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N-ACYL-1-AMINO-1,3-DIENES: 1-AMINO-1,3-DIENE SYNTHETIC EQUIVALENTS FOR THE DIELS-ALDER REACTION

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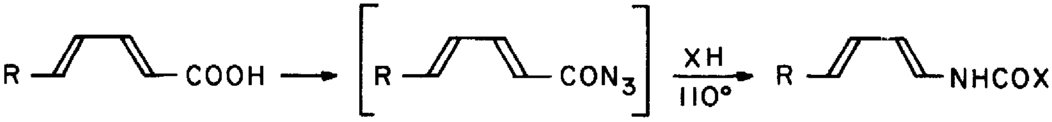
There has been recent interest in the synthesis and Diels-Alder reactions of dienamides.[2,3] The preparation of N-acyl-N-alkyl-1-amino-1,3-butadienes, and their application in synthesis via intramolecular Diels-Alder processes, has been impressively demonstrated by Oppolzer and coworkers.[2] A recent report from our laboratory described a versatile synthetic route to both N-trichloroacetyl-2-amino-1,3-dienes and N-trichloroacetyl-1-amino-1,3-dienes, and illustrated, in a preliminary fashion, their intermolecular Diels-Alder chemistry.[3] Application of these latter dienes in synthesis was limited, however, by their moderate Diels-Alder reactivity, a property attributed to the strong electron withdrawing nature of the trichloroacetyl substituent.[4]

In this letter we report that a variety of crystalline N-acyl-1-amino-1,3-dienes (3) can be prepared in synthetically useful yields by a modified Curtius sequence.[5] Since these dienes are considerably more reactive than the corresponding trichloroacetyl derivatives, they should find application in synthesis.



1 2 3

R = CH_3, H X = OCH_2CH_3, OC_6H_5, SC_6H_5, $N(CH_2)_4$

Dienoic acids 1[6] were readily converted, via the mixed anhydrides,[5] into the azide derivatives 2. The acyl azides were not isolated, but were extracted into toluene and added directly to a refluxing toluene solution containing a trapping reagent XH. Concentration, and filtration through silica gel afforded the pure, crystalline dienes 3[8] in overall yields of 44-80%

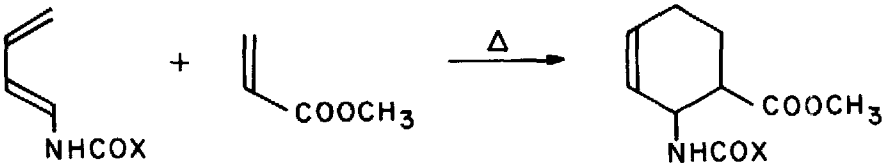
TABLE I. Synthesis of N-acyl-1-amino-1,3-dienes[16]

Diene (3) R	X	Procedure[a]	m.p. (°C)	Isolated Yield (%)
CH_3	OCH_2CH_3	A	91- 92	80
H	OCH_2CH_3	A	44- 45	71[b]
CH_3	OC_6H_5	A	118-120	72
H	OC_6H_5	B[c]	118-119	66
		A		45
CH_3	$N(CH_2)_4$	B	164-165	77
		A		(10)[d]
H	$N(CH_2)_4$	B	163-164	44
CH_3	SC_6H_5	B	116-118	78
H	SC_6H_5	B	92- 93	47

[a] Isocyanate trapped as formed at 110° (procedure A), or isocyanate pre-formed at 110° and trapped at 25° (procedure B); [b] Mean yield of four preparations. All other table entries are nonoptimized yields of a single experiment; [c] A few drops of triethylamine were added; [d] Estimated by pmr.

(Table I).[10] *An alternate procedure (B), in which a solution of the isocyanate was pre-formed* in toluene and cooled to 25° before the trapping agent was added, afforded higher yields in some cases. Since many dienoic acids are available from the Knoevenagel and related reactions,[13] the procedure reported here should allow the preparation of a variety of N-acyl-1-amino-1,3-dienes.

The Diels-Alder reactivities of dienes 3 vary markedly with the nature of the acyl substituent X. The previously reported[3] trichloroacetamido-substituted diene 3 (R = H, X = CCl_3) reacts with methyl acrylate conveniently only at 140° (3 hr) to afford adduct 4



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(X = CCl_3, *cis*/*trans* = 3.5) in 82% yield.[14] In contrast, the diencarbamate **3** (R = H, X = OCH_2CH_3) reacts within 2 hr at 110° (**4**, X = OCH_2CH_3, *cis*/*trans* = 5.4, 78%) and the dienurea **3** (R = H, X = $N(CH_2)_4$) reacts within 8 hr at 80° (**4**, X = $N(CH_2)_4$, *cis*/*trans* >6, 80%).[14] It should be noted that both the latter two dienes react with methyl acrylate faster and more regioselectively than *trans*-2,4-pentadienoic acid (110°, 15 hrs, 85%),[14, 15] and thus an alternate synthetic sequence, in which the Curtius rearrangement is accomplished after cycloaddition, is less attractive. A detailed study of the Diels-Alder reactivity and stereoselectivity of these dienes will be published in due course.

