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CYCLOADDITION REACTIONS OF AZIDES WITH ELECTRON-POOR OLEFINS

ISOMERIZATION AND THERMOLYSIS OF THE RESULTING Δ^2-TRIAZOLINES

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Abstract—The cycloaddition reactions of phenyl azide and butyl azide with monosubstituted electron-poor olefins are highly regioselective (if not regiospecific) and lead to 1,4-disubstituted Δ^2-triazolines or products derived therefrom: aziridines, diazocompounds, pyrazolines and 1,4-trisubstituted triazolines. As expected, the latter three products are not formed when a methyl group is introduced in the geminal position of the olefins, but Δ^2-triazolines and aziridines are then obtained exclusively. In all cases studied the 1,4-substituted Δ^2-triazolines derived from phenyl azide only give aziridines on thermolysis, whereas those derived from alkyl azides are thermally converted into a mixture of aziridine and enamine.

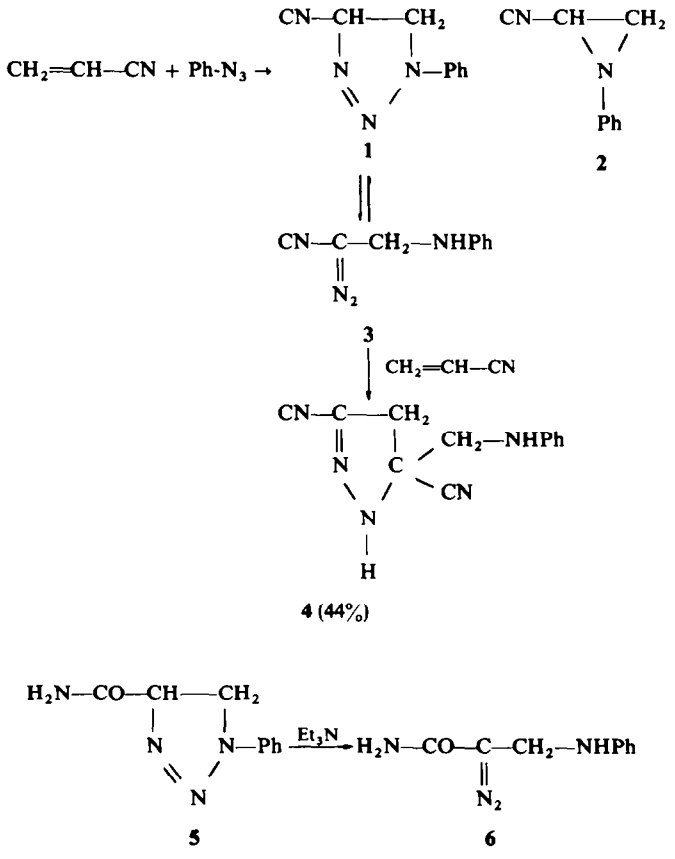
1,3-DIPOLAR cycloaddition reactions of azides with olefins constitute a general method for the synthesis of Δ^2-triazolines.[1] Starting with bisazides and bismaleimides. Gilliams and Smets[2] described the synthesis of poly-Δ^2-triazolines and their thermolysis to polyaziridines. Since little is known about the cycloaddition reactions of azides with asymmetric olefins carrying electron-withdrawing substituents such as ketone, ester, amide and nitrile functions,[3-5] we envisaged a detailed study of this topic, especially focusing on the reactions with butyl azide. Reported here are the formation, isomerization, and thermal decomposition of the resulting Δ^2-triazolines.

