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NUCLEOPHILIC REACTIONS OF N-ETHOXYCARBONYLIMINOPYRIDINIUM YLIDE WITH α,β-UNSATURATED CARBONYL COMPOUNDS[1]

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Abstract—Reactions of N-ethoxycarbonyliminopyridinium ylide (**1**) with α,β-unsaturated carbonyl compounds such as fumarate, maleate, maleic anhydride, N-phenylmaleimide, *p*-benzoquinone, and α-naphthoquinone in the presence of silicic acid gave the corresponding enamines in good yields, providing an efficient synthetic entry to acylenamines. In a similar reaction of tropone with N-ethoxycarbonyliminopyridinium ylide in the presence of silicic acid, 2-aminotropone (**22**) was obtained in quantitative yield. Mechanisms for the formation of the products are discussed.

COMPARED with the 1,3-dipolar cycloaddition reactions of N-ylides with various dipolarophiles, and salt formation of pyridinium N-imine with acyl- and alkylhalides,[2] the nucleophilic reactions of pyridinium N-ylide derivatives with α,β-unsaturated carbonyl compounds have not been well investigated.

Recently, Eicher *et al.*[3] and the present authors[4] have independently reported a novel nucleophilic reaction of pyridinium N-ylide with diphenylcyclopropenone (DPC), which is seemingly initiated by the nucleophilic attack of the N-ylide at the electron deficient carbon of DPC followed by fragmentation of the adduct to give 1,3-oxazine and/or 2-pyrone derivatives with elimination of pyridine.

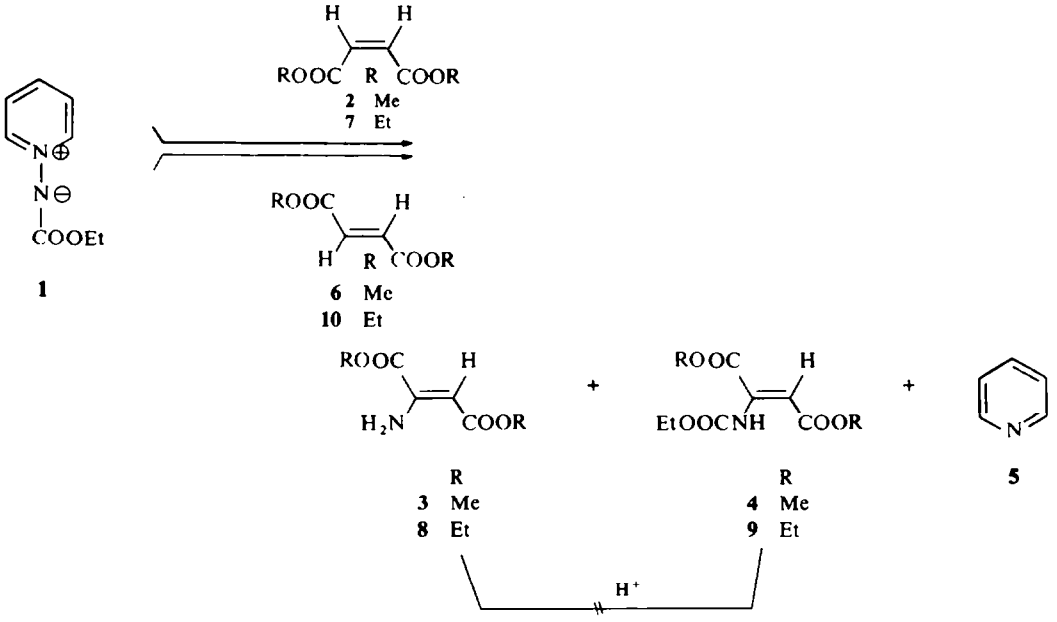
We report a novel enamine synthesis by the nucleophilic reaction of N-ethoxycarbonyliminopyridinium ylide with various α,β-unsaturated carbonyl compounds in the presence of a weakly acidic catalyst such as silicic acid.

