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Stable Biscarbodiimides

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The dehydrosulfurization of bisthioureas containing at least one aromatic residue results in the corresponding biscarbodiimides. Biscarbodiimides with bulky groups, such as *t*-butyl and 2, 6-xylyl, can be isolated without any polymerization and disproportionation; the steric hindrance of the bulky groups makes such isolation possible. Polymerization and disproportionation interrupt the isolation of biscarbodiimides with less bulky groups. Despite their nonpolymerizability, they give rise to the other known addition reaction of aromatic carbodiimides.

Several methods have been tried to prepare biscarbodiimides.[1-5] In most of them, however, isolation was prevented by the labile properties of carbodiimides, causing them to undergo disproportionation and polymerization.[2] Only some special aliphatic biscarbodiimides which have bulky groups like *t*-butyl could be isolated by Nischk[1] and by Schlack and Keil.[3] The preparation of biscarbodiimides containing an aromatic residue has been claimed recently in patents,[4,5] but they were not isolated. Pure biscarbodiimides containing an aromatic residue will offer better monomers for the poly-addition reaction of biscarbodiimides,[6] as the reactivity of carbodiimides is activated by the aromatic residue to nucleophilic reagents.[7,8] We wish to report the preparation of biscarbodiimides with an aromatic residue; several of these biscarbodiimides have been isolated by vacuum distillation or recrystallization for the first time.

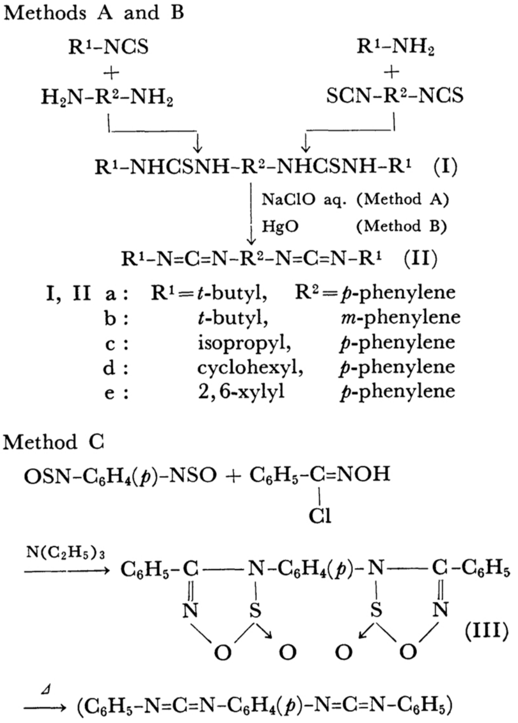
The three methods shown in Scheme 1 were studied for the preparation of biscarbodiimides (II):

Method A: The treatment of bisthiourea (I) with an excess of a strongly alkaline solution of sodium hypochlorite.[9]

Method B: The treatment of I with an excess of yellow mercuric oxide.[9]

Method C: The thermal decomposition of the adduct (III) of thionyl-*p*-phenylenediamine[10] and benzonitrile oxide.[11,12]

Method A offered a good means for the synthesis of II because it had the following advantages in synthetic operation: (a) Cheap sodium hypochlorite could be used as the dehydrosulfurizing agent. (b) The dehydration of the solvent was not required. (c) A large quantity of II was more easily obtained by Method A than by Method B.



I, II	R¹	R²
a:	R^1=*t*-butyl,	R^2=*p*-phenylene
b:	*t*-butyl,	*m*-phenylene
c:	isopropyl,	*p*-phenylene
d:	cyclohexyl,	*p*-phenylene
e:	2, 6-xylyl	*p*-phenylene

Scheme 1

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[1] G. Nischk, German Pat. 924751 (1955).

[2] I. G. Hinton and R. F. Webb, *J. Chem. Soc.*, **1961**, 5051.

[3] a) P. Schlack and G. Keil, *Ann.*, **661**, 164 (1963). b) P. Schlack and G. Keil, German Pat. 1173460 (1962).