Monosubstituted olefins

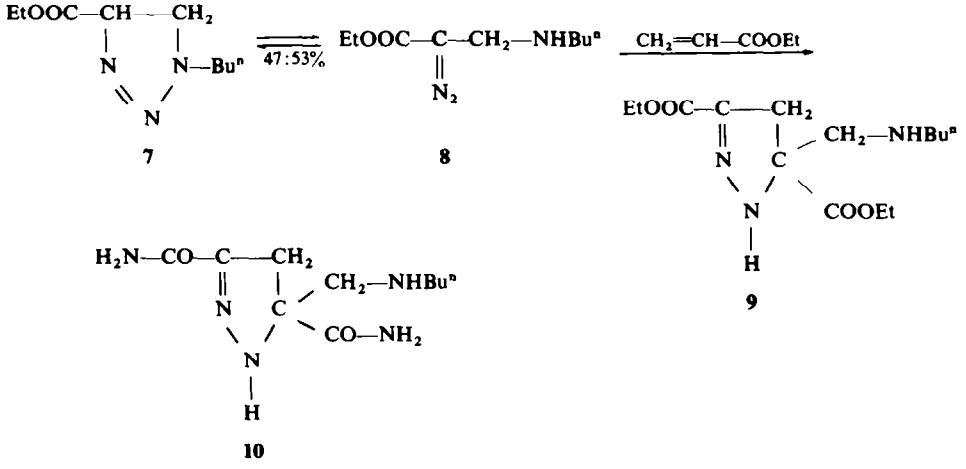
Huisgen *et al.*[3] reported the reaction of phenyl azide with an excess of acrylonitrile at room temperature to give a mixture of 1-phenyl-4-cyano-Δ^2-1,2,3-triazoline (**1**) and 1-phenyl-2-cyanoaziridine (**2**). Besides these two products, we isolated 5-anilinomethyl-3,5-dicyano-Δ^2-pyrazoline (**4**) in 44% yield. Since triazolines with electron-withdrawing substituents in the 4-position are known to isomerize to the open-chain diazocompounds,[3] the formation of **4** is readily rationalized by cycloaddition of 3-anilino-2-diazopropionitrile (**3**) with a second molecule of acrylonitrile.

When phenyl azide was reacted with acrylamide at 25°, triazoline **5** was obtained in 81% yield. On addition of triethylamine (10% solution in DMF), ring cleavage occurred very slowly with formation of 3-anilino-2-diazopropionamide **6** (IR absorption at 2100 cm^{-1}).

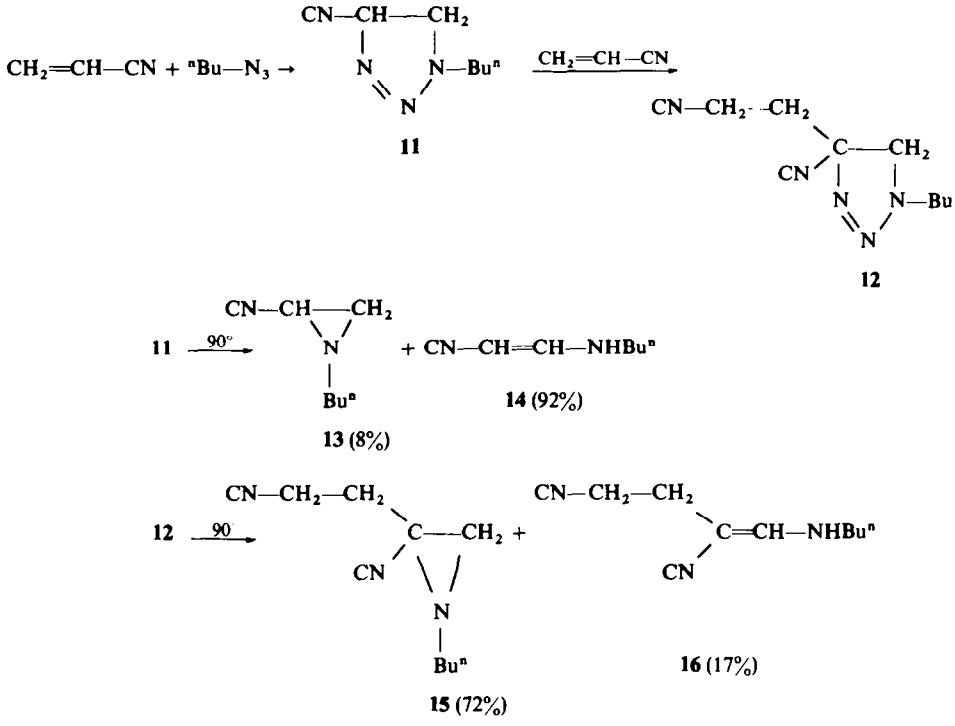
n-Butyl azide did not react with n-butylvinylether, even not at 100°. With ethyl acrylate, however, facile reaction occurred at room temperature to give triazoline **7**. This could be isolated in the pure state, but isomerized spontaneously within a few hours to 3-n-butylamino-2-diazopropionate (**8**) as shown by the appearance of a diazo absorption at 2100 cm^{-1}, a conjugated C=O at 1690 cm^{-1} and a weak N—H



at 3300 cm^{-1}. The diazoester **8** underwent further addition of ethyl acrylate to give the Δ^2-pyrazoline **9** in 95% yield. Similar treatment of n-butyl azide with acrylamide gave the pyrazoline adduct **10** via the corresponding Δ^2-triazoline.