RESULTS AND DISCUSSION

In the absence of an acidic catalyst, N-alkoxycarbonyliminopyridinium ylides did not react, or only very slowly, with α,β-unsaturated carbonyl compounds. In the presence of dilute hydrochloric acid, only N-alkoxycarbonylaminopyridinium chloride was formed and the α,β-unsaturated carbonyl compound was recovered. The present reactions were carried out in refluxing benzene or acetonitrile, or in xylene at 120–130° in a sealed tube, in the presence of silicic acid, the acidity of which seems not as strong as that of hydrochloric acid.

Reactions of the N-*ylide with fumarates and maleates.* Reactions of N-ethoxycarbonyliminopyridinium ylide **1** with alkyl maleates (**2** and **7**) afforded mixtures of the products (**3** and **4**), and (**8** and **9**), respectively. Mixtures of these same products were also formed from alkyl fumarates (**6** and **10**). The *trans*-products were always obtained irrespective of whether the olefin was *trans* or *cis*, and no 1,3-dipolar

cycloadducts were obtained; the product ratios of the reactions differed considerably, as shown in Table 1.



SCHEME 1

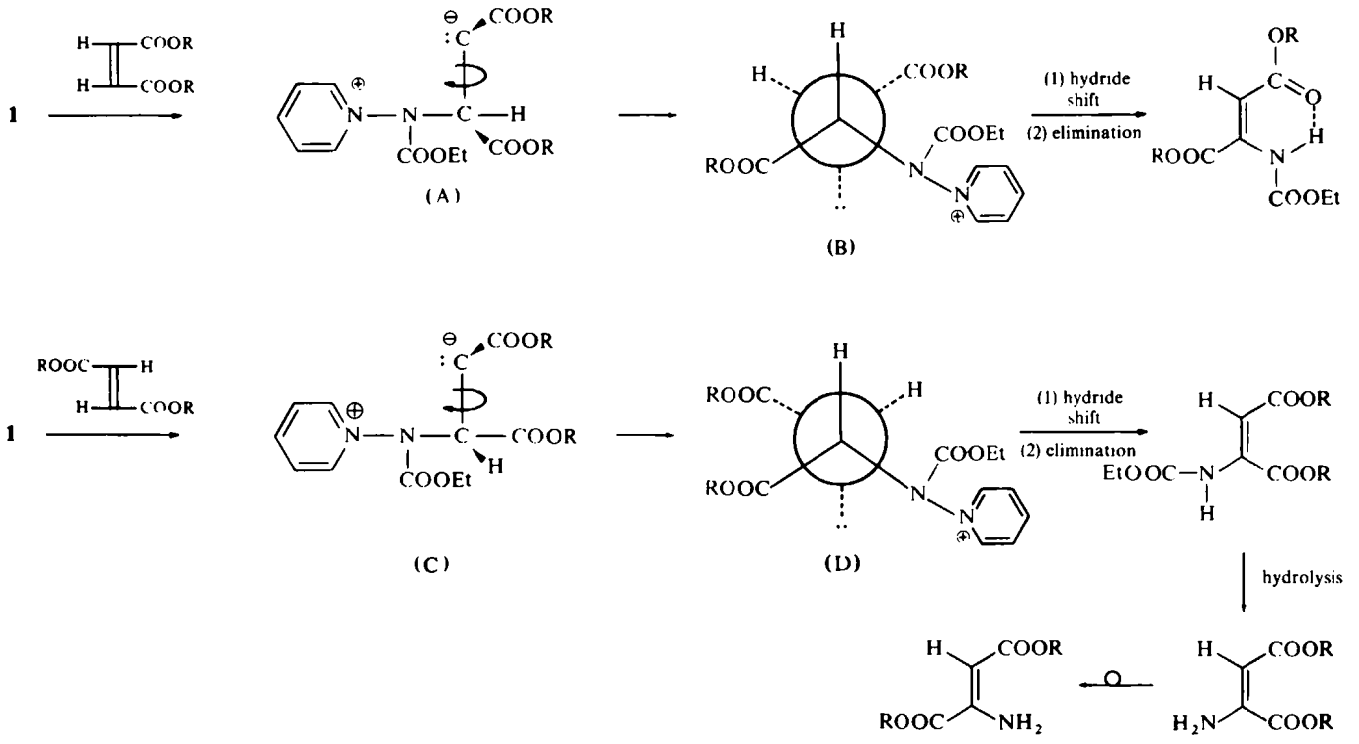
TABLE 1. THE PRODUCT RATIOS OF THE REACTIONS OF 1 AND OLEFINS

N-ylide (1) g	Olefin g	(Compd No.)	Product ratio* (Compd No.)	Total yield g (%)
0·50	0·43	(2)	2 (3):5 (4)	0·42 (68)
0·50	0·43	(6)	5 (3):2 (4)	0·35 (66)
0·33	0·34	(7)	2 (8):5 (9)	0·28 (60)
0·33	0·34	(10)	3 (8):1 (9)	0·21 (50)

* Determined by GLPC.

The structures of **3**, **4**, **8**, and **9** were assigned as dimethyl 2-amino-fumarate, dimethyl 2-ethoxycarbonylamino-fumarate, diethyl 2-amino-fumarate, and diethyl 2-ethoxycarbonylamino-fumarate, respectively.