[4] B. F. Goodrich Co., Netherlands Pat. 6506325 (1965).

[5] Farbenfabriken Bayer A. G., *ibid.*, 6602444 (1966).

[6] Y. Iwakura, R. Tsuzuki and K. Noguchi, *Makromol. Chem.*, **98**, 21 (1966).

[7] H. G. Khorana, *Can. J. Chem.*, **32**, 227 (1954).

[8] M. Szekerke and J. Csazar, *Ann. Univ. Sci. Budapest Rolando Eotvos Nominatae Sect. Chim.*, **1**, 136 (1959); *Chem. Abstr.*, **56**, 4591 (1962).

[9] H. G. Khorana, *Chem. Revs.*, **53**, 145 (1953).

[10] A. Michälis, *Ann.*, **274**, 261 (1893).

[11] A. Werner and H. Buss, *Ber.*, **27**, 2197 (1894).

[12] a) P. Rajagopalan and H. U. Daeniker, *Angew. Chem.*, **75**, 91 (1963). b) P. Rajagopalan and B. G. Advani, *J. Org. Chem.*, **30**, 3369 (1965).

TABLE 1. BISCARBODIIMIDES

R^1-N=C=N-R^2-N=C=N-R^1 (II)

II	R^1	R^2	Method1)	Yield (%)	Bp, °C/mmHg [mp, °C]	Formula	Anal. Found (Calcd) C%	H%	N%	IR (cm^{-1}) (N=C=N)	NMR τ
a	*t*-Butyl	*p*-Phenylene	A B	73 55	168.5—169.5/1 [51.0—52.5]	$C_{16}H_{22}N_4$	71.43 (71.07)	8.37 (8.20)	20.51 (20.73)	2170	8.68 2.95
b	*t*-Butyl	*m*-Phenylene	A	29	137—139/1	$C_{16}H_{22}N_4$	70.92 (71.07)	7.87 (8.20)	20.74 (20.73)	2200	8.82 3.53 3.25
c	Isopropyl	*p*-Phenylene	B	50	138—139/0.12	$C_{14}H_{18}N_4$	69.23 (69.39)	7.18 (7.49)	22.71 (23.12)	2180	—
d	Cyclohexyl2)	*p*-Phenylene	B	(39)3)	—	$C_{20}H_{26}N_4$	— (74.49)	— (8.13)	— (17.18)	2160	—
e	2,6-Xylyl	*p*-Phenylene	A	60	[113—115]	$C_{24}H_{22}N_4$	78.37 (78.66)	5.94 (6.05)	15.16 (15.29)	2170	7.65 2.95 2.82
f	Phenyl2)	*p*-Phenylene	C	(46)4)	—	$C_{20}H_{14}N_4$	— (77.40)	— (4.55)	— (18.06)	2200	—

1) See Scheme 1 and experimental section.
2) Could not be isolated because of polymerization and disproportionation.
3) Dicyclohexylcarbodiimide was obtained in a yield of 39% as a distillate.
4) Diphenylcarbodiimide was obtained in a yield of 46% as a distillate.

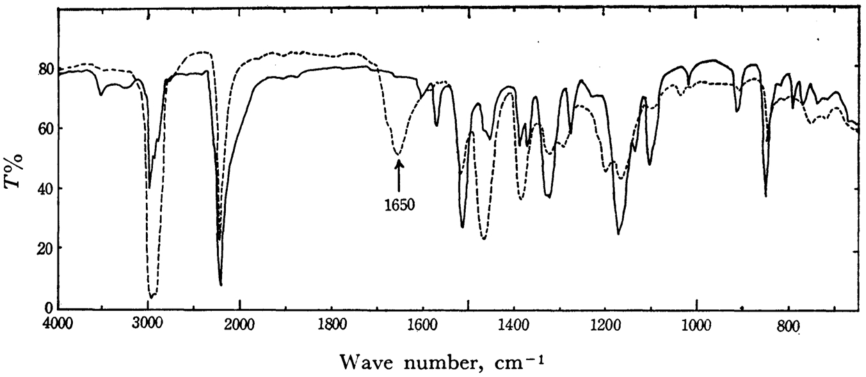


Fig. 1. IR spectra of *p*-phenylenebis(isopropylcarbodiimide) (IIc).
—— Freshly distilled (liquid film)
- - - After 50 days (Nujol mull)