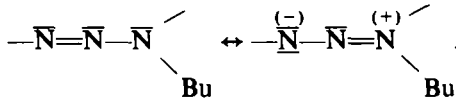
n-Butyl azide added acrylonitrile in two consecutive, but separable steps. When the reaction was worked up after 22 hr, 1-n-butyl-4-cyano-Δ^2-1,2,3-triazoline (**11**) was isolated in the pure state. On prolonged treatment (14 days) **11** reacted slowly with a second molecule of acrylonitrile to give a new Δ^2-triazoline **12**. The structure of this unexpected product was ascertained by spectroscopic analysis and also by thermal decomposition giving a mixture of aziridine **15** and enamine **16**, comparable with decomposition of **11**. Since the cycloaddition step (formation of **11**) was much



faster than the cyanoethylation step (**11** → **12**), a kinetic study of the cycloaddition was undertaken in CCl_4 solution by following the disappearance of the azide band in the IR at about 2100 cm^{-1}. Second order rate constants were determined at 25·8°, 38·5° and 51° and were equal to 5·4, 17·2 and 49·3 × 10^{-7} l $mole^{-1}$ sec^{-1} respectively. The values of the corresponding activation parameters ($\Delta H^{\ddagger}$ = 16·1 kcal $mole^{-1}$, $\Delta S^{\ddagger}$ = −33 e.u.) are typical for a concerted process.[6] It is noteworthy that **11**, in contrast to **1**, did not isomerize to the diazonitrile, CN—C(=N_2)—CH_2—NHBu^n, even after 24 hr in the presence of triethylamine (the IR spectrum was devoid of diazo and conjugated nitrile absorptions).

A concluding remark on the isomerization of Δ^2-triazolines is in order here. A comparison of the results obtained by Huisgen[3] (with phenyl azide adducts) and by ourselves (with butyl azide adducts) indicates that the replacement of a phenyl by a Bu group increases the rate of isomerization, but shifts the equilibrium towards the

triazoline form. Indeed, a Bu group increases the basicity of the N-1 atom, necessary for abstracting the acidic H atom of the 4-position, and therefore increases the rate of isomerization. The equilibrium position, on the other hand, is governed by the stability of both components. Thus, the triazeno group of the triazoline,



, is more stabilized by a butyl (+I-effect than by a phenyl substituent (−I-effect), and the reverse is true for the corresponding diazocompound. Note also that diazonitriles are less stable than diazoesters and diazoketones.

Geminally disubstituted olefins

The introduction of a Me group in the geminal position of the olefin partially modifies the mode of addition on account of its +I-effect. Thus, Huisgen *et al.*[3] briefly reported a non-regiospecific[7] addition of phenyl azide to methyl methacrylate, producing **18a** and **19a** in a ratio of 75: 25%. The authors postulated that **18a** arose from decomposition of the unstable **17a** at room temperature. We obtained similar results by treating phenyl azide with methyl isopropenyl ketone, methacrylonitrile