The structural assignment of product **3** was based mainly on IR and NMR spectral comparisons with an authentic specimen;[5] the IR spectrum of **3** showed absorptions at 1676 and 1730 cm^{-1} due to two CO groups, at 3330 and 3520 cm^{-1} due to a primary amino group, and at 1676 cm^{-1} due to a CO group intramolecular H-bonded with an amino group in the *cis*-position as shown in Scheme 2. The NMR spectrum of **3** in carbon tetrachloride showed a singlet at τ 4·45 for a proton attached to a double bond, Me singlets at τ 6·03 and 6·23 due to two methoxycarbonyl groups, and


1
(A)
(B)
(1) hydride shift
(2) elimination
1
(C)
(D)
(1) hydride shift
(2) elimination
hydrolysis

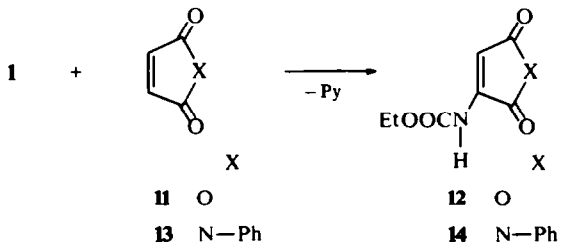
SCHEME 2

a wide broadened signal at τ 2·0 ~ 4·5 attributable to a primary amino group. Similarly, product **4** was assigned as the N-ethoxycarbonyl derivative of **3**, since its IR spectrum exhibited a CO absorption at 1685 cm^{-1}, indicative of the presence of H-bonding; its NMR spectrum showed signals due to a vinyl proton at τ 4·54, an amino proton at τ 0·05, two methoxycarbonyl groups at τ 6·07 (3H) and 6·15 (3H), respectively, and an ethoxycarbonyl group at τ 5·65 (2H) and 8·63 (3H). Compounds **8** and **9** were identified as diethyl analogs of **3** and **4** also by NMR inspection.

Since compounds **4** and **9** were not convertible to compounds **3** and **8** by hydrolysis (Experimental), because of the existence of intramolecular H-bonding, it is possible to consider the intermediacy of N-ethoxycarbonylamino-maleate as a precursor which is converted to 1-aminofumarate by hydrolysis and thermal isomerization. Thus, the reaction mechanism might be explained as an initial nucleophilic attack by the N-ylide at the C=C double bond of the olefin to give carbanion intermediates A and C, these can rotate to give conformers B and D which undergo concerted hydride shift and elimination of the pyridinium moiety as shown in Scheme 2. These paths could be explained regiospecificity to the reaction.

