3×2)	195
d			97	2170,1700,1590	7.82(t,1H,=CH-) 3.0-2.7(m,2H,=CHC$\underline{H}_2$-) 2.7-2.5(m,2H,-COCH_2-)	139
e			38	2150,1685,1600	4.50(bt,1H,>C$\underline{H}$-OCOCH_3) 2.6-0.8(m,19H,-CH_2-×8, >CH-×3) 2.02(s,3H,-COCH_3) 1.26(s,3H,-CH_3) 0.83(s,3H,-CH_3)	387
f		 ***	57	2165,1675,1610	7.43(t,1H,=CH-) 2.41(s,3H,-COCH_3) 2.25(d,3H,=CH-C$\underline{H}_3$)	141

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* Isolated yields after column chromatography were shown.

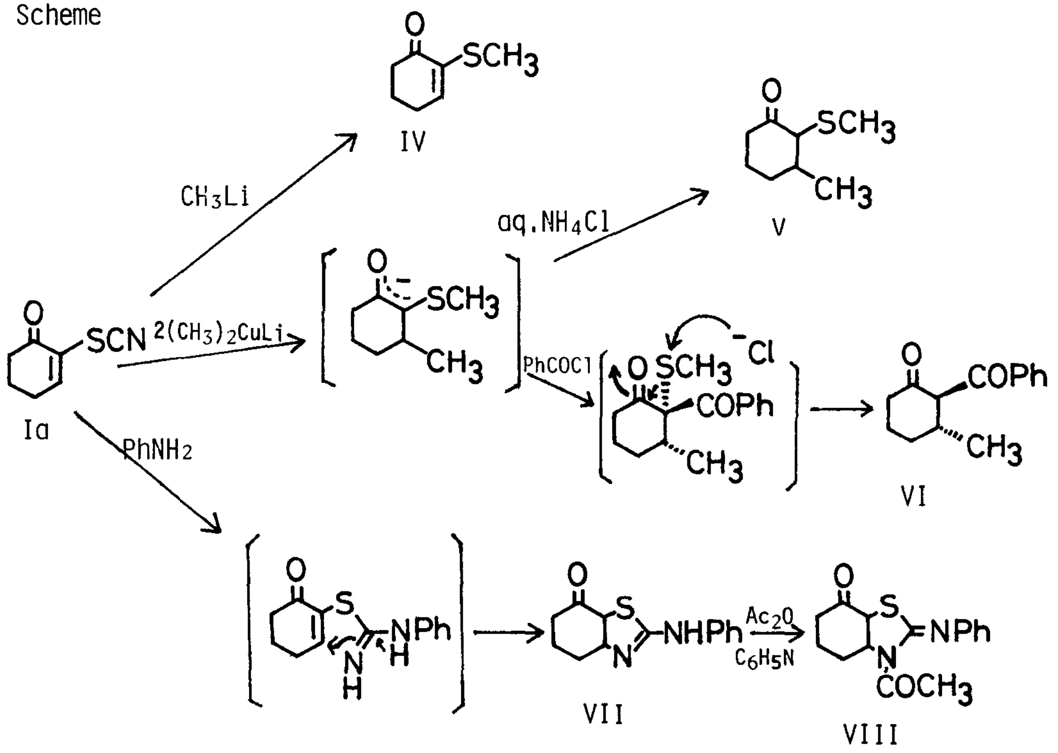
** Satisfactory mass spectral data were obtained for all new compounds.