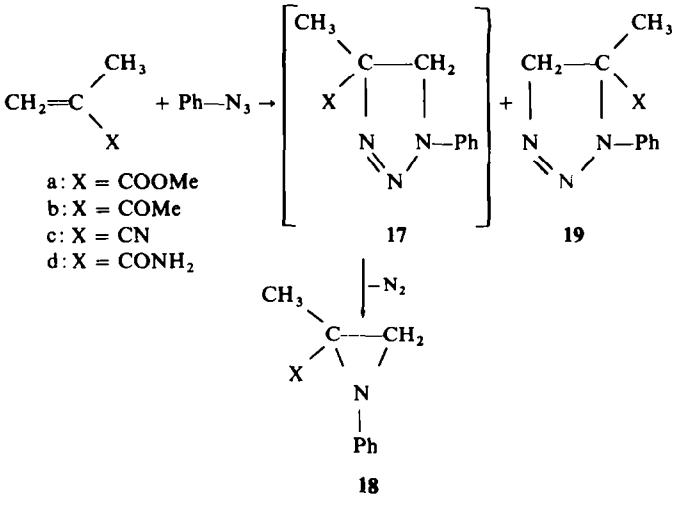


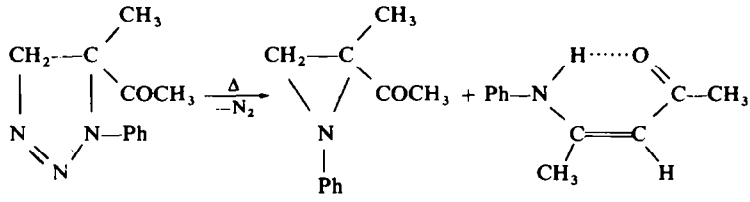
TABLE 1. CYCLOADDITIONS OF PHENYL AZIDE WITH *gem*-DISUBSTITUTED OLEFINS AT 25

X	Reaction time in days	Conversion %	Ratio **18**:**19** by NMR	$10^7 k_2$ (no solvent) 1 mole^{-1} sec^{-1}
a. COOMe[3,6c]	69	—	75:25	0·72*
b: COMe	20	65	70:30	1·9
c: CN	30	10	86:14	~0·04
d. $CONH_2$	150	35	90:10	—

* This value was obtained in CCl_4 as solvent

and methacrylamide (Table 1), and found evidence for the intermediacy of **17** as precursor of **18**. Indeed, when phenyl azide was allowed to react with methyl iso-

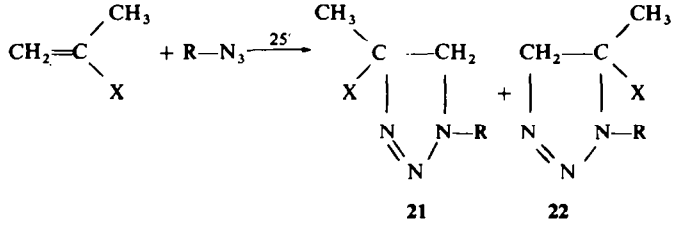
propenyl ketone at 0° for 4 months, triazoline **17b** was obtained and characterized by its NMR spectrum (J_{gem} = 10·5 Hz for the ring-methylene protons). At room temperature **17b** decomposed to **18b**. Its regioisomer[7] **19b**, on the contrary, only decomposed above 100° to give a mixture of the aziridine **18b** and the β-ketoenamine **20**. Structural assignment of **20** was based on spectral analysis and final chemical



19b **18b** **20** (m.p. 48°)

confirmation was secured by an independent synthesis from aniline and acetylacetone.[8]

Methyl azide and butyl azide reacted more regioselectively with *gem*-disubstituted electron-poor olefins than did phenyl azide. In addition, both triazolines **21** and **22** were stable at 25°. The results are summarized in Table 2.



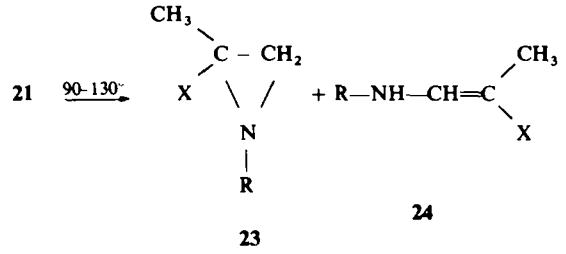
21 **22**

TABLE 2. CYCLOADDITIONS OF ALKYL AZIDES WITH *gem*-DISUBSTITUTED OLEFINS AT 25°

X	R	Reaction time in days	Conversion %	Ratio **21**:**22** by NMR	$10^7 k_2$ (no solvent) 1 mole^{-1} sec^{-1}
a. COOMe	Me	15	65	94:6	1·2
b. COMe	n-Bu	20	70	92:8	2·2
c. CN	n-Bu	30	25	94:6	0·3
d. $CONH_2$	n-Bu	150	55	100	—

An inspection of the kinetic data presented in Table 1 and 2 discloses the following order of reactivity: X = COMe > COOMe > CN > $CONH_2$. This is interpreted in terms of the capability of the X-substituent to stabilize a partial negative charge in the transition state. In addition, the higher reactivity of alkyl azides over phenyl azide further support the *complementary principle* formulated for cycloaddition reactions of azides with dipolarophiles.[6c] This principle states that electron-poor olefins prefer to react with azides carrying electron-releasing substituents, and vice versa. Thus alkyl azides should (and indeed do) react faster than phenyl azide in the examples studied here.