Reactions of the N-*ylide with maleic anhydride,* N-*phenyl maleimide,* p-*benzoquinone, and* α-*naphthoquinone.* With the view of obtaining further mechanistic information on the above-mentioned reactions, similar reactions of **1** with *cis*-locked α,β-unsaturated compounds were investigated.

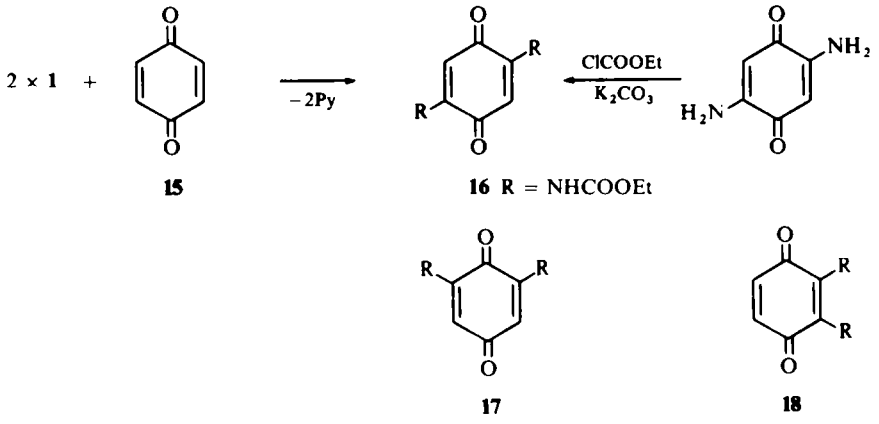
The reactions of **1** with maleic anhydride (**11**) and N-phenylmaleimide (**13**) afforded **12** (73%) and **14** (74%) respectively, together with pyridine.



SCHEME 3

Compounds **12** and **14** were assigned as X-ethoxycarbonylamino-maleic anhydride and α-X-ethoxycarbonylamino-N′-phenylmaleimide, respectively, by comparison of their spectroscopic properties with those of authentic samples.[6]

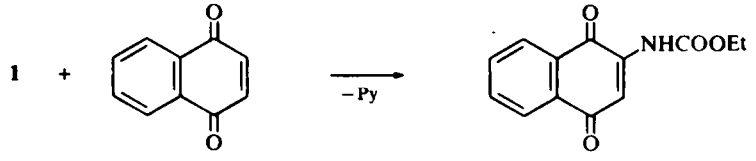
Similar reaction of **1** with *p*-benzoquinone (**15**) gave **16** in 57% yield; the IR and NMR spectra of **16** were also compatible with symmetrical structures such as **17** and **18** shown in Scheme 4, since the IR spectrum displayed, *inter alia*, absorptions at 1730 (ethoxycarbonyl), 1650 (quinone carbonyl), and 3320 cm^{-1} (amino group); and the NMR spectrum exhibited two equivalent vinyl protons as a singlet at τ 2·91. These spectral data could not afford further information for the structure determination. The final assignment was accomplished by an alternative preparation via the N-acylation of 2,5-diamino-1,4-benzoquinone.[7] Thus, **16** was assigned as 2,5-diethoxycarbonylamino-1,4-benzoquinone.



15 16 R = NHCOOEt 17 18

SCHEME 4

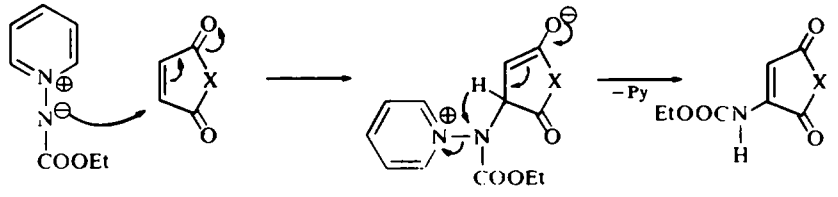
α-Naphthoquinone (**19**) reacted with **1** to give yellow needles (**20**) in 82% yield. The product was identified as 2-ethoxycarbonylamino-1,4-naphthoquinone by NMR spectral comparison with **16**.