The following procedure is representative:

*Ethyl trans-1,3-butadiene-1-carbamate (**3**, R = H, X = OCH_2CH_3).* A solution of ethyl chloroformate (11.9 g, 0.11 mol) in 40 ml of acetone was added dropwise to a stirred solution of *trans*-2,4-pentadienoic acid[6] (8.33 g, 85 mmol), triethylamine (10.2 g, 0.10 mol), and 50 ml of acetone at 0°. After 30 min, a solution of sodium azide (8.45 g, 0.13 mol) and 30 ml of water was added dropwise while maintaining the temperature below 10°. After 1 hr, the reaction mixture was poured into ice-water (~200 ml), extracted three times with 60 ml of toluene, and the toluene solution dried ($MgSO_4$) for 30 min. The azide solution, containing 25 ml of absolute ethanol (0.43 mol), was then added dropwise over 1 hr to 100 ml of refluxing toluene which contained *ca*. 50 mg of 4-*tert*-butylcatechol. Reflux was continued for *ca*. 1 hr after the addition was complete, at which time the azide ir band (2120 cm^{-1}) had disappeared. After cooling to room temperature the solution was concentrated to afford *ca*. 11 g of a yellow, semi-solid material. Purification by chromatography (silica gel, 10:1 hexane:ether) and recrystallization (hexane-ether) afforded 7.1 - 10.8 g (60 - 91%) of pure, white crystalline carbamate: mp 44-45°, ν_{max} (nujol) 3360, 1695, 1665, and 1530 cm^{-1}; pmr ($CDCl_3$, δ) 4.7 - 7.2 (complex m, vinylic and N*H*), 4.15 (q, J = 7Hz, OC*H*$_2$), and 1.25 (t, J = 7Hz, CH_3); cmr ($CDCl_3$, δ TMS) 154.1, 134.8, 127.6, 113.2, 112.1, 61.7, and 14.5; mass spec (m/e) 141.0787 (calc 141.0789).

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References and Notes

1. Alfred P. Sloan Foundation Fellow, 1975-77.
2. W. Oppolzer and W. Fröstl, *Helv. Chim. Acta*, **58**, 587, 590 (1975); W. Oppolzer, W. Fröstl, and H. P. Weber, *ibid.*, **58**, 593 (1975).
3. L. E. Overman and L. A. Clizbe, *J. Amer. Chem. Soc.*, **98**, 2352 (1976).
4. Only Diels-Alder reactions of normal electron demand are considered.
5. J. Weinstock, *J. Org. Chem.*, **26**, 3511 (1961).
6. *Trans,trans*-2,4-hexadienoic (sorbic) acid is commercially available. Trans-2,4-pentadienoic acid was prepared as described,[7] and stored at -20°.
7. R. G. Glushkov and O. Y. Magidson, *Med. Prom. SSSR*, **16**, 27 (1962); *Chem. Abstr.*, **58**, 442c (1963).
8. In contrast to the corresponding N,N-dialkyldienamines,[9] N-acyldienamines **3** are easily handled, reasonably stable, crystalline materials. They have been stored at -20° for up to two weeks without detectable decomposition.
9. S. Hunig and H. Kahanek, *Chem. Ber.*, **90**, 238 (1957).
10. To our knowledge no carbamate or urea derivatives of butadiene have appeared in the literature. The conversion of 1,3-pentadienyl isocyanate to the benzyl urea **3** (R = CH_3, X = $NHCH_2C_6H_5$),[11] and the conversion of *trans,trans*-2,4-hexadienamide, under Hoffmann conditions ($NaOCl/CH_3OH$), to the methyl carbamate **3** (R = CH_3, X = OCH_3)[12] have been reported.
11. F. Tanimoto, T. Tanaka, H. Kitano, and K. Fukui, *Bull. Chem. Soc. Jap.*, **39**, 1922 (1966).
12. V. B. Mochalin, I. S. Varpakhovskaya, and O. P. Beletskaya, *J. Org. Chem. USSR*, **10**, 1556 (1974).
13. "Houben-Weyl," 4th Ed., Vol. 5/1C, Thieme Verlag, Stuttgart, Germany, 1970, pp 519-555.
14. All Diels-Alder reactions were conducted under identical conditions in sealed ampules: diene (1 mmol), methyl acrylate (3 mmol), dioxane (1 ml), and 4-*tert*-butylcatechol (*ca.* 10 mg). Isomer ratios were determined by hplc analysis after the crude reaction mixture was filtered through a short silica gel column.
15. Four adducts were apparent by hplc analysis after esterification (CH_2N_2). The major isomer was formed to the extent of 65%.
16. Satisfactory infrared, nmr, and mass spectra were obtained for all new compounds.