Thermal decomposition of **21** at 90–130° furnished a mixture of aziridine (**23**) and enamine (**24**) (Table 3).

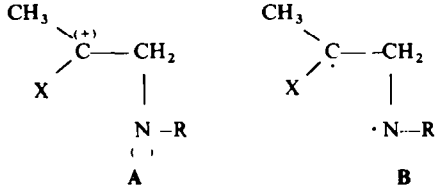


23 **24**

TABLE 3. THERMOLYSIS OF 1-ALKYL-4-DISUBSTITUTED-Δ^2-1,2,3-TRIAZOLINES (**21**)

X	R	Ratio **23**:**24**
a. COOMe	Me	39:61
b. COMe	n-Bu	60:40
c. CN	n-Bu	95:5
d. $CONH_2$	n-Bu	10–20:70–80

The facile thermal decomposition of triazolines carrying an electron-withdrawing X-substituent in the 4-position cannot be explained by a heterolytic cleavage via the zwitterionic intermediate **A**. A radical mechanism, proceeding via **B**, is more probable and in accord with all available evidence. Thus, a 1-phenyl substituent, in comparison with an alkyl substituent, lowers the decomposition temperature of the triazoline because of its radical stabilizing effect. The kinetic measurements by Szeimies and Huisgen[4] on this type of decomposition also provided evidence for a radical pathway.



A **B**

EXPERIMENTAL

Substantial IR and NMR information is available for pyrazolines,[9] aziridines[4,10] and *cis-trans* enamines,[11] and our structure assignments were based thereupon. Triazolines, on the contrary, have apparently received no systematic study, and will therefore be analyzed in detail elsewhere.[12]

5-Anilinomethyl-3,5-dicyano-Δ^2-pyrazoline (**4**). A mixture of phenyl azide (79·7 mmole) and acrylonitrile (277 mmole) was allowed to stand in the dark at room temp for 10 days. The excess of acrylonitrile was distilled off *in vacuo* at room temp and the residual oil (containing **1**, **2** and **4**) was crystallized from benzene–cyclohexane. Recrystallization gave colorless needles of the pyrazoline **4**, m.p. 89°, yield 44%. (Found: C, 64·05; H, 5·05; N, 31·10. Calcd for $C_{12}H_{11}N_5$ (225·1): C, 64·02; H, 4·88; N, 31·09%).

1-Phenyl-4-carboxamido-Δ^2-1,2,3-triazoline (**5**). A soln of 40 mmole phenyl azide and 50 mmole acrylamide in 15 ml 1,2-dimethoxyethane was kept at room temp for 54 days. Triazoline **5** crystallized out (yield 81%) and was recrystallized from EtOAc to give colorless plates, m.p. 147·5–150°. (Found: C, 56·75; H, 5·40; O, 8·40; N, 29·70. Calcd for $C_9H_{10}N_4O$ (190): C, 56·84; H, 5·27; O, 8·44; N, 29·47%).

1-n-*Butyl-4-carbethoxy-*Δ^2*-1,2,3-triazoline* (**7**). n-Butyl azide (120 mmole) and ethyl acrylate (320 mmole) were mixed and kept in the dark at room temp for 24 hr. After removing the excess of reagents *in vacuo*, the remaining colorless liquid (54%) was subjected immediately to analysis and found to be pure **7**.

5-n-*Butylaminomethyl-3,5-dicarbethoxy-*Δ^2*-pyrazoline* (**9**). This compound was obtained when butyl azide (40 mmole) and ethyl acrylate (80 mmole) were allowed to react in the dark at room temp for 10 days. Removal of the excess of reagents *in vacuo* left a colorless oil (**9**) in 95% yield. (Found: C, 55·8; H, 8·30; N, 14·25; O, 21·40. Calcd for $C_{14}H_{25}N_3O_4$ (299): C, 56·0; H, 8·30; N, 14·0; O, 21·35%).

5-n-*Butylaminomethyl-3,5-dicarboxamido-*Δ^2*-pyrazoline* (**10**). This compound crystallized out (yield 51%) when a soln of butyl azide (40 mmole) and acrylamide (50 mmole) in 15 ml 1,2-dimethoxyethane was kept at room temp for 30 days. Recrystallization from MeOH gave a crystalline product, m.p. 149–151·5°. (Found: C, 49·60; H, 7·80; N, 29·00; O, 13·50. Calcd for $C_{10}H_{19}N_5O_2$ (248): C, 49·79; H, 7·58; N, 29·04; O, 13·27%).