19 20

SCHEME 5

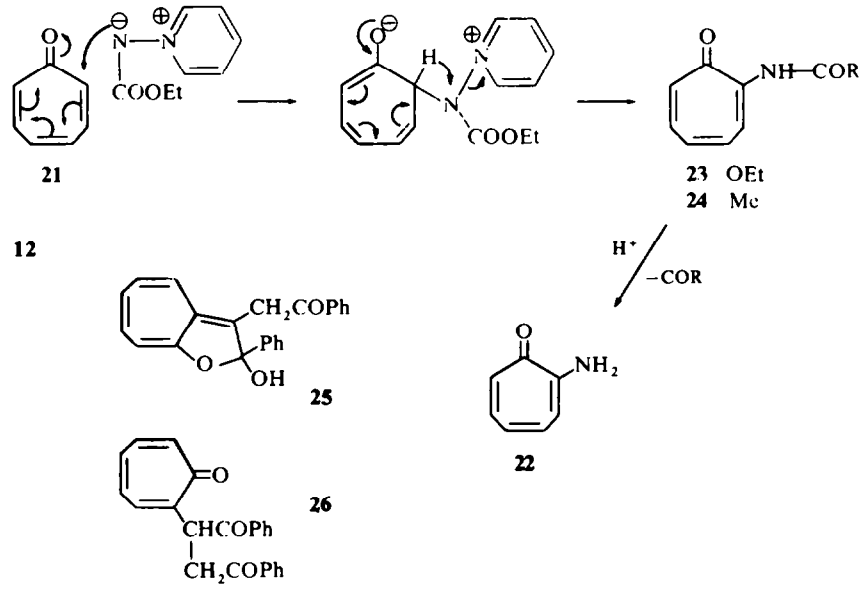
The mechanism for the formation of these cyclic enamines, might be explained as an initial nucleophilic attack of the N-ylide (**1**) at the β-carbon of the double bond in the *cis*-locked compounds followed by loss of pyridine to give the products as shown in Scheme 6.



SCHEME 6

Reaction of the N*-ylide with tropone.* Tropone (**21**) reacted with **1** to give yellow crystals (**22**) in quantitative yield. The NMR spectrum of **22** exhibited a signal at τ 3·60 (2H, br s) due to a primary amino group but no characteristic signals for an ethoxycarbonyl group. Compound **22** was readily converted to N-ethoxycarbonyl- (**23**) and N-acetyl- (**24**) derivatives by treatment with ethyl chloroformate and acetic anhydride, respectively. From these data, **22** was assigned as 2-aminotropone, the IR

spectrum of which was identical with that of an authentic sample prepared from 2-methoxy-tropone and ammonia.[8] In addition, **23** was shown to be sensitive to hydrolysis in the presence of silicic acid. It is interesting to compare this reaction of N-alkoxycarbonyliminopyridinium ylides and tropone with that of the isoelectronic pyridinium methylides and tropone to give 1:2 adducts (**25** and **26**).[9]



SCHEME 7

EXPERIMENTAL

M.ps were measured with a Yanagimoto micromelting point apparatus and are uncorrected. Microanalyses were performed on a Perkin–Elmer 240 Elemental Analyser. The UV spectra were determined with a Jasco Model ORD/UV-5 recorder. The NMR spectra were taken with a Japan Electric Optics La., Co., Ltd., Model C-60-XL NMR spectrometer and with a Varian A-60 recording spectrometer with TMS as an internal standard. Chemical shifts are expressed in τ values. The IR spectra were taken with a Jasco Model IR-S spectrophotometer. The GLPC was done isothermally on a Hitachi K-23 Gas Chromatograph with a 3 ft, 5 wt% SE 30 (chromosorb G-NAW) column (flame-isomerization detector). A Varian aerograph model 700 (hydrogen flame ionization detector, nitrogen carrier gas, fitted with a 5 ft $\frac{1}{8}$ in column containing 12% Dow Corning Silicone oil 550 on 80–100 Chromosorb W) was used for preparative separations.