TABLE 2. BISUREAS[1]
R^1-NHCONH-R^2-NHCONH-R^1 (VI)

VI	R^1	R^2	Yield %	Mp, °C	Solvent for recrystallization	Formula	Anal. Found (Calcd) C%	H%	N%
a	*t*-Butyl	*p*-Phenylene	49	>360	Ethanol	$C_{16}H_{26}N_4O_2$	68.11 (62.72)	8.52 (8.55)	18.27 (18.29)
b	*t*-Butyl	*m*-Phenylene	36	243—245 (dec.)	Ethanol	$C_{16}H_{26}N_4O_2$	63.00 (62.72)	8.60 (8.55)	18.24 (18.29)
c	Isopropyl	*p*-Phenylene	68	>300	DMF[3]	$C_{14}H_{22}N_4O_2$	60.54 (60.41)	7.78 (7.97)	20.10 (20.13)
d	Cyclohexyl	*p*-Phenylene	63[2]	>360	DMF[3]	$C_{20}H_{30}N_4O_2$	67.16 (67.01)	8.30 (8.44)	15.39 (15.63)
e	2, 6-Xylyl	*p*-Phenylene	51	>300	DMF[3]	$C_{24}H_{26}N_4O_2$	71.44 (71.62)	6.53 (6.51)	13.79 (13.92)
f	Phenyl	*p*-Phenylene	33[2]	>300	DMF[3]	$C_{20}H_{18}N_4O_2$	— (69.35)	— (5.24)	— (16.18)[4]

1) To a solution of biscarbodiimide (II) in acetone was added dropwise a large excess of 1 N hydrochloric acid. Crystals precipitated were collected by filtration, washed with acetone and dried to give bisureas.
2) Overall yield of bisurea from bisthiourea.
3) Dimethylformamide.
4) VIf was determined by the coincidence of IR spectrum with that of authentic sample prepared from *p*-phenylenediamine and phenyl isocyanate.

II did not react with water, even in such strongly alkaline conditions, and no formation of bisureas was observed. As, moreover, the yields were quite high, this method was most suitable for the synthesis of II. Method B is a conventional one and has the advantage that free sulfur is not formed because it is removed as mercuric sulfide. However, the yellow mercuric oxide used as the dehydrosulfurizing agent is expensive and, moreover, very toxic. In Method C, none of the raw materials except that for IIf were easily available.

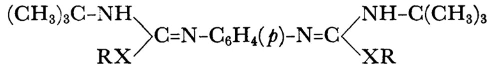
The results of the preparation of II are summarized in Table 1. IIa, IIb, and IIe could be isolated by vacuum distillation or by recrystallization and stored for weeks without any change, as they were free from polymerization and disproportionation by the steric hindrance of *t*-butyl or 2, 6-xylyl groups. IId and IIf, on the other hand, underwent disproportionation upon vacuum distillation, thus forming dicyclohexylcarbodiimide (IVa) or diphenylcarbodiimide (IVb), and could not be isolated, as has been reported by Hinton and Webb in connection with hexamethylenebis(cyclohexylcarbodiimide).[2] However, the formation of IId and IIf was confirmed by the analysis of the IR spectra of the reaction products remaining after evaporating the solvent.

$$\text{IId and IIf} \xrightarrow{\text{distillation}}$$

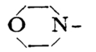
$$\underset{\text{(IV)}}{R^1\text{-N=C=N-}R^1} + \underset{\text{(V)}}{\text{-(-}R^2\text{-N=C=N-)-}_n}$$