1-n-*Butyl-4-cyano-*Δ^2*-1,2,3-triazoline* (**11**). A mixture of butyl azide (45 mmole) and acrylonitrile (156 mmole) was kept in the dark at room temp for 22 hr. Removal of the excess of reagents left a colorless liquid of pure **11**. (Found: C, 54·80; H, 8·20; N, 36·60. Calcd for $C_7H_{12}N_4$ (152): C, 54·90; H, 8·49; N, 36·60%).

1-n-*Butyl-4-cyano-4-*β*-cyanoethyl-*Δ^2*-1,2,3-triazoline* (**12**). This compound was obtained when butyl azide (79 mmole) and acrylonitrile (277 mmole) were allowed to react in the dark at room temp for 10 days. Removal of the excess of reagents *in vacuo* left a yellow-red oil of **12** (90%) which could not be crystallized. (Found: C, 59·00; H, 7·30; N, 34·15. Calcd for $C_{10}H_{15}N_5$ (205): C, 58·53; H, 7·31; N, 34·19%).

Thermolysis of 1-n-*butyl-4-cyano-*Δ^2*-1,2,3-triazoline* (**11**). Triazoline **11** in 10 ml toluene was heated at 90° for 24 hr. Removal of the solvent left a red-brown oil composed of **13** and **14** in a ratio of 8 : 92% by NMR. Aziridine **13**, present in only small amounts, could not be isolated in the pure state. Pure **14** was obtained by vacuum distillation (78–80° at 0·2 mm). The NMR spectrum (CCl_4) indicated that both *cis* and *trans*-isomers were present in a ratio of 12 : 88%. (Found: C, 67·72; H, 9·68; N, 22·48. Calcd for $C_7H_{12}N_2$ (124): C, 67·75; H, 9·67; N, 22·58%).

Thermolysis of 1-n-*butyl-4-cyano-4-*β*-cyanoethyl-*Δ^2*-1,2,3-triazoline* (**12**). Triazoline **12** was heated at 90° for 22 hr. Vacuum distillation afforded two fractions. The first colorless fraction (108–110° at 0·5 mm) was pure **15**. (Found: C, 67·72; H, 8·48; N, 23·66. Calcd for $C_{10}H_{15}N_3$ (177): C, 67·80; H, 8·47; N, 23·73%). The second yellow-red fraction (160° at 0·5 mm) was mainly **16** but was contaminated with 30% of **15**.

Reactions of gem-*disubstituted olefins with azides.* A mixture of olefin and azide was allowed to react in the dark at room temp, and the reaction was followed spectroscopically. After removing the excess of reagents *in vacuo*, the products were analyzed as a mixture by NMR (Tables 1 and 2). The following two aziridines were isolated in the pure state:

18c: colorless liquid, b.p. 108° at 1 mm, $\eta^{25} = 1{\cdot}5390$. (Found: C, 75·70; H, 6·30; N, 17·82. Calcd for $C_{10}H_{10}N_2$ (158): C, 75·95; H, 6·33; N, 17·72%).

18d: m.p. 100·5–102·5° (benzene–cyclohexane). (Found: C, 68·40; H, 6·85; N, 15·95; O, 9·35. Calcd for $C_{10}H_{12}N_2O$ (176): C, 68·18; H, 6·81; N, 15·90; O, 9·09%).

Thermolysis of triazolines **21**. The triazolines **21** were heated at 90–130° for an appropriate time and thereafter analyzed as a mixture (Table 3). Fractional distillation at reduced pressure afforded **23** in the pure state.

23a: liquid, b.p. 50° at 10 mm. (Found: C, 55·85; H, 8·45; N, 10·80. Calcd for $C_6H_{11}NO_2$ (129): C, 55·81; H, 8·55; N, 10·83%).

23b: colorless liquid, b.p. 83° at 12 mm, $\eta^{25} = 1{\cdot}4440$. (Found: C, 69·60; H, 11·00; N, 9·00; O, 10·40. Calcd for $C_9H_{17}NO$ (155): C, 69·68; H, 10·97; N, 9·03; O, 10·32%).