Reactions of N-*ethoxycarbonyliminopyridinium ylide* (**1**) *with olefins*

General procedure. To an equimolar mixture of **1** and the olefin (**2**, **6**, **7**, or **10**) in xylene (20 ml), silicic acid (1–2 g) was added. The mixture was heated at 120–130° in a sealed tube for 12–48 hr, then cooled to room temp. Silicic acid was removed by filtration and the filtrate was concentrated *in vacuo*. The residual oil was separated by preparative gas chromatography into the products. The product ratio of each reaction and the physical and spectral data are summarized in Tables 1 and 2.

1-Ethoxycarbonylamino-fumarate derivatives (**4** and **9**) could not be converted to 1-aminofumarate derivatives (**3** and **8**) by heating in the presence or absence of silicic acid.

Reaction of **1** *with maleic anhydride.* A mixture of **1** (0·33 g, 2 mmol), **11** (0·33 g, 2 mmol) and silicic acid (2 g) in acetonitrile was heated at reflux temp in a water bath for 5 hr then filtered to remove silicic acid. The

TABLE 2. PHYSICAL AND SPECTRAL DATA OF THE PRODUCTS

Cmpd No.*	n_D (°C)	IR (cm^{-1}) NH	IR (cm^{-1}) CO	UV λ_{max}^{EtOH} nm (ε)	NMR (CCl_4) Chemical shifts (τ) and Coupling constants (J in Hz)
3	1·5132 (21)	3520, 3330	1730, 1676	307 (3·48 × 10^3)	6·23 (3H, s, OMe), 6·03 (3H, s, Ome), 4·45 (1H, s, vinyl-H), 2·0 4·5 (2H, br, NH_2)
4	1·4874 (20)	3310,	1750, 1735, 1685	264 (7·23 × 10^3)	8·63 (3H, t, J = 7·0, O—CH_2—C$\underline{H}_3$), 6·15 (3H, s, Ome), 6·07 (3H, s, Ome), 5·65 (2H, q, J = 7·0, O—C$\underline{H}_2$) 4·54 (1H, s, vinyl-H), 0·05 (1H, br s, NH)
8	1·4915 (24)	3520, 3370	1726, 1676	305 (8·70 × 10^3)	8·75 (3H, t, J = 7·0, O—CH_2—C$\underline{H}_3$), 8·66 (3H, t, J = 7·0, O—CH_2 C$\underline{H}_3$), 5·95 (2H, q, J = 7·0, O—C$\underline{H}_2$), 5·79 (2H, q, J = 7·0, OC$\underline{H}_2$), 4·70 (1H, s, vinyl-H), 2·5–5·0 (2H, br s, NH_2)
9	1·4789 (21)	3320	1740, 1682	263 (5·71 × 10^3)	8·45–8·85 (9H, m, 3 × OCH_2—C$\underline{H}_3$), 5·55 6·05 (6H, m, 3 OCH_2 –), 4·87 (1H, s, vinyl-H), 0·47 (1H, br s, NH)

* **3**: Found: C, 45·00; H, 5·69; N, 8·85. Calcd for $C_6H_9NO_4$: C, 45·28; H, 5·70; N, 8·80%. **4**: Found: C, 46·80; H, 5·60; N, 5·79. Calcd for $C_9H_{13}NO_6$: C, 46·75; H, 5·67; N, 6·06%. **8**: Found: C, 51·50; H, 6·88; N, 7·36. Calcd for $C_8H_{13}NO_4$: C, 51·33; H, 7·00, N, 7·48%. **9**: Found: C, 51·00; H, 6·90; N, 5·40. Calcd for $C_{11}H_{17}NO_6$: C, 50·96; H, 6·61; N, 5·40%.