IVa: R^1=cyclohexyl, IVb: R^1=phenyl
V: R^2=*p*-phenylene

TABLE 3. ADDITION PRODUDTS OF *p*-PHENYLENEBIS(*t*-BUTYLCARBODIIMIDE) (IIa) WITH ACTIVE HYDROGEN COMPOUNDS[1]

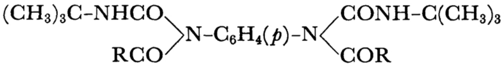


$$\begin{matrix}(CH_3)_3C\text{-}NH \\ RX\end{matrix}\!\!>C=N\text{-}C_6H_4(p)\text{-}N=C\!<\!\!\begin{matrix}NH\text{-}C(CH_3)_3 \\ XR\end{matrix}$$

RX-	Yield %	Mp, °C	Solvent for recrystallization	Formula	Anal. Found (Calcd) C%	H%	N%
$C_6H_5CH_2NH$-	57	122.5—123.5	Cyclohexane	$C_{30}H_{40}N_6$	74.29 (74.34)	8.40 (8.32)	17.33 (17.34)
cyclo-$C_6H_{11}NH$-	71	137.0—138.0	Isopropyl ether	$C_{28}H_{48}N_6$	71.90 (71.75)	10.25 (10.32)	18.03 (17.93)
	64	172.5—173.5	Ethyl acetate	$C_{24}H_{40}N_6O_2$	64.80 (64.83)	8.76 (9.07)	18.92 (18.90)
$C_6H_5CH_2O$-[2]	41	192.0—193.0	Benzene	$C_{30}H_{38}N_4O_2$	73.62 (74.04)	7.42 (7.87)	11.45 (11.51)
m-CH_3-C_6H_4O-	18	151.0—155.0	*n*-Hexane	$C_{30}H_{38}N_4O_2$	74.22 (74.04)	7.78 (7.87)	11.55 (11.51)
C_6H_5S-	58	159.0—163.0	Ethyl acetate	$C_{28}H_{34}N_4S_2$	68.74 (68.55)	7.00 (6.99)	11.70 (11.42)

1) Both reactants were mixed and kept at room temperature till the whole inhalt had solidified.
2) Cuprous chloride was added as a catalyst.[13]

TABLE 4. BISACYLUREAS DERIVED FROM *p*-PHENYLENEBIS(*t*-BUTYLCARBODIIMIDE) (IIa) AND CARBOXYLIC ACIDS[1]



$$\begin{matrix}(CH_3)_3C\text{-}NHCO \\ RCO\end{matrix}\!\!>N\text{-}C_6H_4(p)\text{-}N\!<\!\!\begin{matrix}CONH\text{-}C(CH_3)_3 \\ COR\end{matrix}$$

R	Yield %	Mp, °C	Solvent for recrystallization	Formula	Anal. Found (Calcd) C%	H%	N%
cyclo-C_6H_{11}-	38	318.0—318.5	Ethyl acetate	$C_{30}H_{46}N_4O_4$	68.71 (68.41)	8.60 (8.80)	10.50 (10.64)
C_2H_5-	32	283.0—283.5	Ethyl acetate	$C_{22}H_{34}N_4O_4$	63.33 (63.13)	8.27 (8.19)	13.27 (13.39)

1) Crystals, formed soon after carboxylic acid had been added to a solution of IIa in dioxane, were filtered and dried to give bisacylureas.

The formation of IId and IIf is also indicated by the fact that the corresponding ureas (VId and VIf) were obtained by the addition of dilute hydrochloric acid to the acetone solution of the residue remaining after evaporating the solvent. IVa and IVb were identified by means of the coincidence of their IR spectra with those of authentic samples. IIc could be distilled under a high vacuum as a slightly yellowish viscous liquid, but it gradually polymerized to a white waxy mass. The occurrence of polymerization, which seemed to be trimerization,[9] was confirmed by the IR spectra, as is shown in Fig. 1. The intensity of the absorption at 2180 cm^{-1} (-N=C=N-) gradually diminished and, in turn, that at 1650 cm^{-1} (>C=N-) which might originate in a trimeric structure,*[1] appeared and gradually increased. IIa, IIb and IIe were identified by elementary analyses, their IR and NMR spectra, and the chemical reactions. A strong absorption at 2160—2200 cm^{-1} in the IR spectra is characteristic of the carbodiimide linkage.[9]