*** Although it is a single isomer (checked by t.l.c. and n.m.r.), the stereochemistry is unclear.

Reactions of 2-Thiocyanato-2-ethylenic Carbonyl Compounds

The importance of the 2-thiocyanato-2-ethylenic carbonyl compounds (I) is demonstrated by some useful transformations of (Ia) to the compounds (IV-VIII) as exemplified in the following Scheme. Treatment of (Ia; 1 mmole in 3 ml ether) with CH_3Li (1 mmole in 2 ml ether) at -70° for 30 min gave 2-methylthio-2-cyclohexenone (IV) [2,4-dinitrophenyl hydrazone, mp 216-219° (lit. 222-224°[10])] in 34% yield and with $(CH_3)_2CuLi$ (2 mmole in 15 ml ether) at -70° for 30 min followed by working-up with aq. NH_4Cl or benzoyl chloride (1 mmole) gave 3-methyl-2-methylthiocyclohexanone (V) [mixture of two isomers, i.r. $\nu_{max}^{CHCl_3}$ cm^{-1} 1685, n.m.r. δ (CCl_4) 2.80 (m, 1H, $-COC\underline{H}SCH_3$), 2.5-1.2 (m, 7H, $-CH_2-\times 3$, and $-CHCH_3$), 2.00 (s, 3H, $-SCH_3$) and 1.15 (d, 3H, $-CH_3$), m/e 158 (M^+)] or 2-benzoyl-3-methylcyclohexanone (VI) [trans isomer, mp 65-66.5° (pet. ether), i.r. $\nu_{max}^{CHCl_3}$ cm^{-1} 1700 and 1670, n.m.r. δ ($CDCl_3$) 7.8-7.6 (m, 2H, ArH), 7.5-7.2 (m, 3H, ArH), 3.90 (d, J 10Hz, 1H, -COCHCO), 2.7-1.1 (m, 7H, $-CH_2\times 3$ and CH-) and 0.95 (d, 3H, $-CH_3$), m/e 216 (M^+)] in 47% or 51% yield, respectively. When (Ia, 1 mmole) was reacted with aniline (1 mmole) in ethanol (3 ml) at reflux for 6 hr, nucleophilic attack of aniline on the sulfenyl cyanide group of (Ia) followed by subsequent intramolecular Michael addition occurred to give the 2-iminothiazoline (VII) [mp 245° (acetone), i.r. $\nu_{max}^{CHCl_3}$ cm^{-1} 3150 and 1700, n.m.r.

Scheme



δ (d_6-DMSO) 8.80 (bs, 1H, NH), 7.8-6.9 (m, 5H, ArH), 5.0 (m, 1H, >CH-N), 4.38 (bd, 1H, -COCH-S) and 2.9-1.5 (m, 6H, $-CH_2-\times 3$), m/e 246 (M^+)] in 46% yield, which was acetylated to (VIII) [mp 170° (methanol), i.r. $\nu_{max}^{CHCl_3}$ cm^{-1} 1710 and 1680, n.m.r. δ ($CDCl_3$) 2.89 (s, 3H, $N-COCH_3$), m/e 288 (M^+)] by treatment with acetic anhydride in dry pyridine. Although none of these reactions has been optimized, (Ia) was found to be a useful intermediate for the preparation of 2,3-disubstituted cyclohexanones and for the some sulfur containing heterocycles Further potentialities of these types of thiocyanates (I) are now under investigation.

References and Notes

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8 The treatment of KSCN with isophorone oxide (IIc) in protic solvent did not give (Ic) at all, but afforded bis-(3,5,5-trimethyl-2-cyclohexen-1-on-2-yl)-sulfide [m.p. 90-91° (pet. ether-ether), $\nu_{max}^{CHCl_3}$ cm^{-1} 1665 and 1590, δ ($CDCl_3$) 2.35 (s, 2H×2, $-CH_2$), 2.31 (s, 3H×2, $-CH_3$), 2.23 (s, 2H×2, $-CH_2$) and 1.0 (s, 3H×4, $-CH_3$), m/e 306 (M^+)] in 53% yield and that of NH_4SCN with (IIc) gave low yield of (Ic) accompanied with more than three complex mixtures.

9 The reaction of TPPT with alcohols and carboxylic acids leading to the formation of thiocyanates and acylisothiocyanates has been reported in the following papers; Y. Tamura, T. Kawasaki, M. Adachi, M. Tanio and Y. Kita, *Tet. Letters*, 1977, 4417; Y. Tamura, T. Kawasaki, M. Tanio and Y. Kita, *Chem. & Ind.*, 1978, 806.

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