filtrate was concentrated *in vacuo* to give **12**, which was recrystallized from EtOAc to give colourless crystals (0·27 g, 73%); m.p. 118–120°, spectroscopic properties identical with an authentic sample.[6]

Reaction of **1** *with* N-*phenylmaleimide.* A mixture of **1** (0·33 g), **13** (0·35 g, 2 mmol), and benzene (20 ml) was heated at reflux temp for 5 hr then filtered to remove silicic acid. The filtrate was concentrated *in vacuo* to give **14** (0·40 g, 74%) as yellow needles; m.p. 134–136°, spectroscopic properties identical with an authentic sample.[6] The product (**14**) was also obtained, but in less yield (54%), when the reaction was carried out at room temp.

Reaction of **1** *with* 1,4-*benzoquinone.* A mixture of a benzene solution of **1** (0·66 g, 4 mmol) and **15** (0·22 g, 2 mmol) and silicic acid (2 g) was stirred overnight at room temp and then silicic acid was removed by filtration. The filtrate was concentrated *in vacuo* to give **16**, which was recrystallized from chloroform–ether to give orange prisms (0·32 g, 57%); m.p. 219–220°, IR (KBr) 3320 (NH), 1730 (urethane CO) and 1650 cm^{-1} (quinone CO), λ_{max}^{EtOH} 307 nm (ε 2·28 × 10^4) and 222 (1·96 × 10^4), τ ($CDCl_3$) 8·68 (6H, t, J = 7·0, $OCH_2C\underline{H}_3$ × 2), 5·79 (4H, q, J = 7·0, OCH_2 × 2), 2·91 (2H, s, vinyl-H), and 2·27 (2H, br s, NH). (Found: C, 50·76; H, 4·94; N, 9·79. Calcd for $C_{12}H_{14}N_2O_6$: C, 51·06; H, 5·00; N, 9·93%).

This compound was also identified by mixed m.p's with a material prepared by the reaction of 2,5-diamino-1,4-benzoquinone and ethyl chloroformate in the presence of potassium carbonate in chloroform.

Reaction of **1** *with* α-*naphthoquinone.* Compound **20** was obtained in 82% yield from the reaction of **1** (0·17 g, 1 mmol), **20** (0·16 g, 1 mmol), and silicic acid (1 g) in a sealed tube at 120–130° for 20 hr. Recrystallization from chloroform-n-hexane gave yellow prisms (**20**) (0·20 g): m.p. 160–163°, IR (KBr) 3300 (NH), 1723 (urethane CO) and 1666 cm^{-1} (quinone CO), λ_{max}^{EtOH} 334 nm (ε 2·04 × 10^3), 285 (9·81 × 10^3), 251 (1·70 × 10^4), 246 (1·57 × 10^4) and 241 (1·25 × 10^4), τ ($CDCl_3$) 8·65 (3H, t, J = 7·0, $OCH_2C\underline{H}_3$), 5·75 (2H, q, J = 7·0, O –CH_2), 2·57 (1H, s, vinyl-H), and 1·8–2·5 (5H, m, aromatic and amino protons). (Found: C, 63·89; H, 4·63; N, 5·78. Calcd for $C_{13}H_{11}NO_4$: C, 63·67; H, 4·52; N, 5·71%).

Reaction of **1** *with tropone.* 1-Aminotropone (**22**) was obtained in quantitative yield from the reaction of **1** (0·33 g), **21** (0·21 g) and silicic acid (1 g) by the conditions described. Recrystallization from chloroform-n-hexane gave yellow prisms (**22**); m.p. 101–104°, τ ($CDCl_3$) 3·60 (2H, br s, NH_2) and 2·50–3·50 (5H, m ring protons). The product was found to be identical with an authentic sample.[8]