II reacted with water in the presence of an acid catalyst[9] to give the corresponding bisureas (VI). The data on VI are summarized in Table 2.

$$II + H_2O \xrightarrow{H^+} R^1\text{-}NHCONH\text{-}R^2\text{-}NHCONH\text{-}R^1 \qquad (VI)$$

The sterically-hindered biscarbodiimides (IIa, IIb, and IIe) still cause an addition reaction with active hydrogen compounds, in spite of their lack of reactivity in polymerization. They added amines, phenols, aromatic mercaptans, and carboxylic acids without a catalyst, and alcohols in the presence of cuprous chloride as a catalyst.[13] Typical results of the addition reaction of IIa are summarized in Table 3 and 4.

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*[1] The well-known diphenylcarbodiimide trimer[9] was found to have an absorption band at 1660 cm^{-1} due to a carbon-nitrogen double bond.

13) E. Schmidt and F. Moosmüller, *Ann.*, **597,** 235 (1955).

TABLE 5. BISTHIOUREAS

R¹-NHCSNH-R²-NHCSNH-R¹ (I)

I	R¹	R²	Procedure1)	Yield %	Dp2) (°C)	Solvent for recrystallization	Formula	Nitrogen contents, %	
								Calcd	Found
a	*t*-Butyl	*p*-Phenylene	A	95	197	DMF3)-water	$C_{16}H_{26}N_4S_2$	16.56	16.50
b	*t*-Butyl	*m*-Phenylene	A	96	193	Methanol	$C_{16}H_{26}N_4S_2$	16.56	16.16
c	Isopropyl	*p*-Phenylene	B	78	1964)	DMF3)-water	$C_{14}H_{22}N_4S_2$	18.05	17.87
d	Cyclohexyl	*p*-Phenylene	B	73	203	DMF3)	$C_{20}H_{30}N_4S_2$	14.35	14.78
e	2,6-Xylyl	*p*-Phenylene	A	88	214	—5)	$C_{24}H_{26}N_4S_2$	12.90	—

1) Procedure A; A solution of diisothiocyanate and amine in acetone was stirred for three hours at room temperature.
Procedure B; A solution of isothiocyanate and diamine in acetone was refluxed for forty hours.
2) Decomposition point.
3) Dimethylformamide.
4) Lit. mp 220—221°C, K. Ganapathi and B. S. Kulkarni, *Proc. Indian Acad. Sci.*, **37A**, 643 (1953).
5) Could not be recrystallized from any solvent tried.

Experimental

Starting Materials. *p*-Phenylenediisothiocyanate,14) isopropyl- and cyclohexyl-isothiocyanate,15) thionyl-*p*-phenylenediamine,10) and benzhydroxamoyl chloride11) were prepared according to the literature. *m*-Phenylenediisothiocyanate was prepared principally by the same method as *p*-phenylenediisothiocyanate.14) The procedure was as follows:

To a mixture of *m*-phenylenediamine (54 g) and carbon disulfide (85 g), a 28% aqueous ammonia solution (185 m*l*) was gradually added on an ice bath. The reaction mixture was stirred for three hours on the ice bath, and then for an additional three hours at room temperature. The precipitates were filtered, washed with 3% aqueous ammonium chloride, and dried to give diammonium *m*-phenylenebis(dithiocarbamate) (139 g, 95%). The salt was suspended in water (200 m*l*) and acetone (100 m*l*). To the suspension, ethyl chlorocarbonate (108 g) was added, drop by drop, at about −10°C. After the addition, the mixture was stirred for one hour at room temperature. A solution of sodium hydroxide (20 g) in water (50 m*l*) was added, drop by drop, to the mixture at about 0°C. Chloroform (300 m*l*) was added after thirty minutes of stirring at room temperature. An aqueous layer was then separated and extracted with chloroform three times. The combined chloroform solution was washed with water to make it neutral and dried over calcium chloride. The chloroform was then evaporated under reduced pressure, and the residue was distilled rapidly. The distillate was rectified to give *m*-phenylenediisothiocyanate (60 g, 63%) as a slightly yellowish solid. It boiled at 123—125°C/<1 mmHg and melted at 49—52°C.16)