23c: colorless liquid, b.p. 32° at 4 mm, $\eta^{25} = 1{\cdot}4334$. (Found: C, 69·70; H, 10·40; N, 20·00. Calcd for $C_8H_{14}N$ (124): C, 69·56; H, 10·15; N, 20·29%).

The following two enamines **24** were also isolated in the pure state:

24a: liquid, b.p. 49° at 2 mm. (Found: C, 55·75; H, 8·65; N, 10·90. Calcd for $C_6H_{11}NO_2$ (129): C, 55·81; H, 8·55; N, 10·83%).

(E)-24b:[13] white crystalline product, m.p. 54–55° (light petroleum). (Found: C, 69·35; H, 11·05; N, 8·90; O, 10·15. Calcd for $C_9H_{17}NO$ (155): C, 69·68; H, 10·98; N, 9·03; O, 10·32%).

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REFERENCES

[1] G. L'abbé, *Chem. Rev.* **69**, 345 (1969)

[2] Y. Gilliams and G. Smets, *Makromol. Chem.* **117**, 1 (1968); *Ibid.* **128**, 263 (1969)

[3] R. Huisgen, G. Szeimies and L. Möbius, *Chem. Ber.* **99**, 475 (1966)

[4] G. Szeimies and R. Huisgen, *Ibid.* **99**, 491 (1966)

[5] F. Texier and R. Carrié, *Tetrahedron Letters* 823 (1969); F. Texier and R. Carrié, *C.R. Acad. Sci., Paris* **268**, 139 (1969 and **271**, 958 (1970)

[6] [a] P. Scheiner, J. H. Schomaker, S. Deming, W. J. Libbey and G. P. Nowack, *J. Am. Chem. Soc.* **87**, 306 (1965);

[b] A. S. Bailey and J. E. White, *J. Chem. Soc.* B. 819 (1966);

[c] R. Huisgen, G. Szeimies and L. Möbius, *Chem. Ber.* **100**, 2494 (1967);

[d] A. C. Oehlschlager, R. S. McDaniel, A. Thakore, P. Tillman and L. H. Zalkow, *Canad. J. Chem.* **47**, 4367 (1969);

[e] see also R. Huisgen, *Angew. Chem.* Int. Edit. Engl. **2**, 633 (1963)

[7] For a definition of this term, see A. Hassner, *J. Org. Chem.* **33**, 2684 (1968)

[8] E. Roberts and E. E. Turner, *J. Chem. Soc.* 1832 (1927)

[9] G. P. Mueller and B. Riegel, *J. Am. Chem. Soc.* **76**, 3686 (1954); J. A. Moore, *J. Org. Chem.* **20**, 1607 (1955); W. S. Brey and C. M. Valentia, *Canad. J. Chem.* **46**, 810 (1968)

[10] N. H. Cromwell, R. E. Bambury and J. L. Adelfang, *J. Am. Chem. Soc.* **82**, 4241 (1960); S. J. Brois, *J. Org. Chem.* **27**, 3532 (1962); S. L. Manatt, D. D. Elleman and S. J. Brois, *J. Am. Chem. Soc.* **87**, 2220 (1965); S. J. Brois, *Tetrahedron* **26**, 227 (1970); M. J. Tempé, *C. R. Acad. Sci. Paris*, **259**, 1717 (1964); H. L. Spell, *Analyt. Chem.* **39**, 185 (1967)

[11] J. Dabrowski, *Spectrochim. Acta* **19**, 475 (1963); J. Dabrowski and K. Kamieńska-Trela, *Ibid.* **22**, 211 (1966); J. Dabrowski and U. Dabrowska, *Chem. Ber.* **101**, 3392 (1968); H. Dodziuk, K. Kamieńska-Trela and J. Dabrowski, *Rocz. Chem.* **44**, 393 (1970); G. O. Dudek and G. P. Volpp, *J. Am. Chem. Soc.* **85**, 2697 (1963); R. Huisgen, K. Herbig, A. Siegl and H. Huber, *Chem. Ber.* **99**, 2526 (1966); W. Bottomley, J. N. Phillips and J. G. Wilson, *Tetrahedron Letters* 2957 (1967)

[12] W. Broeckx, M. C. Delvaux de Fenffe, S. Toppet and G. Smets, in preparation

[13] For the nomenclature of *cis-trans* isomers according to the sequence rule, see *J. Org. Chem.* **35**, 2849 (1970)