Preparation of 2-*ethoxycarbonylaminotropone.* A chloroform solution of **21** (0·10 g) and ethyl chloroformate (0·1 g) in the presence of K_2CO_3 (1 g) was stirred overnight at room temp. The insoluble ppt was removed by filtration and the filtrate was concentrated *in vacuo*. The crude **23** was recrystallized from n-hexane to give pale yellow prisms (0·15 g, 95%); m.p. 70–71°, IR (KBr) 3310 (NH) and 1730 cm^{-1} (urethane CO), λ_{max}^{EtOH} 378 nm (ε 3·63 × 10^3), 361 (4·39 × 10^3), 329 (5·20 × 10^3), 248 (1·06 × 10^4), and 228 (1·28 × 10^4), τ ($CDCl_3$) 8·67 (3H, t, J = 7·0, $OCH_2C\underline{H}_3$), 5·79 (2H, q, J = 7·0, OCH_2), 2·6–3·3 (4H, m, H_4 and H_7), 1·46 (1H, dd, J = 9·0 and 1·5, H_3), and 1·16 (1H, br s, NH). (Found: C, 62·25; H, 5·75; N, 7·23. Calcd for $C_{10}H_{11}NO_3$: C, 62·16; H, 5·74; N, 7·25%).

Preparation of 2-*acetylaminotropone.* 2-Aminotropone was allowed to react with excess of Ac_2O without solvent at room temp for 1 hr to give **24** in a quantitative yield; m.p. 102–105°, IR (KBr) 3260 (NH) and 1688 cm^{-1} (amide CO), λ_{max}^{EtOH} 379 nm (ε 4·08 × 10^3), 362 (5·90 × 10^3), 330 (6·91 × 10^3), 250 (1·28 × 10^4), and 233 (1·39 × 10^4), τ ($CDCl_3$) 7·72 (3H, s, OMe), 2·55–3·20 (4H, m, H_4 and H_7), 1·06 (1H, dd, J = 9·0 and 1·5, H_3), and 0·66 (1H, br s, NH). Compound **24** was found to have identical spectroscopic properties with the material reported by Nozoe *et al.*[8]

Thermal degradation of **23**. A mixture of **23** (0·1 g) and silicic acid (0·1 g) in xylene (10 ml) was heated overnight at 120–130° in a sealed tube and then silicic acid was removed by filtration. The filtrate was concentrated to give 2-aminotropone in quantitative yield. However, when **23** was refluxed in xylene without catalyst under same conditions, **22** could not be detected in the reaction mixture.

REFERENCES

[1] Studies of Heteroaromaticity. Part LVIII. Part LVII of this series, T. Sasaki, K. Kanematsu and S. Ochiai, *Annual Report of the Asahi Glass Foundation for the Contribution to Industry & Technology* Vol. **18**, 77 (1971)

[2] [a] R. Huisgen, R. Grashey and J. Sauer, *Cycloaddition reactions of Alkenes* in *The Chemistry of Alkenes* (Edited by S. Patai) p. 739. Interscience (1964); [b] T. Okamoto, M. Hirobe and A. Ohsawa, *Chem. Pharm. Bull. Tokyo*, **14**, 518 (1966)

[3] T. Eicher, E. von Angerer and A. Hansen, *Liebigs Ann.* **746**, 102 (1971)

[4] T. Sasaki, K. Kanematsu and A. Kakehi, *J. Org. Chem.* **36**, 2451 (1971)

[5] R. Huisgen, K. Herbig, A. Siegl and H. Huber, *Chem. Ber.* **99**, 2526 (1966)

[6] M. R. Atkinson, M. H. Maguire, R. K. Ralph, G. Shaw and R. N. Warrener, *J. Chem. Soc.* 2363 (1957)

[7] H. W. Moore, H R Shelden and D. R. Shellhamer, *J. Org. Chem.* **34**, 1999 (1969)

[8] T. Nozoe and Y. Kitahara, *Proc. Japan Acad.* **30**, 204 (1954)

[9] Y. Sugimura, I. Kawamoto, K. Ihno and N. Soma, Abstracts of Papers in *International Symposium of the Chemistry of Non-benzenoid Aromatic Compounds* p. 67. Sendai, Japan (1970)