Bisthioureas (I). Bisthioureas were prepared either from diisothiocyanate and monoamine (Procedure A) or from monoisothiocyanate and diamine (Procedure B). They could be used for the synthesis of biscarbodiimides without recrystallization. The results are summarized in Table 5.

Cycloadduct (III) of Thionyl-*p*-phenylenediamine and Benzonitrile Oxide.12,17) To a solution of thionyl-*p*-phenylenediamine10) (17.7 g) and benzhydroxamoyl chloride11) (27.5 g) in ether (420 m*l*), triethylamine (20.0 g) was added, drop by drop, below 5°C. After the solution had been refluxed for one hour, the precipitates were collected by filtration and steeped in methanol. The insoluble part was collected by filtration, washed with methanol, and dried to give III (34.0 g, 87%) as slightly yellowish crystals. It was recrystallized from dioxane-methanol, and it decomposed at 116.5—117.0°C.

Found: C, 55.18; H, 3.55; N, 12.91%. Calcd for $C_{20}H_{14}N_4O_4S_2$: C, 54.80; H, 3.22; N, 12.78%.

Biscarbodiimides (II). Method A: *Sodium Hypochlorite Method.* An example is as follows.

***p*-Phenylenebis(*t*-butylcarbodiimide) (IIa).** A mixture of Ia (68 g), commercial antiformin18) (active chlorine 10%, 1760 g), a 40% aqueous sodium hydroxide solution (500 g) and toluene (400 m*l*) was stirred for two hours at 70°C. After the reaction mixture had then cooled, the aqueous layer was separated and extracted with toluene three times. The combined toluene solution was washed with water and dried over anhydrous sodium sulfate. After the evaporation of the toluene, the residue was distilled in the presence of an active copper powder.6,19) The distillate was rectified to give IIa (40 g, 73%) as a white solid.

Method B: *Mercuric Oxide Method.* An example is as follows.

***p*-Phenylenebis(*t*-butylcarbodiimide) (IIa).** Three portions of yellow mercuric oxide (250 g) were, added to a refluxing suspension of Ia (33.8 g) in anhydous benzene at 30-min intervals. After four hours

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14) Y. Iwakura and S. Asakuno, *Preprint of Symposium on Polymer Science* (Japan) at Nagoya (1957), p. 88.

15) J. E. Hodgkins and M. G. Ettlinger, *J. Org. Chem.*, **21**, 404 (1956).

16) Lit. mp 53°C; O. Billeder and A. Steiner, *Ber.*, **20**, 230 (1887).

17) F. Eloy and R. Lenaers, *Bull. Soc. Chem. Belges,* **74**, 129 (1965); *Chem. Abstr.*, **63**, 5630 (1965).

18) A strongly alkaline solution of sodium hypochlorite (active chlorine 10%).

19) R. Q. Brewster and T. Groening, "Organic Syntheses," Coll. Vol. III, p. 445 (1961).

the reaction mixture was cooled, filtered and washed with anhydrous benzene. The combined benzene solution was dried over anhydrous sodium sulfate. The solvent was evaporated, and the residual oil was distilled to give IIa (15.0 g, 56%) as a white solid.

Method C: The cycloadduct (III) (3.0 g) of thionyl-*p*-phenylenediamine10) and benzonitrile oxide11) was decomposed at 120—125°C in a distilling apparatus. The residue, however, was distilled to give diphenylcarbodiimide (0.6 g, 46%).